UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

(Mark One)

☒ **ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934**

For the fiscal year ended December 31, 2021

OR

☐ **TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934 FOR THE TRANSITION PERIOD FROM TO**

Commission File Number 001-39247

IMARA INC.

(Exact name of Registrant as specified in its charter)

Delaware	**81-1523849**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
116 Huntington Avenue, 6th Floor	
Boston, Massachusetts	**02116**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 206-2020

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common stock, par value $0.001 per share	IMRA	The Nasdaq Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act: **None**

Indicate by check mark if the Registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. YES ☐ NO ☒

Indicate by check mark if the Registrant is not required to file reports pursuant to Section 13 or 15(d) of the Act. YES ☐ NO ☒

Indicate by check mark whether the Registrant: (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the Registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. YES ☒ NO ☐

Indicate by check mark whether the Registrant has submitted electronically every Interactive Data File required to be submitted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the Registrant was required to submit such files). YES ☒ NO ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, a smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large accelerated filer	☐	Accelerated filer	☐
Non-accelerated filer	☒	Smaller reporting company	☒
Emerging growth company	☒		

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant has filed a report on and attestation to its management's assessment of the effectiveness of its internal control over financial reporting under Section 404(b) of the Sarbanes-Oxley Act (15 U.S.C. 7262(b)) by the registered public accounting firm that prepared or issued its audit report. ☐

Indicate by check mark whether the Registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). YES ☐ NO ☒

The aggregate market value of the voting and non-voting common equity held by non-affiliates of the Registrant, based on the closing price of the shares of common stock on the Nasdaq Global Select Market on June 30, 2021 was $87,931,922.

The number of shares of Registrant's Common Stock outstanding as of March 1, 2022 was 26,287,264.

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CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS AND INDUSTRY DATA

This Annual Report on Form 10-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995 that involve substantial risks and uncertainties. All statements, other than statements of historical fact, contained in this Annual Report on Form 10-K, including statements regarding our strategy, future operations, future financial position, future revenue, projected costs, prospects, plans and objectives of management, are forward-looking statements. The words “anticipate,” “believe,” “continue,” “could,” “estimate,” “expect,” “intend,” “may,” “might,” “plan,” “potential,” “predict,” “project,” “should,” “target,” “would,” and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words.

The forward-looking statements in this Annual Report on Form 10-K include, among other things, statements about:

- the impact of the ongoing COVID-19 pandemic and our response to it;
- the initiation, timing, progress and results of our current and future preclinical studies and clinical trials, including our ongoing Ardent and Forte Phase 2b clinical trials of tovinontrine (IMR-687) in sickle cell disease, or SCD, and ß-thalassemia, our open label extension clinical trial of tovinontrine in SCD and our planned clinical development of tovinontrine in heart failure with preserved ejection fraction;
- our planned research and development activities for any additional product candidates we may develop, including IMR-261;
- our estimates regarding expenses, future revenue, timing of any future revenue, capital requirements and need for additional financing;
- our plans to develop and, if approved, subsequently commercialize tovinontrine and any other product candidates, including in combination with other drugs and therapies;
- the timing of and our ability to submit applications for, obtain and maintain regulatory approvals for tovinontrine and any other product candidates we may identify and pursue;
- our expectations regarding our ability to fund our operating expenses and capital expenditure requirements with our cash, cash equivalents and investments;
- the potential advantages or differentiating features of tovinontrine and any other product candidates we may identify and pursue;
- the rate and degree of market acceptance and clinical utility of tovinontrine and any other product candidates we may identify and pursue;
- our estimates regarding the potential market opportunity for tovinontrine and any other product candidates we may identify and pursue;
- our commercialization, marketing and manufacturing capabilities and strategy;
- our expectations regarding our ability to obtain and maintain intellectual property protection for tovinontrine and any other product candidates we may identify and pursue;
- our ability to identify additional products, product candidates or technologies with significant commercial potential that are consistent with our commercial objectives;
- the impact of government laws and regulations;
- our competitive position and expectations regarding developments and projections relating to our competitors and any competing therapies that are or become available;
- our ability to maintain and establish collaborations or obtain additional funding;
- our ability to continue as a going concern; and
- our expectations regarding the time during which we will be an emerging growth company under the JOBS Act.

We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. In addition, statements that “we believe” and similar statements reflect our beliefs and opinions on the relevant subject. These statements are based upon information available to us as of the date of this Annual Report on Form 10-K, and while we believe such information forms a reasonable basis for such statements, such information may be limited or incomplete, and our statements should not be read to indicate that we have conducted an exhaustive inquiry into, or review of, all potentially available relevant information. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-looking statements we

make. We have included important factors in the cautionary statements included in this Annual Report on Form 10-K, particularly in the "Risk Factors" section, that we believe could cause actual results or events to differ materially from the forward-looking statements that we make.

You should read this Annual Report on Form 10-K and the documents that we have filed as exhibits to Annual Report on Form 10-K completely and with the understanding that our actual future results may be materially different from what we expect. The forward-looking statements contained in this Annual Report on Form 10-K are made as of the date of this Annual Report on Form 10-K, and we do not assume any obligation to update any forward-looking statements, whether as a result of new information, future events or otherwise, except as required by applicable law.

This Annual Report on Form 10-K includes statistical and other industry and market data that we obtained from industry publications and research, surveys and studies conducted by third parties as well as our own estimates of potential market opportunities. All of the market data used in this Annual Report on Form 10-K involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such data. Industry publications and third-party research, surveys and studies generally indicate that their information has been obtained from sources believed to be reliable, although they do not guarantee the accuracy or completeness of such information. Our estimates of the potential market opportunities for our product candidates include several key assumptions based on our industry knowledge, industry publications, third-party research and other surveys, which may be based on a small sample size and may fail to accurately reflect market opportunities. While we believe that our internal assumptions are reasonable, no independent source has verified such assumptions.

RISK FACTOR SUMMARY

Our business is subject to a number of risks that if realized could materially affect our business, financial condition, results of operations, cash flows and access to liquidity. These risks are discussed more fully in Part I, Item 1A. “Risk Factors” of this Annual Report on Form 10-K. Our principal risks include the following:

- We have incurred significant losses since our inception, and we expect to incur losses over the next several years.
- We are heavily dependent on the success of tovinontrine, our only product candidate currently in clinical development. If we are unable to successfully complete clinical development, obtain regulatory approval for, and commercialize tovinontrine, or experience delays in doing so, our business will be materially harmed.
- We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.
- We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.
- Our limited operating history may make it difficult for you to evaluate the success of our business to date and to assess our future viability.
- Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers.
- Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.
- We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.
- If we fail to comply with our obligations under our existing license agreements, or under any future intellectual property licenses, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.
- If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.
- Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

PART I

Item 1. Business.

Overview

We are a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin, known as hemoglobinopathies, and other serious diseases. Our pipeline is built on the differentiated therapeutic potential of our lead product candidate, tovinontrine (IMR-687), which is an oral, highly selective, potent small molecule inhibitor of phosphodiesterase-9, or PDE9. Tovinontrine is currently in Phase 2b clinical development for the treatment of sickle cell disease, or SCD, and β-thalassemia and we expect to begin clinical development of tovinontrine in heart failure with preserved ejection fraction, or HFpEF, in the second quarter of 2022. We are also advancing IMR-261, an oral, clinic-ready activator of nuclear factor erythroid 2–related factor 2, or Nrf2.

Disease Areas

Hemoglobinopathies

Hemoglobinopathies are a diverse range of rare inherited genetic disorders in which there is abnormal or decreased production of hemoglobin, the iron-containing protein in red blood cells, or RBCs, responsible for transporting oxygen in the blood. Hemoglobinopathies can be broadly categorized into two groups. The first group, which includes SCD, results from structural abnormalities in hemoglobin that cause RBCs to become inflexible and elongated (sickle-shaped), ultimately blocking blood flow to organs, which can lead to vaso-occlusive crises, or VOCs. SCD is characterized by debilitating pain, progressive multi-organ damage and early death. The global prevalence of SCD is estimated to be approximately 4.4 million patients, including approximately 100,000 patients in the United States and 134,000 patients in the European Union.

The second group of hemoglobinopathies, which includes β-thalassemia, results from decreased production of hemoglobin or ineffective erythropoiesis (RBC production), leading to fewer, smaller, paler RBCs and chronic anemia. β-thalassemia is often grouped into two subsets: patients with non-transfusion dependent thalassemia, or NTDT, and patients with transfusion dependent thalassemia, or TDT. If left untreated, β-thalassemia causes severe anemia, splenomegaly, skeletal abnormalities, leg ulcers, iron overload, and organ failure, often leading to early death. The global prevalence of β-thalassemia is estimated to be approximately 288,000 patients, with the total combined prevalence in the United States and the European Union estimated to be approximately 19,000 patients.

SCD and β-thalassemia are both designated as rare diseases in the United States and the European Union.

Heart Failure with Preserved Ejection Fraction

Heart failure with preserved ejection fraction, or HFpEF, also known as diastolic heart failure, is typically caused by abnormalities of cardiac filling, which leads to symptoms such as shortness of breath, exercise intolerance and fluid retention. Characteristics of HFpEF are heterogeneous, but commonly include ventricular hypertrophy, diastolic dysfunction, endothelial dysfunction, insulin resistance, and inflammation. Comorbidities, such as hypertension, anemia, chronic kidney disease, diabetes, and obesity, are also common in HFpEF and are thought to contribute to its development. HFpEF accounts for approximately half of all cases of heart failure and has become the predominant form of heart failure over time. Prevalence in the United States is estimated to be approximately 3-4 million patients. In contrast to heart failure with reduced ejection fraction, or HFrEF, there are relatively few treatment options to improve symptoms and outcomes for patients and there are currently only two FDA-approved products (Entresto and Jardiance) for the treatment of HFpEF.

Product Candidates

Tovinontrine (IMR-687)

Our lead candidate, tovinontrine, is a highly selective and potent small molecule inhibitor of PDE9. PDE9 selectively degrades cyclic guanosine monophosphate, or cGMP, an active signaling molecule that plays an important role in vascular biology. Lower levels of cGMP are found in patients with SCD and β-thalassemia and are associated with reduced blood flow, increased inflammation, greater cell adhesion and reduced nitric oxide mediated vasodilation. Blocking PDE9 acts to increase cGMP levels, which is associated with several benefits including the potential reactivation of fetal hemoglobin, or HbF, a natural hemoglobin produced during fetal development, lower white blood cell, or WBC, activation and reduced adhesion across various cell types. Increased levels of HbF in RBCs have been demonstrated to improve symptomology and substantially lower disease burden in both patients with SCD and patients with β-thalassemia and, along with reduced WBC adhesion and platelet aggregation, may result in fewer VOCs for SCD patients.

In addition, levels of cGMP are often reduced in patients with heart failure. Augmenting cGMP through the natriuretic peptide-cGMP pathway has been shown to mediate cardioprotective effects that lead to reduced heart failure disease progression and fewer cardiac events.

We believe tovinontrine may have advantages over other therapies, including having a multimodal approach and being an oral dosing regimen. In addition, tovinontrine tablets have been shown to be stable at high temperatures and in humid conditions, potentially enabling worldwide access, including in areas where SCD and ß-thalassemia are endemic.

SCD Program

We are currently conducting the Ardent Phase 2b clinical trial of tovinontrine, a randomized, double-blind, placebo-controlled trial in approximately 115 adult patients with SCD. We have completed enrollment in the Ardent clinical trial and expect to report interim data from this trial in the first week of April 2022 and final data in the second half of 2022. In November 2021, we made the decision to change the primary endpoint of the Ardent trial to annualized rate of VOCs following a written recommendation from the FDA. HbF response, which was previously the primary endpoint, will continue to be evaluated as a key secondary endpoint.

The Ardent trial follows completion of our Phase 2a clinical trial of tovinontrine in SCD, which demonstrated a well-tolerated safety profile for tovinontrine and potential benefits from tovinontrine with respect to VOCs. Changes in SCD-related biomarkers were variable.

We are also conducting a long-term open label extension, or OLE, clinical trial of tovinontrine, which is comprised of patients who completed our Phase 2a clinical trial of tovinontrine. Data from the OLE trial presented at the American Society of Hematology (ASH) Annual Meeting in December 2021 demonstrated a well-tolerated safety profile for tovinontrine, potential benefits from tovinontrine with respect to VOCs and improvements in certain SCD-related biomarkers, including HbF and F-cells, through 12 months of treatment on the OLE trial.

In the second quarter of 2022, we expect to initiate a new, long-term OLE trial of tovinontrine for patients who complete the Ardent Phase 2b clinical trial in SCD. In addition to patients from the Ardent trial, we expect patients from the ongoing Phase 2a OLE trial to roll over into this new OLE trial, resulting in one OLE trial with patients from both the Phase 2a clinical trial and the Ardent Phase 2b clinical trial.

ß-thalassemia Program

We are also conducting the Forte Phase 2b clinical trial of tovinontrine, a randomized, double-blind, placebo-controlled trial in approximately 120 TDT and NTDT patients with ß-thalassemia. In November 2021, we presented data from a pre-specified interim analysis from the Forte trial in TDT patients. The interim analysis data demonstrated a well-tolerated safety profile for tovinontrine and a trend for reduced transfusion burden in the higher dose cohort. We expect to report additional interim data for TDT and NTDT patients from the Forte trial in the first week of April 2022 and data from the final analysis of the Forte clinical trial in the second half of 2022.

HFpEF Program

In the second quarter of 2022, we expect to dose the first patient in the SP_9IN Phase 2 clinical trial of tovinontrine in HFpEF. The SP_9IN trial will be a randomized, placebo-controlled trial of approximately 170 patients 45 years of age or older with enriched PDE9 expression and persistent symptoms of HFpEF. The primary endpoint of the trial will be the change in N-terminal pro b-type natriuretic peptide, or NT-proBNP, levels.

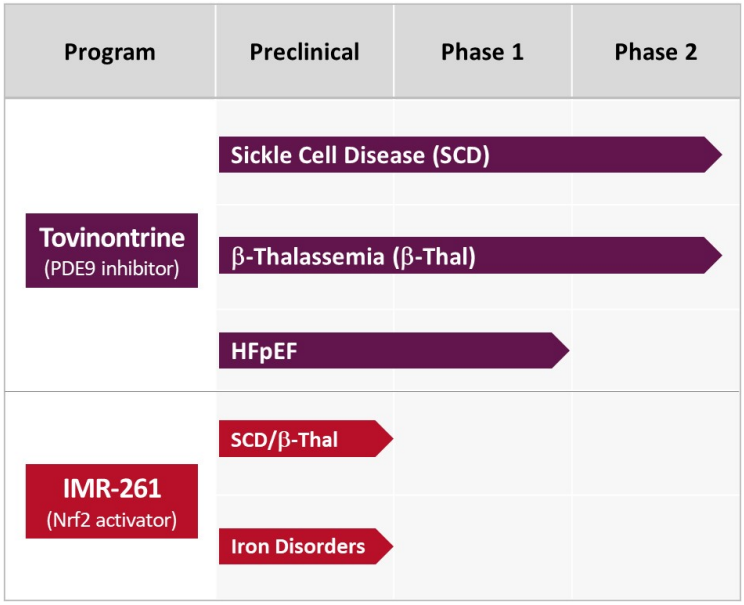
IMR-261

We have commenced research activities for IMR-261 (formerly CXA-10), an oral, clinical-ready activator of Nrf2. In pre-clinical models of SCD, IMR-261 was observed to activate expression of HbF and reduce VOCs. Furthermore, in a preclinical model of ß-thalassemia, IMR-261 was observed to increase hemoglobin and enhance RBC maturation. We have initiated work on drug product manufacturing for IMR-261 as we explore potential clinical development paths in hemoglobinopathies, iron disorders and potentially other areas.

Prior to its acquisition by us, IMR-261 was evaluated by Complexa, Inc. in Phase 2 clinical trials in focal segmental glomerulosclerosis, or FSGS, and pulmonary arterial hypertension, or PAH, and independent medical literature suggests potential in a broad array of RBC diseases, including disorders of hemoglobin, and iron overload diseases.

Our Pipeline

We are advancing a pipeline of therapeutic programs to address diseases with significant unmet medical need. The following chart summarizes key information about our programs:



Our Strategy

Our goal is to become a leading biopharmaceutical company focused on the development and commercialization of novel therapies. To achieve this, we are focused on the following key strategies:

- ***Rapidly advance tovinontrine through clinical development for the treatment of SCD and ß-thalassemia.*** There remains a significant need to develop additional differentiated disease-modifying, oral therapies to treat SCD and β-thalassemia. We are currently conducting Phase 2b clinical trials of tovinontrine for SCD and ß-thalassemia and expect to report interim data from each trial in the first week of April 2022.
- ***Expand clinical development of tovinontrine for the treatment of HFpEF.*** Published literature suggests that the inhibition of PDE9, and resulting increases in cGMP through natriuretic peptide modulation, can serve as an attractive target for the prevention and treatment of vascular disease, including HFpEF. Data from three preclinical mouse models of tovinontrine showed that selective inhibition of PDE9 with tovinontrine was effective for prevention and treatment of cardiac hypertrophy and renal dysfunction, indicating that tovinontrine may be a promising treatment option for patients suffering from HFpEF. We expect to begin clinical development of tovinontrine in HFpEF in the second quarter of 2022.
- ***Continue efforts to expand our pipeline.*** We have commenced research activities for IMR-261, an activator of Nrf2. In pre-clinical models of SCD, IMR-261 was observed to activate expression of HbF and reduce VOCs. Furthermore, in a preclinical model of ß-thalassemia, IMR-261 was observed to increase hemoglobin and enhance RBC maturation. We have initiated work on drug product manufacturing for IMR-261 as we explore potential clinical development paths. We are also exploring business development opportunities to identify novel product candidates.
- ***Maximize the commercial opportunity of our product portfolio.*** We have retained worldwide development and commercial rights to tovinontrine and are pursuing a clinical and regulatory development strategy for tovinontrine in the United States, Europe and certain other international regions. As we advance tovinontrine through clinical development, we intend to establish a focused marketing and sales infrastructure in order to maximize the commercial opportunity in the United States and Europe, and potentially other international regions.

- ***Strategically evaluate licensing and collaboration opportunities to maximize value.*** We may selectively evaluate the merits of entering into licensing and collaboration agreements for regions in which we are unlikely to pursue independent development and commercialization, or where a collaborator could provide specialized expertise and capabilities to create additional value.

Sickle Cell Disease Overview

SCD is the most common type of inherited hemoglobinopathy. SCD is characterized by debilitating pain, progressive multi-organ damage and early death. Beginning early in life, patients suffer from blocked blood flow to tissues, known as vaso-occlusion, destruction of RBCs, known as hemolysis, and inadequate oxygen delivery, or hypoxia. The most common complication of SCD is pain, often a consequence of VOCs. A VOC occurs when circulation is obstructed by sickled RBCs, causing tissue damage to the organ and resultant pain. The outcomes of these events begin presenting early in childhood and quickly lead to heart and lung complications, renal disfunction, prolonged refractory penile erection (known as priapism), spleen enlargement and failure, stroke, retinopathy and mental and physical disabilities. Given the constellation of these comorbidities, patients with SCD have a diminished quality of life and on average have a significantly shorter lifespan than normal healthy adults, sometimes up to 20 to 30 years shorter.

SCD is caused by a single mutation in the gene that expresses the beta globin subunit of hemoglobin. Hemoglobin in RBCs consists of two beta globin and two alpha globin subunits. Hemoglobin's primary function is to transport oxygen from the lungs to tissues throughout the body and return carbon dioxide back to the lungs. In oxygen rich environments, like the lungs, hemoglobin has a high affinity for oxygen and binds to it rapidly. In lower oxygen surroundings, like peripheral tissues, hemoglobin has a low affinity for oxygen and releases it quickly. The beta globin subunit mutation in SCD leads to the production of abnormal hemoglobin known as sickle hemoglobin, or HbS. HbS is comprised of two mutant beta globin and two normal alpha globin subunits. In reduced oxygen settings, HbS permits hydrophobic associations between the mutated beta globin subunits and the normal alpha subunits. This causes the oxygen deficient hemoglobin units to assemble into long chains in an event known as polymerization. These long, fixed chains of hemoglobin distort the flexible disc-like RBC into an inflexible crescent or "sickled" shape. Although the sickled RBC may convert back into a regular RBC in oxygen rich environments, it will return to its sickled form in lower oxygen environments and ultimately may be permanently sickled and/or be destroyed.

Although patients with SCD often present a spectrum of symptoms that can vary over time, patients are often grouped by their predominant symptomology: those that present with hemolytic anemia, which is largely driven by sickled RBCs, and those that present with painful VOCs, where RBCs, WBCs and other cell types play a role.

The Role of Fetal Hemoglobin on RBC Pathophysiology and SCD

One way to prevent the polymerization of HbS that results in sickled RBCs is to enhance the overall affinity of hemoglobin for oxygen, which reduces sickling in low oxygen environments and ameliorates pathophysiology of the disease. A promising approach to enhance hemoglobin-oxygen affinity is to reactivate production of inactive HbF, which we refer to as HbF induction. HbF is a natural hemoglobin that is activated during fetal development and is designed to give the growing fetus better access to oxygen from the maternal bloodstream. HbF has higher affinity for oxygen and ceases production approximately six months after birth, at which time it is replaced by adult hemoglobin that has lower oxygen affinity. Accordingly, newborns with SCD do not experience RBC sickling or resulting symptomology in the first four to five months of life. As HbF production declines and mutated HbS is produced in its place, SCD clinical manifestations begin to rapidly emerge. Some children with SCD mature into adulthood with persistence of HbF, otherwise known as hereditary persistence of HbF, and this reduces the long-term clinical manifestations of SCD. In some cases, these patients are essentially asymptomatic. A systematic literature review and series of quantitative meta-analyses revealed statistically significant associations between increases in HbF and clinical outcomes in SCD including mortality, stroke, acute chest syndrome, pain, blood transfusion, retinopathy and splenomegaly.

The Role of Other Cell Types in SCD

While HbF induction focuses primarily on the RBC aspect of SCD pathophysiology, non-RBC factors also play an important role in SCD. Several other cell types contribute to SCD, including WBCs, endothelial cells and platelets. Dysfunction of these cells, their inter-relationship and resulting downstream inflammatory processes contribute to numerous acute symptoms in SCD patients, such as painful VOCs and multi-organ damage. Third-party clinical data suggest that elevated WBCs are a predictor of increased risk of early death in patients with SCD. Furthermore, in patients with SCD, WBCs are activated and express higher levels of cell surface markers associated with adhesion, such as CD11a, CD11b and CD18. WBCs also interact with sickled RBCs and endothelial cells causing both cell aggregation and adhesion within the blood vessel. As a result, endothelial cells are damaged and secrete inflammatory signals that can ultimately lead to organ

damage. Platelets exacerbate this inflammatory cascade by releasing cell signaling molecules known as cytokines and further contribute to the cellular blockage in blood vessels that causes VOCs.

The Role of Adhesion Mediators in SCD

In addition to specific cell types playing a role in SCD, adhesion mediators cause RBCs, WBCs, endothelial cells and platelets to stick to one another. These adhesion mediators, known as cell adhesion molecules include selectins and vascular factors that form a multi-cellular lattice that contributes to blood vessel blockage. Inhibition of different types of adhesion mediators has recently become an approach to ameliorate SCD pathophysiology, which is distinct from approaches that solely target the underlying sickled RBC. Adhesion mediators can also be easily measured and therefore serve as reproducible biomarkers across RBCs, WBCs, endothelial cells and platelets.

Addressable Patient Population

The global incidence of SCD is estimated to be approximately 300,000 births annually, and by 2050, incidence is expected to rise to approximately 400,000 births annually. In the United States, where newborn screening for SCD is mandatory, the estimated prevalence is approximately 100,000 individuals. In the European Union, the estimated prevalence is approximately 134,000 individuals. The global prevalence of SCD is estimated to be approximately 4.4 million patients. SCD is most common among people of African, Middle Eastern and South Asian descent.

Approved and Emerging Modalities and Their Limitations

Approved Treatments

Managing SCD and its various clinical manifestations is complex, and patients have historically had limited options for treatment. In November 2019, the FDA granted accelerated approval for Oxbryta (voxelotor) for the treatment of SCD in patients 12 years of age and older and its label has subsequently been expanded to include patients four years of age and older. In February 2022, the European Commission approved Oxbryta for the treatment of hemolytic anemia in patients with SCD 12 years of age and older. Oxbryta is an oral therapy taken once daily and is the first approved treatment that directly inhibits sickle hemoglobin polymerization. In November 2019, the FDA also approved Adakveo (crizanlizumab), which has been demonstrated to reduce the frequency of VOCs in adult and pediatric patients aged 16 years and older with SCD. Adakveo received conditional approval in the European Union in October 2020 for the prevention of recurrent VOCs in SCD patients aged 16 years and older. Adakveo is administered intravenously and binds to P-selectin, which is a cell adhesion protein that plays a central role in the multicellular interactions that can lead to VOCs.

While these approvals are important milestones for patients with SCD, we believe that there remains a significant unmet need for SCD therapies. Oxbryta was approved by the FDA on an accelerated basis based on improvements in hemoglobin levels as a surrogate endpoint reasonably likely to predict clinical benefit. Continued approval for this indication may be contingent upon verification and description of the clinical benefit in a confirmatory study which is currently ongoing and is evaluating cerebral blood flow velocity. Adakveo does not treat the underlying cause of SCD and is only available through intravenous administration, not in oral form.

Prior to the approval of Oxbryta and Adakveo for SCD, there were only two FDA-approved drugs in the United States to treat SCD: Hydroxyurea, or HU, and Endari (L-glutamine); and only one approved drug in the European Union: HU. These therapies have significant limitations in their safety, dosing regimen, efficacy and long-term effects.

HU, an oral chemotherapy that induces HbF and decreases sickling of the RBC, was first approved by the FDA for the treatment of SCD in 1998 and approved in the European Union in 2007. Despite numerous benefits, HU remains a suboptimal therapy for several reasons:

- Safety Concerns: HU has a boxed warning because of its cancer-causing potential.
- Complex Dosing Regimen: Due to HU's myelosuppressive effects, which can lead to reduced WBC and platelet counts, patients need to be frequently monitored and HU must be titrated over many months, which prevents many patients from achieving an optimal dose of therapy.
- Variable Responses: Patients treated with HU have significant nonresponse rates, and HU may have a delayed onset of activity.
- Potential Long-Term Effects of Use: Long-term effects include the potential for infertility in both males and females.

Endari, an oral powder form of L-glutamine, was approved by the FDA in 2017. L-glutamine is an amino acid precursor to nicotinamide adenine dinucleotide, or NAD, and is thought to reduce the oxidative stress that is present in patients with SCD. In September 2019, Emmaus Life Sciences, Inc. withdrew its marketing application to the European Medicines Agency, or EMA, for Endari.

Blood transfusions are another suboptimal treatment option for patients with SCD. Transfusions can transiently bolster hemoglobin levels by adding functional RBCs but can lead to several complications that include iron overload, adverse immune response and transmission of transfusion-associated infections. Due to the lack of uniform accessibility to blood transfusions, they are not widely employed for the treatment of SCD. Allogeneic hematopoietic stem cell transplant, or HSCT, is available as a potentially curative treatment for SCD and acts by halting sickled RBC production from the affected marrow and replacing it with healthy hematopoietic stem cells from a matched donor. HSCT is rarely used due to the difficulty in finding a matched donor, the potential for infection and an approximately 5% mortality rate. The possibility of increased mortality risk relegates this to a last option, often utilized only in the most severe cases.

Due to the limitations of existing therapies, we believe there remains a critical need to develop new preventative therapies that are easy to access, safe for long-term use and address the multiple aspects of SCD pathology.

Emerging Modalities

There has recently been an increased focus on the development of new treatments for SCD with a spectrum of different approaches, but none address the multifactorial pathology of SCD with an oral once-a-day tablet. These approaches can be broadly categorized as follows:

Anti-Polymerization Agents: Anti-polymerization agents, such as Oxbryta, are designed to prevent polymerization of hemoglobin and sickling of RBCs by increasing hemoglobin's affinity for oxygen and maintaining hemoglobin in an oxygenated state. However, approaches that are solely focused on reducing polymerization may not address the complex symptomology of SCD and the clinical impact of Oxbryta on VOCs remains a question.

HbF Inducers: HbF inducers seek to reactivate production of HbF in an effort to enhance hemoglobin-oxygen affinity. Examples include FTX-6058, under development by Fulcrum Therapeutics, Inc., or Fulcrum, and EPI-01, under development by Novo Nordisk A/S, or Novo Nordisk (in collaboration with EpiDestiny, Inc., or EpiDestiny).

PKR Activators: Pyruvate kinase-R, or PKR, is an enzyme that is involved in the conversion of sugar into energy and is critical for the survival of RBCs. Mutations in PKR cause deficiencies in this process which results in a shortened lifespan for RBCs. This has led to the hypothesis that PKR activation can overturn this deficiency and may lead to a therapeutic benefit in patients with SCD. Examples include mitapivat (AG-348), under development by Agios Pharmaceuticals, Inc., or Agios, and etavopivat (FT-4202), which is under development by Forma Therapeutics, Inc., or Forma.

Selectin Inhibitors: Pan selectin and specific P-selectin inhibitors, such as Adakveo, are designed to reduce adhesion of WBCs to the endothelial cell wall and reduce VOCs; however, selectin inhibitors do not ultimately prevent the sickling of RBCs in SCD. Furthermore, Adakveo requires lengthy infusion treatments every three to four weeks. Global Blood Therapeutics, Inc, or GBT, is also developing inclacumab, a specific P-selectin inhibitor that was previously under development for non-SCD indications.

Gene Therapy/Editing: Gene-based therapy is an innovative and potentially curative approach to SCD treatment. Like HSCT, gene therapy for SCD involves several pre-treatment steps that can include chemotherapy, which carry significant standalone risks. bluebird bio, Inc., or bluebird, and Aruvant Sciences, Inc., or Aruvant, are each developing gene therapies which aim to deliver a functional copy of the human beta-globin gene. Gene editing, including CRISPR-Cas9, is an alternative approach to gene modification that has recently advanced in clinical development. Examples of gene editing approaches include CTX-001, currently in development by CRISPR Therapeutics AG, or CRISPR (in collaboration with Vertex Pharmaceuticals Incorporated, or Vertex). Numerous questions remain with respect to the gene editing approach, including off-target mutagenesis and the ultimate potential reach of such therapeutics. More studies are needed to establish durability and safety of these potential treatments.

The Role of Phosphodiesterase-9 in SCD

Tovinontrine is being developed to inhibit PDE9. PDE9 decreases cGMP, an active signaling molecule that plays an important role in vascular biology. Lower levels of cGMP, as found in patients with SCD, are associated with reduced blood

flow, increased inflammation, greater cell adhesion and reduced nitric oxide-mediated vasodilation. In addition, PDE9 is highly expressed in cells of interest in SCD, specifically reticulocytes, which are an important cell type for HbF induction. Furthermore, PDE9 has high expression in WBCs and in areas where RBCs are formed. In preclinical studies, PDE9 inhibitors have been shown to increase cGMP concentrations, induce HbF and F-cells, reduce WBC activation and adhesion across other cell types and modulate adhesion mediators. This was further demonstrated in preclinical SCD models of tovinontrine, where we observed that tovinontrine is a potent cGMP inducer and had a multimodal mechanism of action, acting to increase HbF expression in RBCs, reduce RBC sickling and decrease expression of WBC adhesion molecules.

Our Solution for Sickle Cell Disease: Tovinontrine as a Differentiated PDE9 Inhibitor

Our approach to address SCD is fundamentally distinct from other therapies. Tovinontrine is being developed to directly and potently inhibit PDE9, which represents a differentiated approach to increase cGMP levels, with a selectivity for PDE9 that we believe will make it amenable for long-term use. We believe tovinontrine may have advantages over other therapies in SCD, including a multimodal approach and an oral, once daily dosing regimen. In addition, tovinontrine tablets have been shown to be stable at high temperatures and in humid conditions, potentially enabling worldwide access, including in areas where SCD and ß-thalassemia are endemic.

We believe tovinontrine has several differentiating features relative to other PDE9 inhibitors:

Highly Potent PDE9 Inhibitor: Tovinontrine is a highly potent PDE9 inhibitor, as measured by induction of cGMP across escalating doses. Tovinontrine has been designed to rapidly increase cGMP, which translates to HbF induction and potentially reduced WBC adhesion.

Differentiated Selectivity and Tolerability Profile: Tovinontrine is highly specific to PDE9 and not selective for other phosphodiesterase family members. Toxicology studies of tovinontrine, including fertility and juvenile studies, support its potential benefit as a long-term therapy in adults and children. We believe this selectivity will allow us to optimize dose while minimizing off-target effects.

Minimal Brain Penetration: Tovinontrine was observed to have minimal brain penetration in preclinical *in vivo* models relative to other PDE9 inhibitors that have been studied. We believe this will reduce the potential impact of PDE9 inhibition on central nervous system development and function.

Drug Product Stability: Tovinontrine tablets have been shown to be stable at high temperatures and in humid conditions, potentially enabling worldwide access, including in underserved regions where SCD and β-thalassemia are endemic.

Preclinical and Healthy Volunteer Data

In preclinical SCD models, we observed that tovinontrine is a potent cGMP inducer and had a multimodal mechanism of action, acting to increase HbF expression in RBCs, reduce RBC sickling and decrease expression of WBC adhesion molecules.

In an SCD *in vitro* model, we measured the ability of tovinontrine to increase cGMP levels in an RBC cell line as compared to HU. In this study, we observed that tovinontrine induced cGMP production in a dose-dependent manner at an approximately 30-fold lower drug concentration than HU. In addition, at an equivalent drug concentration of 10 µM of tovinontrine, we observed an approximately ten-fold increase in cGMP levels as compared to HU. We also evaluated tovinontrine in a mouse model of SCD that expresses human sickle hemoglobin. We observed that tovinontrine demonstrated statistically significant increases in F-cells, statistically significant decreases in the percentage of sickled RBCs and decreases in markers of hemolysis, or destruction of RBCs, and WBC adhesion.

In 2016, we initiated a Phase 1 randomized, double-blind, placebo-controlled clinical trial of tovinontrine in healthy volunteers. In that trial, single and multiple ascending doses of tovinontrine were reported to be well tolerated to a maximum dose of 4.5 mg/kg per day and no serious adverse events were reported. In 2021, we conducted a second healthy volunteer clinical trial of tovinontrine to explore higher doses of tovinontrine. This single ascending dose followed by a multiple dose trial tested doses of up to 13 mg/kg per day. The results demonstrated that doses of up to 8 mg/kg per day were well tolerated and no dose limiting toxicities or serious adverse events were reported at any dose tested.

Phase 2a Clinical Trial of Tovinontrine in SCD

Our Phase 2a clinical trial was a randomized, double-blind, placebo-controlled clinical trial in adult patients with SCD and was conducted at clinical centers in the United States and the United Kingdom. The trial evaluated the safety, tolerability, pharmacokinetics, or PK, and exploratory pharmacodynamic, or PD, and clinical outcomes of escalating doses of tovinontrine administered once daily for 16 to 24 weeks, either as a monotherapy or in combination with HU. A total of 93 patients were dosed in the trial, of which 58 patients were on monotherapy and 35 patients were treated in combination with HU. Patients on treatment in the monotherapy arm received an escalating dose of tovinontrine of up to 200 mg per day, while patients in the combination arm received an escalating dose of tovinontrine of up to 100 mg per day in addition to HU.

The data from the Phase 2a clinical trial demonstrated that tovinontrine was well tolerated as a monotherapy and in combination with HU at all dose levels. Changes in SCD-related biomarkers were variable across the trial. A post-hoc analysis of the pooled results further showed that when compared to placebo (N=30), patients on tovinontrine (N=63) had:

- a 40% lower mean annualized rate of VOCs;
- a 38% lower mean annualized rate of VOC-related hospitalizations;
- an increase in time to first VOC of 169 days for patients treated with tovinontrine versus 87 days for placebo groups; and
- improvements in the patient-reported VOC pain severity score.

Phase 2a Open Label Extension of Tovinontrine in SCD

We are conducting a four-year OLE clinical trial which allows patients from the Phase 2a clinical trial to enroll in a long-term safety and tolerability study of tovinontrine following completion of the Phase 2a clinical trial. Patients in the OLE clinical trial initially received a once-daily dose of tovinontrine of 200 mg and have subsequently been escalated to a once-daily dose of up to 400 mg.

In December 2021, we presented 12-month data from the OLE trial at the American Society of Hematology (ASH) Annual Meeting. Of the 26 subjects enrolled, 21 were evaluable at month 12 (as of the data cut-off). Tovinontrine was generally well-tolerated as a monotherapy as well as in combination with HU. There were no clinically significant changes in lab safety data, electrocardiogram data or vital signs, and no patients discontinued from the study due to adverse events.

The median annualized VOC rate was reduced by 38% in subjects previously in the placebo group in the Phase 2a clinical trial (N=7), with median annualized VOC rates of 5.0 (Phase 2a) and 3.1 (OLE) per year, with a median duration of treatment of 6.4 months and 11.6 months, respectively.

The low median annualized VOC rate for tovinontrine-treated patients in the Phase 2a clinical trial was maintained in subjects in the OLE clinical trial (N=14), with median annualized VOC rates of 0 (Phase 2a) and 2.0 (OLE) per year, with a median duration of treatment of 6.4 months and 11.8 months, respectively.

22% (4/18) of evaluable patients had an absolute increase in HbF greater than 3%. 47% (9/19) of patients had an absolute increase in F-cells greater than 6%, and F-cell increases were observed in 18 out of 19 evaluable patients.

Ardent Phase 2b Clinical Trial of Tovinontrine in SCD

We are currently conducting the Ardent Phase 2b clinical trial of tovinontrine in SCD, a randomized, double-blind, placebo-controlled, multicenter study of approximately 115 adult patients with SCD. Patients were initially randomly assigned in a 2:1 ratio to receive either low dose tovinontrine (once daily dose of 200 mg or 300 mg based on patient weight) or placebo. In the first quarter of 2021, an independent data monitoring committee for the Ardent trial recommended opening of the high dose tovinontrine treatment arm following review of available safety and tolerability data. After this point, patients were randomly assigned in a 1:2:1 ratio to receive low dose tovinontrine (once daily dose of 200 mg or 300 mg based on patient weight), high dose tovinontrine (once daily dose of 300 mg or 400 mg based on patient weight) or placebo. We completed enrollment in the Ardent trial in the third quarter of 2021.

The planned primary efficacy endpoint of the Ardent trial is annualized rate of VOCs, and the trial is powered for statistical significance with respect to this endpoint. We decided to change the primary endpoint of the Ardent trial from HbF response, defined as an increase of ≥3% in HbF, to annualized rate of VOCs following a written recommendation from the FDA in November 2021. HbF response will continue to be evaluated as one of two key secondary endpoints, with an

evaluation of time to first VOC as the other key secondary endpoint. In addition, other secondary endpoints include the evaluation of the effect of tovinontrine versus placebo on (i) the percent of patients who are VOC-free, time to second VOC, VOC-related hospitalizations, (ii) HbF-associated biomarkers, (iii) indices of red cell hemolysis, (iv) indices of WBC adhesion, and (v) quality of life measures.

We plan to conduct an interim analysis from the Ardent trial of patients who have reached at least 24 weeks of dosing and expect to report data related to the primary endpoint from this interim analysis in the first week of April 2022. We expect to report final data from the Ardent trial through 52 weeks of treatment in the second half of 2022.

In the second quarter of 2022, we expect to initiate long-term OLE clinical trial of tovinontrine for patients who complete the Ardent Phase 2b clinical trial in SCD. In addition to patients from the Ardent trial, we expect patients from the ongoing Phase 2a OLE trial to roll over into this new OLE trial, resulting in one OLE trial with patients from both the Phase 2a clinical trial and the Ardent Phase 2b clinical trial.

β-thalassemia Disorder Overview

β-thalassemia is a rare inherited RBC disorder. Unlike patients with SCD, patients with β-thalassemia have a mutation that causes the absence or decreased synthesis of the beta globin subunit of hemoglobin, thereby creating an over-abundance of the alpha globin subunit. This causes the formation and aggregation of insoluble clumps that lead to ineffective RBC production and a reduction in the number of functioning RBCs. Furthermore, the RBCs that do survive have shorter lifespans and are smaller, paler and less efficient at transporting oxygen throughout tissues of the body. Oftentimes, RBCs of smaller size, measured as mean corpuscular volume, is a first indication of β-thalassemia prior to genotyping. If left untreated, β-thalassemia causes severe anemia, splenomegaly, skeletal abnormalities, organ failure and early death.

β-thalassemia presents as a spectrum of disease, with patients categorized based on hemoglobin levels and clinical manifestations. Although β-thalassemia can be classified as “major,” “intermedia,” and “minor,” a more recent classification is based on a patient’s dependency on blood transfusion. Most β-thalassemia major patients are classified as TDT, while intermedia and minor patients are classified as NTDT. TDT patients have a transfusion regimen that is well established and generally lifelong. NTDT patients are a clinically diverse group, with transfusions required intermittently during periods of RBC stress, such as pregnancy, infection, surgery, times of rapid growth and sometimes later in life.

As in SCD, a promising way to address the missing or decreased presence of the beta globin subunit is to induce HbF production. In addition to resolving persistent anemia, HbF induction rectifies the missing or mutated beta globin subunit and thereby reduces the overabundance of free-floating alpha globin subunits. These benefits have the potential to result in increased functional RBC production, higher hemoglobin levels, reduced hemolysis and the reduction of adhesion and inflammation. In addition to HbF induction, independent research suggests activation of the nitric oxide-cGMP signaling pathway may induce RBC production, which is associated with increases in RBC counts and hemoglobin levels. We believe this is an important mechanism of action to that could be relevant in reducing disease burden. Furthermore, adhesion mediators are also highly upregulated in patients with β-thalassemia and may contribute to the increased number of clots in their blood vessels, known as a hypercoagulability state. Specifically, data show that two adhesion markers, ICAM-1 and VCAM-1, are over-expressed in patients with β-thalassemia as compared to controls. Furthermore, there is evidence that WBCs in patients with β-thalassemia express higher levels of CD11b and CD18, two important biomarkers in the WBC activation cascade.

Addressable Patient Population

The prevalence of β-thalassemia globally is estimated to be 288,000, with an incidence of 60,000 births per year. The total combined prevalence of β-thalassemia in the United States and European Union is estimated to be approximately 19,000 patients. Of the patients currently treated in the United States and European Union, we believe approximately 50% and 10%, respectively, are transfusion dependent. β-thalassemia is especially prevalent in developing countries of Africa, South Asia, Southeast Asia, the Mediterranean region and the Middle East. Although historically prevalent in Mediterranean North Africa and South Asia, thalassemias are now encountered in other regions as a result of changing migration patterns. As such, there is a growing focus on developing new therapeutics aimed at improving quality of life for this significant unmet medical need.

Approved and Emerging Modalities and Their Limitations

Approved Treatments

Blood transfusions have been the standard of care treatment for β-thalassemia. The risks associated with transfusions are similar to those seen in the SCD population, but higher frequency of use often results in iron overload toxicities, a secondary complication of this treatment. Over time, iron becomes trapped in the tissues of vital organs, which can lead to diabetes, cirrhosis, osteoarthritis, heart attack and hormone imbalances. If not addressed, excess iron can result in organ failure and death. There are several approved agents that remove iron from the body, known as iron chelators, but they have significant challenges including high costs, the requirement for frequent monitoring, therapy complications and patient incompatibility.

HSCT is a potential curative therapy for β-thalassemia and has demonstrated successful outcomes across patient types. However, as in SCD, there are numerous barriers to use, including increased mortality risk, that have limited its broader adoption. Recently, the European Commission granted conditional marketing authorization for Zynteglo, a gene therapy approach to β-thalassemia for patients 12 years and older with TDT and for whom HSCT is appropriate, but a donor has not yet been matched or been made available. The long-term efficacy of the therapy remains unknown, as do many of the associated risks.

In November 2019, the FDA approved Reblozyl (luspatercept-aamt) for the treatment of anemia in adult patients with β-thalassemia who require regular RBC transfusions. Reblozyl was approved by the European Commission in June 2020 to treat adult patients with transfusion-dependent anemia associated with ß-thalassemia. Reblozyl is a modified receptor protein that promotes RBC maturation and increases overall RBC production, but does not address other cell types implicated in β-thalassemia. Reblozyl is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia. Reblozyl is the first and only FDA-approved erythroid maturation agent, representing a new class of therapy which works by regulating late-stage RBC maturation to help patients reduce their RBC transfusion burden.

Emerging Modalities

There has been increased development of new treatments for β-thalassemia, but no clinical-stage program addresses the full spectrum of the disease in an oral, once-a-day tablet. These treatments can be broadly categorized into the following approaches:

RBC Maturation: Clinical stage programs in this category generally are aimed at promoting RBC maturation and/or increasing overall RBC production, but do not address other cell types implicated in b-thalassemia. Several molecules targeting this pathway to treat chronic anemia associated with ineffective erythropoiesis and iron overload are in development. These include IONIS-TMPRss6-LRx, under development by Ionis Pharmaceuticals, Inc., or Ionis Pharmaceuticals, SLN-124, under development by Silence Therapeutics PLC, or Silence Therapeutics, and VIT-2763, under development by Vifor Pharma Ltd, or Vifor.

Gene Therapy/Editing: As with SCD, gene therapy and gene editing approaches are also being developed as potential curative therapies for b-thalassemia. beti-cel is a gene therapy treatment in development by bluebird, while CTX-001 is a gene editing therapy currently in development by CRISPR (in collaboration with Vertex). Gene therapy involves pretreatment regimens associated with standalone risk which may limit its use in broad patient populations, and gene editing approaches still have many unanswered questions, including off-target mutagenesis.

PKR Activators: Drug candidates are being developed that activate PKR, an enzyme that is involved in the conversion of sugar into energy and is critical for the survival of RBCs. Examples include mitapivat, under development by Agios, and etavopivat, under development by Forma in TDT and NTDT patients with ß-thalassemia.

Our Solution for β-thalassemia: Tovinontrine as a Differentiated PDE9 Inhibitor

PDE9 is a potent and highly selective mechanism that uniquely targets cGMP degradation, making it a promising pathway to increase cGMP, reactivate HbF, enhance RBC production, enable RBC maturation, and reduce WBC activation in β-thalassemia. We believe tovinontrine is a differentiated PDE9 inhibitor that is highly potent, selective for its target, minimally brain penetrating, and is delivered in an oral, once-a-day therapy, which could be used globally.

Preclinical Data of Tovinontrine in ß-thalassemia

We conducted preclinical studies in a ß-thalassemia mouse model that recapitulates the human NTDT condition. This mouse model lacks a functional beta globin subunit, leading to deficits in hemoglobin and RBCs, as well as slowed RBC maturation. After 30 days of treatment at two different doses, we observed that tovinontrine induced statistically significant increases in functional hemoglobin and total RBC counts in a dose dependent way, with the 60mg/kg dose outperforming the 30mg/kg dose. Allometric scaling to reflect dose conversion from mouse to human indicates that the 30mg/kg mouse dose is equivalent to a human dose of approximately 2.4mg/kg and the 60mg/kg mouse dose is equivalent to a human dose of approximately 4.9mg/kg.

Promotion of RBC maturation, a key mechanistic component in reducing ß-thalassemia pathology, was also observed in preclinical studies. After 30 days of once-a-day treatment with 30 mg/kg and 60 mg/kg of tovinontrine, we observed that erythroblast maturation was significantly improved as reflected by an increase in the amount of Ery.C, which is the population of mature erythroblasts, in comparison to Ery.B, which are more immature erythroblasts. These changes were also associated with a decrease on the ratio of Ery.B to Ery.C, otherwise known as a maturation index, where lower ratio indicates progression to maturity.

Forte Phase 2b Clinical Trial of Tovinontrine in ß-thalassemia

We are currently conducting the Forte Phase 2b clinical trial of tovinontrine in ß-thalassemia, a randomized, double-blind, placebo-controlled trial, evaluating the safety and tolerability of tovinontrine in approximately 120 adult patients with ß-thalassemia. Similar to the Ardent SCD trial, patients were initially randomly assigned in a 2:1 ratio to receive either low dose tovinontrine (once daily dose of 200 mg or 300 mg based on patient weight) or placebo. In the first quarter of 2021, an independent data monitoring committee for the Forte trial recommended opening of the high dose tovinontrine treatment arm following review of available safety and tolerability data. After this point, patients have been randomly assigned in a 1:2:1 ratio to receive low dose tovinontrine (once daily dose of 200 mg or 300 mg based on patient weight), high dose tovinontrine (once daily dose of 300 mg or 400 mg based on patient weight) or placebo.

In addition to safety, for TDT patients, we are evaluating the effect of tovinontrine versus placebo in reducing the number of RBC units transfused in any 12-week interval as compared to the 12-week interval prior to randomization, known as the transfusion burden. For NTDT patients, we are evaluating the effect of tovinontrine versus placebo on HbF and hemoglobin, or Hb. The Forte trial will also examine additional exploratory efficacy endpoints as well as additional safety and PK endpoints.

In November 2021, we conducted a pre-specified protocol-driven interim analyses in approximately 43 TDT patients, 35 of whom completed at least 12 weeks of treatment and were in the analysis population for transfusion burden. The median baseline transfusion burden in each of the high dose tovinontrine and placebo groups was 7.5 RBC units/12 weeks. Furthermore, 54% of the subjects in the analysis population (19/35) had the more severe β^0/β^0 genotype. The interim data demonstrated tovinontrine was well-tolerated, with the most frequent adverse events (at least 10% of subjects in pooled tovinontrine dose groups) being nausea, headache and dizziness. Four (9.3%) patients discontinued due to adverse events considered at least possibly related to study drug.

The proportion of patients who had at least a33% reduction in transfusion burden (of at least 2 units) in any 12-week interval as compared to the 12-week interval prior to randomization was greater in the high dose tovinontrine group (7/8) versus placebo, despite an unexpectedly high response rate in the placebo group (8/12). Additionally, the proportion of patients who had at least a 33% reduction in transfusion burden (of at least 2 units) in any 14-week interval as compared to the 12-week interval prior to randomization was also greater in the high dose tovinontrine group (5/8) versus the placebo group (5/12). Low dose tovinontrine did not show a higher response rate when compared to the placebo group. No substantial differences between groups were observed in transfusion burden response rate using a fixed interval (weeks 13-24). RBC markers were not evaluable in these regularly transfused subjects.

We expect to report data from an additional interim analysis in approximately 50 TDT patients and 30 NTDT patients through 24 weeks of dosing in the first week of April 2022 and final data from the Forte trial in the second half of 2022.

HFpEF Disease Overview

HFpEF, also known as diastolic heart failure, is typically caused by abnormalities of cardiac filling, which leads to symptoms such as shortness of breath, exercise intolerance and fluid retention. Characteristics of HFpEF are heterogeneous, but commonly include ventricular hypertrophy, diastolic dysfunction, endothelial dysfunction, insulin resistance, and inflammation. Comorbidities, such as hypertension, anemia, chronic kidney disease, diabetes, and obesity, are also common

in HFpEF, which are thought to contribute to its development. HFpEF accounts for approximately half of all cases of heart failure and is becoming the predominant form of heart failure over time. Prevalence in the United States is estimated to be approximately 3-4 million patients. In contrast to heart failure with reduced ejection fraction, or HFrEF, there are relatively few treatment options to improve symptoms and outcomes for patients.

Our Solution for HFpEF: Tovinontrine as a Differentiated PDE9 Inhibitor

cGMP is known to play a pivotal role in cardiovascular and metabolic health. For example, increased cGMP signaling promotes vasodilation, natriuresis, diuresis, insulin sensitivity and lipolysis, and can inhibit cardiac hypertrophy, inflammation and adverse platelet-leukocyte-endothelial interactions. Therefore, increasing cGMP by PDE9 inhibition may be an attractive target for the treatment of HFpEF. We believe tovinontrine is a differentiated PDE9 inhibitor that is highly potent, selective for its target, minimally brain penetrating, and is delivered in an oral, once-a-day therapy.

Preclinical Data of Tovinontrine in HFpEF

We conducted *in vivo* studies with tovinontrine in three different established mouse models for HFpEF in collaboration with the Necker Institute of Paris, France. In the first model, we tested whether tovinontrine could prevent the development of HFpEF induced by unilateral nephrectomy and six-week continuous infusion of d-aldosterone. Tovinontrine was administered at doses of 60 mg/kg or 100 mg/kg concurrently with d-aldosterone for six weeks. The results showed that tovinontrine significantly attenuated the development of cardiac and cardiomyocyte hypertrophy and limited the increase in biomarkers of myocardial inflammation and fibrosis. Congruent findings were obtained in the second model, in which mice received continuous infusion of angiotensin II for six weeks to produce the HFpEF phenotype. Tovinontrine was administered at doses of 60 or 100 mg/kg concurrently with angiotensin II infusion for six weeks. The results showed that tovinontrine attenuated cardiac and cardiomyocyte hypertrophy and limited the increase in biomarkers of myocardial inflammation and fibrosis. In addition to these two preventive models, a third model was employed to test the therapeutic potential of tovinontrine to treat prevalent HFpEF. In this study, 20 week-old diabetic prone obese mice that displayed the HFpEF phenotype were assigned to receive vehicle or tovinontrine at 60- or 100-mg/kg for eight weeks. The mice treated with tovinontrine displayed significantly less cardiomyocyte hypertrophy and lower levels of biomarkers of myocardial inflammation and fibrosis. In the control arms of all three models, we found increased myocardial transcript levels of PDE9, atrial natriuretic peptide, or ANP, and B-type natriuretic peptide, or BNP. In all three models, we found that tovinontrine significantly reduced PDE9, ANP and BNP transcript levels in a dose-dependent manner.

Planned Phase 2 Clinical Trial of Tovinontrine in HFpEF

In the second quarter of 2022, we expect to dose the first patient in the SP$_9$IN Phase 2 clinical trial of tovinontrine in HFpEF. The SP$_9$IN trial will be a randomized, placebo-controlled trial of approximately 170 patients 45 years of age or older with enriched PDE9 expression and persistent symptoms of HFpEF. Patients will receive either tovinontrine (twice daily dose of 300 mg or 400 mg based on patient weight) or placebo for 16 weeks. The primary endpoint will be the change in NT-proBNP levels, with secondary endpoints that include safety and tolerability as well as quality of life measures such as Kansas City Cardiomyopathy Questionnaire (KCCQ) and New York Heart Association (NYHA) classification. Exploratory measures are expected to include a clinical composite score, 6-minute walk test and evaluation of cardiac structure and function.

IMR-261 (formerly CXA-10)

Overview

We have commenced research activities for IMR-261 (formerly CXA-10), an oral, clinic-ready activator of Nrf2. Nrf2 coordinates the expression of antioxidant genes in response to oxidative stress, regulates inflammation, inhibits the NF-kB pathway and has been shown to increase HbF. Prior to its acquisition by us, IMR-261 was evaluated by Complexa, Inc. in Phase 2 clinical trials in FSGS and PAH, and independent medical literature suggests potential in a broad array of RBC diseases, including disorders of hemoglobin and iron overload diseases. We have initiated work on drug product manufacturing for IMR-261 as we explore potential clinical development paths in hemoglobinopathies, iron disorders and potentially other areas.

Preclinical Data for IMR-261

We evaluated IMR-261 in preclinical studies using *in-vitro* cell cultures and *in-vivo* mouse models of SCD and b-thalassemia. In CD34+ cells from sickle cell and healthy donors, high dose IMR-261 increased HbF expression by approximately 7-fold versus placebo, whereas lower dose IMR-261 increased HbF expression by approximately 4-fold versus placebo. Furthermore, an approximately 3-fold increase in F-cells was seen in both high dose and low dose groups when compared to placebo. In the Townes mouse model of SCD, high dose IMR-261 induced HbF by approximately 2.2-fold when compared to placebo (8.3 ng/ml versus 3.7 ng/ml). In addition, high dose tovinontrine significantly decreased select markers of hemolysis and increased Hb by approximately 1.1 g/dL when compared to placebo (8.7 g/dL versus 7.6 g/dL).

In a separate experiment in Townes SCD mice that assessed VOC reduction after administration of TNF-alpha, IMR-261 significantly reduced the presence of RBC on occluded vessels when compared to placebo. IMR-261 was also tested in a mouse model of b-thalassemia ($Hbb^{th1/th1}$) and showed significant increases in Hb and improvements in ineffective erythropoiesis at the high dose.

License and Acquisition Agreements

Tovinontrine – Exclusive License with Lundbeck

In April 2016, we entered into an agreement, or the Lundbeck Agreement, with H. Lundbeck A/S, or Lundbeck, for a worldwide license under certain patent rights and certain know-how owned or otherwise controlled by Lundbeck within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, excluding diseases or disorders of the central nervous system, which we refer to as the Lundbeck Field. The Lundbeck Agreement was amended in July 2016 and October 2017.

The Lundbeck Agreement grants us an exclusive license under the licensed technology, including the right to grant sublicenses with certain restrictions, to research, develop, make, have made, use, sell, have sold, offer to sell, import, export and commercialize any product comprising or containing certain PDE9 inhibitors, in the Lundbeck Field. We call such products Lundbeck Licensed Products. Subject to certain restrictions, under the agreement, we grant Lundbeck a non-exclusive, irrevocable, perpetual, worldwide, sub-licenseable, and fully paid-up right and license under patent rights we control to the extent necessary for Lundbeck to research, develop, make, have made, use, sell, have sold, offer to sell, import, export and commercialize Lundbeck Licensed Products outside of the Lundbeck Field.

The Lundbeck Agreement also grants us a non-exclusive license under the licensed technology to research and develop, and make, have made, use, import and export for purposes of enabling such research and development, enhancements, improvements, modifications or derivatives to licensed products, until but not beyond a specified pre-commercialization developmental stage with respect to each such enhancement, improvement, modification or derivative. We have the right to request that Lundbeck grant us an exclusive development and commercialization license to one or more compounds identified through these activities as a back-up compound.

As partial consideration for the licenses granted under the Lundbeck Agreement, we issued an aggregate of 443,271 shares of our common stock to Lundbeck between April 2016 and August 2017. We are also obligated to make milestone payments to Lundbeck aggregating up to (i) $23.5 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any licensed product and (ii) $11.8 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any Imara product that is or comprises a PDE9 inhibitor but is not a Lundbeck Licensed Product, which is referred to as a PDE9 Product, if any. We are obligated to pay tiered royalties of low-to-mid single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of Lundbeck Licensed Products, and tiered royalties of low single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of PDE9 Products, if any. The royalties are payable on a product-by-product and country-by-country basis. Our obligation to make royalty payments extends with respect to a Lundbeck Licensed Products in a country until the later of ten years after the first commercial sale of that Lundbeck Licensed Product in that country and the expiration of the last-to-expire valid claim of a patent or patent application licensed from Lundbeck covering the Lundbeck Licensed Product or any constituent licensed compound in that country. Our obligation to make royalty payments extends with respect to a PDE9 Product in a country until the ten years after the first commercial sale of such PDE9 Product in that country. To date pursuant to this agreement, we have made cash payments to Lundbeck of $1.8 million consisting of an upfront payment and ongoing milestone payments.

The Lundbeck Agreement obligates us to use commercially reasonable efforts to develop, seek regulatory approval for, manufacture, market and otherwise commercialize at least one licensed product, in accordance with a development plan and a development milestone timetable specified in the Lundbeck Agreement. We have the option to extend the development milestone timetable up to two times by agreeing to additional payment obligations.

Both we and Lundbeck have the right to terminate the Lundbeck Agreement if the other party materially breaches the Lundbeck Agreement and fails to cure such breach within specified cure periods or in the event the other party undergoes certain bankruptcy events. Lundbeck may terminate the Lundbeck Agreement if we or any of our affiliates, sublicensees or subcontractors bring specified patent challenges against Lundbeck or assist others in bringing such a patent challenge against Lundbeck and fail to cease such challenge within a specified period of time. We have the right to terminate the Lundbeck Agreement for our convenience at any time on six months' prior written notice to Lundbeck.

IMR-261 – Asset Purchase Agreement with Complexa (assignment for the benefit of creditors), LLC

In October 2020, we entered into an asset purchase agreement, or the Complexa APA, with Complexa (assignment for the benefit of creditors), LLC, or Complexa ABC, pursuant to which we acquired all of Complexa ABC's right, title and interest in and to the assets comprising the Nrf2 program, including CXA-10 (subsequently renamed IMR-261), previously held by Complexa, Inc. Complexa, Inc. had previously assigned all such assets to Complexa ABC pursuant to a general assignment entered into in August 2020 between Complexa, Inc. and Complexa ABC.

As consideration for the assets acquired under the Complexa APA, we made a one-time payment of approximately $0.1 million and agreed to pay up to an additional approximately $3.8 million in milestone payments based on the achievement of specified clinical and commercial sale milestones as set for the in the Complexa APA. As part of the acquisition, Complexa ABC assigned to us all of its rights under license agreements with The UAB Research Foundation and the University of Pittsburgh, each as discussed below.

IMR-261 – Exclusive License Agreement with UAB Foundation

In October 2020, we took assignment to an exclusive license agreement, or the UAB Agreement, originally entered into between The UAB Research Foundation, or UAB, and Complexa, Inc. in April 2012. The UAB Agreement grants us an exclusive worldwide license to practice and fully exploit certain patent rights and to make, have made, develop, use, lease, offer to sell, sell, import and export products covered by such patents within the field of human therapeutics and diagnostics. We call such products UAB Licensed Products. We have the right to grant sublicenses with certain restrictions, including obtaining the consent of UAB, which consent may not be unreasonably withheld, conditioned or delayed.

We are obligated to make milestone payments to UAB aggregating up to approximately $0.3 million upon the achievement of specified commercial sale milestones by any UAB Licensed Product and to pay a low single-digit percentage royalty to UAB based on our, and any of our affiliates' and sublicensees', net sales of UAB Licensed Products, if any, subject to a minimum annual royalty payment specified in the UAB Agreement. Our obligation to make royalty payments extends with respect to a UAB Licensed Product until the expiration of the last-to-expire valid claim of a patent licensed from UAB covering the UAB Licensed Product. The patents subject to the license under the UAB Agreement only have valid claims in the United States. The royalties are payable on a product-by-product basis.

The UAB Agreement obligates us to use commercially reasonable efforts to develop, manufacture, commercialize and market at least one UAB Licensed Product, in accordance with a development plan and a development milestone timetable specified in the UAB Agreement.

The UAB Agreement expires based upon the expiration of the last-to-expire valid claim of a patent licensed from UAB. We have the right to terminate the UAB Agreement for our convenience at any time on 90 days' prior written notice to UAB. UAB has the right to terminate the UAB Agreement if, amongst other reasons, we are in material default of the UAB Agreement and fail to cure such breach within specified cure periods or in the event we undergo certain bankruptcy events.

IMR-261 – Non-Exclusive License Agreement with University of Pittsburgh

In October 2020, we took assignment to an exclusive license agreement, or the Original Pittsburgh Agreement, originally entered into between University of Pittsburgh – Of the Commonwealth System of Higher Education, or University

of Pittsburgh, and Complexa, Inc. in August 2014. The Original Pittsburgh Agreement was terminated in its entirety in November 2020 and in May 2021, we and the University of Pittsburgh entered into a new license agreement, or the New Pittsburgh Agreement, to replace the Original Pittsburgh Agreement. The New Pittsburgh Agreement was amended in December 2021.

The New Pittsburgh Agreement grants us a non-exclusive worldwide license to make, have made, manufacture, research, develop, use, sell, offer for sale and commercialize certain products covered by certain patents within the field of hemoglobinopathies, red cell anemias and iron disorders. We call such products Pittsburgh Licensed Products. We have the right to grant sublicenses with certain restrictions, including obtaining the consent of Pittsburgh, which consent may not be unreasonably withheld.

As partial consideration New Pittsburgh Agreement, we made upfront payments aggregating to less than $0.1 million. We are obligated to make milestone payments to the University of Pittsburgh of up to approximately $0.3 million in the aggregate upon the achievement of specified clinical and commercial sale milestones by any Pittsburgh Licensed Product and to pay a low single-digit percentage royalty to the University of Pittsburgh based on our, and any of our affiliates' and sublicensees', net sales of Pittsburgh Licensed Product, if any, subject to a minimum annual royalty payment specified in the New Pittsburgh Agreement. Our obligation to make royalty payments extends with respect to a Pittsburgh Licensed Products until the expiration of the last-to-expire valid claim of a patent licensed from the University of Pittsburgh covering the Pittsburgh Licensed Product. The patents subject to the license under the New Pittsburgh Agreement only have valid claims in the United States.

The New Pittsburgh Agreement obligates us to use commercially reasonable efforts to develop and obtain FDA approval for Pittsburgh Licensed Products, in accordance with a development milestone timetable specified in the New Pittsburgh Agreement.

The New Pittsburgh Agreement expires upon the expiration of the last-to-expire valid claim of a patent licensed from the University of Pittsburgh. We have the right to terminate the New Pittsburgh Agreement for our convenience at any time on 90 days' prior written notice to the University of Pittsburgh. The University of Pittsburgh has the right to terminate the New Pittsburgh Agreement if, amongst other reasons, we default in the performance of any of our obligations under the New Pittsburgh Agreement and fail to cure such breach within specified cure periods or in the event we undergo certain bankruptcy events.

Competition

The biopharmaceutical industry is characterized by rapidly advancing technologies, intense competition and strong emphasis on proprietary products. While we believe that our technology, knowledge, experience and scientific resources provide us with competitive advantages, we face potential competition from many sources, including major pharmaceutical, specialty pharmaceutical and biotechnology companies, academic institutions and government agencies and public and private research institutions. Any product candidates that we successfully develop and commercialize will compete with existing therapies and new therapies that may become available in the future.

Our competitors may have significantly greater financial resources, established presence in the market, expertise in research and development, manufacturing, preclinical and clinical testing, obtaining regulatory approvals and reimbursement and marketing approved products than we do. These competitors may also compete with us in recruiting and retaining qualified scientific, sales, marketing and management personnel, and establishing clinical trial sites and patient registration for clinical trials. Smaller or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies.

If our lead product candidate tovinontrine is approved for the indications that we are currently targeting, it will likely compete with the currently marketed drugs and, if approved, the therapies in development discussed below.

Sickle Cell Disease

Approved drug treatments for SCD focus primarily on the management of anemia and reduction of VOCs. Until November 2019, there were only two drug treatments approved in the United States: HU and Endari; and only one approved drug treatment in the European Union: HU. HU, marketed under trade names including Droxia by Bristol-Myers Squibb Company, as well as in generic form, is approved for the treatment of anemia related to SCD, to reduce the frequency of

VOCs and the need for blood transfusions. Endari, marketed by Emmaus Life Sciences, Inc., is an oral powder form of L-glutamine approved to reduce severe complications associated with the disorder.

In November 2019, the FDA granted accelerated approval for Oxbryta (voxelotor) for the treatment of SCD in patients 12 years of age and older and its label was subsequently expanded to include patients four years of age and older. Oxbryta is an oral therapy taken once daily and is the first approved treatment that directly inhibits sickle hemoglobin polymerization. In February 2022, the European Commission approved Oxbryta for the treatment of hemolytic anemia in patients with SCD 12 years of age and older. In addition, in November 2019, the FDA approved Adakveo (crizanlizumab), to reduce the frequency of VOCs in adult and pediatric patients aged 16 years and older with SCD. Adakveo received conditional approval in the European Union in October 2020 for the prevention of recurrent VOCs in SCD patients aged 16 years and older. Adakveo is administered intravenously and binds to P-selectin, which is a cell adhesion protein that plays a central role in the multicellular interactions that can lead to vaso-occlusion.

Blood transfusions are also used to treat SCD and can transiently bolster hemoglobin levels by adding functional RBCs. There are a number of limitations associated with this therapeutic approach, including limited patient access and serious complications such as iron overload. The only potentially curative treatment currently approved for severe SCD is HSCT. However, this treatment option is not commonly used given the difficulties of finding a suitable matched donor and the risks associated with the treatment, which include an approximately 5% mortality rate. HSCT is more commonly offered to pediatric patients with available sibling-matched donors.

Tovinontrine could face competition from a number of different therapeutic approaches in development for patients with SCD. For example, there are a number of companies in clinical development for gene editing/therapy treatments, including bluebird, Aruvant, CRISPR (in collaboration with Vertex), Sangamo Therapeutics, Inc. (in collaboration with Sanofi), Intellia Therapeutics, Inc. (in collaboration with Novartis), Graphite Bio, Inc. and Editas Medicine, Inc. There are also several companies advancing therapeutic approaches outside of gene editing/therapy, including GBT, Agios, Forma, Vifor, Novo Nordisk (in collaboration with EpiDestiny), Fulcrum, CSL Ltd. and Pfizer.

ß-thalassemia

Until November 2019, there were no approved drug therapies for ß-thalassemia in the United States. The current standard of care for many patients with ß-thalassemia has been frequent blood transfusions to manage anemia. A potentially curative therapy for ß-thalassemia is HSCT, which is associated with serious risk and is limited to patients with a suitable donor.

In November 2019, the FDA approved Reblozyl for the treatment of anemia in adult patients with ß-thalassemia who require regular RBC transfusions. Reblozyl was approved by the European Commission in June 2020 to treat adult patients with transfusion-dependent anemia associated with ß-thalassemia. Reblozyl is a modified receptor protein that promotes RBC maturation and increases overall RBC production, but does not address other cell types implicated in ß-thalassemia. Reblozyl is not indicated for use as a substitute for RBC transfusions in patients who require immediate correction of anemia. Reblozyl is dosed subcutaneously and is administered every three weeks in an outpatient setting.

In June 2019, the European Commission granted conditional marketing authorization for Zynteglo, a gene therapy developed by bluebird bio for the treatment of adult and adolescent patients with transfusion-dependent ß-thalassemia and with certain genotypes. Bluebird bio submitted its rolling BLA to the FDA which it has announced that it plans to complete in 2021.

Tovinontrine could face competition from a number of different therapeutic approaches that are in development as a therapeutic option for patients with TDT or NTDT ß-thalassemia. For example, there are a number of companies in clinical development for gene editing/therapy treatments, including bluebird, CRISPR (in collaboration with Vertex) and Ionis Pharmaceuticals. There are also several companies advancing therapeutic approaches outside of gene editing/therapy, including Agios, Forma, Silence Therapeutics and Vifor.

HFpEF

In the area of HFpEF, tovinontrine could face competition from Entresto (marketed by Novartis) and Jardiance (marketed by Eli Lilly & Co.) which are currently the only FDA-approved therapies for HFpEF. We are also aware of several drugs approved for other indications that are likely to seek near-term marketing approval for the treatment of HFpEF including Farxiga (Astra Zeneca, PLC), Invokana (Johnson & Johnson) and Zynquista (Lexicon Pharmaceuticals, Inc). In

addition, Bristol-Myers Squibb Co., Cytokinetics, Inc., Acceleron Pharma, Inc., Palatin Technologies, Inc., Cardurion Pharmaceuticals, Inc. and TransThera Biosciences Co., Ltd., among potentially other companies, are also developing therapeutic approaches for patients with HFpEF.

Intellectual Property

We strive to protect and enhance the proprietary technology, inventions and improvements that are commercially important to the development of our business, including by seeking, maintaining and defending patent rights, whether developed internally or licensed from third parties. We also rely on trade secrets, know-how, continuing technological innovation and in-licensing opportunities to develop, strengthen and maintain our proprietary position in our field.

Our future commercial success depends, in part, on our ability to: obtain and maintain patent and other proprietary protection for commercially important technology, inventions and know-how related to our business; defend and enforce in our intellectual property rights, in particular our patent rights; preserve the confidentiality of our trade secrets; and operate without infringing, misappropriating or violating the valid and enforceable patents and proprietary rights of third parties. Our ability to stop third parties from making, using, selling, offering to sell or importing any products we develop may depend on the extent to which we have rights under valid and enforceable patents or trade secrets that cover these activities.

The patent positions of biopharmaceutical companies like ours are generally uncertain and can involve complex legal, scientific and factual issues. We cannot predict whether the patent applications we are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient proprietary protection from competitors. We also cannot ensure that patents will issue with respect to any patent applications that we or our licensors may file in the future, nor can we ensure that any of our owned or licensed patents or future patents will be commercially useful in protecting our product candidates and methods of manufacturing the same. In addition, the coverage claimed in a patent application may be significantly reduced before a patent is issued, and its scope can be reinterpreted and even challenged after issuance. As a result, we cannot guarantee that any products we develop will be protected or remain protectable by enforceable patents. Moreover, any patents that we hold may be challenged, circumvented or invalidated by third parties. See “Risk Factors—Risks Related to Our Intellectual Property” for a more comprehensive description of risks related to our intellectual property.

We generally file patent applications directed to our key programs in an effort to secure our intellectual property positions vis-a-vis these programs. The intellectual property portfolio for tovinontrine and IMR-261, is summarized below. Prosecution is a lengthy process, during which the scope of the claims initially submitted for examination by the U.S. Patent and Trademark Office may be significantly narrowed before issuance, if issued at all. We expect this may be the case with respect to some of our pending patent applications referred to below.

Tovinontrine (IMR-687)

The patent portfolio for our tovinontrine program includes at least six published patent families. As of December 31, 2021, we owned, co-owned, or held exclusive license rights to numerous patent and patent applications, including at least six issued or allowed U.S. patents, nine U.S. pending non-provisional patent applications, 82 issued or allowed non-U.S. patents, including five European patent applications which have been validated among individual European Patent Convention nations, 95 non-U.S. pending patent applications, and four pending Patent Cooperation Treaty, or PCT, applications relating to our tovinontrine program. These patents and patent applications comprise the following patent families:

The issued patents include coverage of the tovinontrine composition of matter. The issued patents include US 9,643,970 (exclusively licensed to us from Lundbeck A/S), which issued May 2017. This U.S. patent and related international family members are directed to the tovinontrine composition of matter, including racemic mixtures. The expected expiry date of US 9,643,970, including 63 days of Patent Term Adjustment, based on a 20-year term, is December 2032, absent any other patent term extensions available.

The issued patents also include US 9,434,733 (exclusively licensed to us from Lundbeck A/S), which issued September 2016. This U.S. patent and related international family members are directed to the alternative PDE9 inhibitor compositions of matter, including racemic mixtures. The expected expiry date, based on a 20-year term is January 2033, absent any patent term extensions available.

The issued patents also include US 10,513,524 (exclusively licensed to us from Lundbeck A/S), which issued December 2019. This U.S. patent and related international family members provide further protection for the tovinontrine

composition of matter, including the enantiomer, in addition to coverage of therapeutic methods of treating sickle cell disease with tovinontrine . The expected expiry date, based on a 20-year term, is July 2036, absent any patent term extensions available.

The pending applications include an additional patent family directed to therapeutic methods with a priority filing date of July 2016. A patent in Morocco has been allowed in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is June 2037, absent any patent term extensions available.

The pending applications also include a patent family directed to process chemistry for manufacturing with a priority date of May 2017. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2038, absent any patent term extensions available.

The PCT applications include a patent family directed to polymorphs of tovinontrine with a priority filing date of May 2018. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2039, absent any patent term extensions available.

The pending PCT applications also include a PCT application directed to solid dose formulations of tovinontrine with a priority filing date of August 2018. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is August 2039, absent any patent term extensions available.

The pending PCT applications also include a PCT application directed to liquid solution formulations of tovinontrine with a priority filing date of April 2019. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is April 2040, absent any patent term extensions available.

The pending PCT applications also include a PCT application directed to therapeutic methods of treating thalassemia with a priority date of May 2019. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2040, absent any patent term extensions available.

While we believe that the specific and generic claims contained in our owned and licensed pending U.S., non-U.S., and PCT applications provide protection for the claimed pharmaceutical compositions and methods of use, third parties may nevertheless challenge such claims.

IMR-261

The patent portfolio for our IMR-261 program includes at least four published patent families. As of December 31, 2021, we owned, co-owned, or held exclusive license rights to numerous patent and patent applications, including at least seven issued or allowed U.S. patents, one U.S. pending non-provisional patent applications, 20 non-U.S. pending patent applications, and two pending PCT application relating to our IMR-261 program. These patents and patent applications comprise the following patent families:

The issued patents include coverage of the IMR-261 composition of matter. The issued patents include US 8,309,526 (exclusively licensed to us from UAB), which issued November 13, 2012. The expected expiry date of US 8,309,526, based on a 20-year term, is April 2025, absent any other patent term extensions available.

The issued patents also include four patents (US 7,776,916, US 9,522,156, US 9,006,473 and 9,867,795, each exclusively licensed to us from UAB), which issued between August 17, 2010 and January 16, 2018. These U.S. patents provide coverage of therapeutic methods of treating certain inflammatory and vascular diseases, including sickle cell disease, with IMR-261. The expected expiry date of these patents, based on a 20-year term, ranges between April 2025 and March 2027, absent any patent term extensions available.

The pending applications include a patent family directed to therapeutic methods of treating certain diseases, including sickle cell disease, at specified doses, with a priority date of October 2015. No patents covering therapeutic methods of treating sickle cell disease have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is October 2036, absent any patent term extensions available.

The PCT applications include a patent family directed to therapeutic methods of treating certain diseases, including sickle cell disease, at additional specified doses, with a priority filing date of May 2020. No patents have issued in this patent family, and the expected expiry date of this patent family, based on a 20-year term, is May 2041, absent any patent term extensions available.

In addition to the above, we have licensed on a non-exclusive basis from the University of Pittsburgh, rights to U.S. issued patents covering pharmaceutical compositions of nitro oleic acids, including IMR-261. The expected expiry date of these patents, based on a 20-year term, is in mid-2028, absent any other patent term extensions available.

The term of individual patents depends upon the legal term of the patents in the countries in which they are obtained. In most countries in which we file, the patent term is 20 years from the earliest date of filing a non-provisional patent application.

In the United States, the term of a patent covering an FDA-approved drug may, in certain cases, be eligible for a patent term extension under the Drug Price Competition and Patent Term Restoration Act of 1984 as compensation for the loss of patent term during the FDA regulatory review process. The period of extension may be up to five years, but cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval. Only one patent among those eligible for an extension and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and in certain other jurisdictions to extend the term of a patent that covers an approved drug. It is possible that issued U.S. patents covering tovinontrine may be entitled to patent term extensions. If our use of drug candidates or the drug candidate itself receive FDA approval, we intend to apply for patent term extensions, if available, to extend the term of patents that cover the approved use or drug candidate. We also intend to seek patent term extensions in any jurisdictions where available, however, there is no guarantee that the applicable authorities, including the FDA, will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions.

In addition to patent protection, we rely upon unpatented trade secrets and confidential know-how and continuing technological innovation to develop and maintain our competitive position. However, trade secrets and confidential know-how are difficult to protect. We seek to protect our proprietary information, in part, using confidentiality agreements with any collaborators, scientific advisors, employees and consultants and invention assignment agreements with our employees. We also have agreements requiring assignment of inventions with selected consultants, scientific advisors and collaborators. These agreements may not provide meaningful protection. These agreements may also be breached, and we may not have an adequate remedy for any such breach. In addition, our trade secrets and/or confidential know-how may become known or be independently developed by a third party, or misused by any collaborator to whom we disclose such information. Despite any measures taken to protect our intellectual property, unauthorized parties may attempt to copy aspects of our products or to obtain or use information that we regard as proprietary. Although we take steps to protect our proprietary information, third parties may independently develop the same or similar proprietary information or may otherwise gain access to our proprietary information. As a result, we may be unable to meaningfully protect our trade secrets and proprietary information. See “Risk Factors—Risks Related to Our Intellectual Property” for a more comprehensive description of risks related to our intellectual property.

Manufacturing

We currently contract with third parties for the manufacture of our product candidates for preclinical studies and clinical trials and intend to do so in the future. We do not own or operate manufacturing facilities for the production of clinical or commercial quantities of our product candidates. We currently have no plans to build our own clinical or commercial scale manufacturing capabilities. To date, our third-party manufacturers have met our manufacturing requirements. We expect third-party manufacturers to be capable of providing sufficient quantities of our program materials to meet anticipated clinical-trial scale demands. To meet our projected needs for commercial manufacturing, third parties with whom we currently work will need to increase their scale of production or we will need to secure alternate suppliers. We believe that there are alternate sources of supply that can satisfy our clinical and commercial requirements, although we cannot be certain that identifying and establishing relationships with such sources, if necessary, would not result in significant delay or material additional costs. Although we rely on contract manufacturers, we have personnel with manufacturing experience to oversee our relationships with contract manufacturers.

Sales and Marketing

In light of our stage of development, we have not yet established a commercial organization or distribution capabilities. We have retained worldwide commercial rights for our product candidates. If our product candidates receive marketing approval, we plan to commercialize them in the United States and Europe and potentially other international regions with our own sales force.

Government Regulation and Product Approvals

Government authorities in the United States at the federal, state and local level, and in other countries and jurisdictions, such as the European Union, or EU, extensively regulate, among other things, the research, development, testing, manufacture, pricing, quality control, approval, packaging, storage, recordkeeping, labeling, advertising, promotion, distribution, marketing, post-approval monitoring and reporting, and import and export of biopharmaceutical products. The processes for obtaining marketing approvals in the United States and in foreign countries and jurisdictions, along with compliance with applicable statutes and regulations and other regulatory authorities, require the expenditure of substantial time and financial resources.

Approval and Regulation of Drugs in the United States

In the United States, drug products are approved and regulated under the Federal Food, Drug and Cosmetic Act, or FDCA, and applicable implementing regulations and guidance. A company, institution or organization that takes responsibility for the initiation and management of a clinical development program for such products, and for their regulatory approval, is typically referred to as a sponsor. The failure of a sponsor to comply with the applicable regulatory requirements at any time during the product development process may result in delays to the conduct of a study, regulatory review and approval and/or administrative or judicial sanctions.

A sponsor seeking approval to market and distribute a new drug in the United States generally must satisfactorily complete each of the following steps before the product candidate will be approved by the FDA:

- preclinical testing including laboratory tests, animal studies and formulation studies, which must be performed in accordance with the FDA's good laboratory practice, or GLP, regulations and standards;
- design of a clinical protocol and submission to the FDA of an IND for human clinical testing, which must become effective before human clinical trials may begin;
- approval by an independent institutional review board, or IRB, representing each clinical site before each clinical trial may be initiated;
- performance of adequate and well-controlled human clinical trials to establish the safety, potency and purity of the product candidate for each proposed indication, in accordance with current good clinical practices, or GCP;
- preparation and submission to the FDA of a new drug application, or NDA, for a drug product which includes not only the results of the clinical trials, but also, detailed information on the chemistry, manufacture and quality controls for the product candidate and proposed labelling for one or more proposed indication(s);
- review of the product candidate by an FDA advisory committee, where appropriate or if applicable;
- satisfactory completion of an FDA inspection of the manufacturing facility or facilities, including those of third parties, at which the product candidate or components thereof are manufactured to assess compliance with current good manufacturing practices, or cGMP, requirements and to assure that the facilities, methods and controls are adequate to preserve the product's identity, strength, quality and purity;
- satisfactory completion of any FDA audits of the non-clinical and clinical trial sites to assure compliance with GCP and the integrity of clinical data in support of the NDA;
- payment of user fees and securing FDA approval of the NDA to allow marketing of the new drug product; and
- compliance with any post-approval requirements, including the potential requirement to implement a Risk Evaluation and Mitigation Strategy, or REMS, and the potential requirement to conduct any post-approval studies required by the FDA.

Preclinical Studies

Before a sponsor begins testing a product candidate with potential therapeutic value in humans, the product candidate enters the preclinical testing stage. Preclinical tests include laboratory evaluations of product chemistry, formulation and stability, as well as other studies to evaluate, among other things, the toxicity of the product candidate. The conduct of the preclinical tests and formulation of the compounds for testing must comply with federal regulations and requirements, including GLP regulations and standards and the United States Department of Agriculture's Animal Welfare Act, if applicable. Some long-term preclinical testing, such as animal tests of reproductive adverse events and carcinogenicity and long-term toxicity studies may continue after the IND is submitted.

The IND and IRB Processes

An IND is a request for FDA authorization to administer such investigational product to humans. Such authorization must be secured prior to interstate shipment and administration of any product candidate that is not the subject of an approved NDA. In support of a request for an IND, sponsors must submit a protocol for the clinical trial, and any subsequent protocol amendments must be submitted to the FDA as part of the IND application. In addition, the results of the preclinical tests, together with manufacturing information, analytical data, any available clinical data or literature and plans for clinical trials, among other things, must be submitted to the FDA as part of an IND. The FDA requires a 30-day waiting period after the filing of each IND before clinical trials may begin. This waiting period is designed to allow the FDA to review the IND to determine whether human research subjects will be exposed to unreasonable health risks. At any time during this 30- day period, the FDA may raise concerns or questions about the conduct of the trials as outlined in the IND and impose a clinical hold or partial clinical hold. In this case, the IND sponsor and the FDA must resolve any outstanding concerns before clinical trials can begin.

Following commencement of a clinical trial under an IND, the FDA may also place a clinical hold or partial clinical hold on that trial. A clinical hold is an order issued by the FDA to the sponsor to delay a proposed clinical investigation or to suspend an ongoing investigation. A partial clinical hold is a delay or suspension of only part of the clinical work requested under the IND. For example, a specific protocol or part of a protocol is not allowed to proceed, while other protocols may do so. No more than 30 days after imposition of a clinical hold or partial clinical hold, the FDA will provide the sponsor a written explanation of the basis for the hold. Following issuance of a clinical hold or partial clinical hold, an investigation may only resume after the FDA has so notified the sponsor that the investigation may proceed. The FDA will base that determination on information provided by the sponsor correcting the deficiencies previously cited or otherwise satisfying the FDA that the investigation can proceed.

A sponsor may choose, but is not required, to conduct a foreign clinical study under an IND. When a foreign clinical study is conducted under an IND, all FDA IND requirements must be met unless waived. When a foreign clinical study is not conducted under an IND, the sponsor must ensure that the study complies with certain regulatory requirements of the FDA in order to use the study as support for an IND or application for marketing approval. The FDA's regulations are intended to help ensure the protection of human subjects enrolled in non-IND foreign clinical studies, as well as the quality and integrity of the resulting data. They further help ensure that non-IND foreign studies are conducted in a manner comparable to that required for IND studies.

In addition to the foregoing IND requirements, an IRB representing each institution participating in the clinical trial must review and approve the plan for any clinical trial before it commences at that institution, and the IRB must conduct continuing review and reapprove the study at least annually. The IRB must review and approve, among other things, the study protocol and informed consent information to be provided to study subjects. An IRB must operate in compliance with FDA regulations. An IRB can suspend or terminate approval of a clinical trial at its institution, or an institution it represents, if the clinical trial is not being conducted in accordance with the IRB's requirements or if the product candidate has been associated with unexpected serious harm to patients.

Additionally, some trials are overseen by an independent group of qualified experts organized by the trial sponsor, known as a data safety monitoring board or committee, or DSMB. This group provides a recommendation as to whether or not a trial may move forward at designated check points based on access that only the group maintains to available data from the study. Suspension or termination of development during any phase of clinical trials can occur if it is determined that the participants or patients are being exposed to an unacceptable health risk. Other reasons for suspension or termination may be made by us based on evolving business objectives and/or the competitive climate.

Expanded Access to an Investigational Drug for Treatment Use

Expanded access, sometimes called "compassionate use," is the use of investigational new drug products outside of clinical trials to treat patients with serious or immediately life-threatening diseases or conditions when there are no comparable or satisfactory alternative treatment options. The rules and regulations related to expanded access are intended to improve access to investigational drugs for patients who may benefit from investigational therapies. FDA regulations allow access to investigational drugs under an IND by the company or the treating physician for treatment purposes on a case-by-case basis for: individual patients (single-patient IND applications for treatment in emergency settings and non-emergency settings); intermediate-size patient populations; and larger populations for use of the drug under a treatment protocol or Treatment IND Application.

When considering an IND application for expanded access to an investigational product with the purpose of treating a patient or a group of patients, the sponsor and treating physicians or investigators will determine suitability when all of the following criteria apply: patient(s) have a serious or immediately life-threatening disease or condition, and there is no comparable or satisfactory alternative therapy to diagnose, monitor, or treat the disease or condition; the potential patient benefit justifies the potential risks of the treatment and the potential risks are not unreasonable in the context or condition to be treated; and the expanded use of the investigational drug for the requested treatment will not interfere with the initiation, conduct, or completion of clinical investigations that could support marketing approval of the product or otherwise compromise the potential development of the product. Sponsors of one or more investigational drugs for the treatment of a serious disease(s) or condition(s) must make publicly available their policy for evaluating and responding to requests for expanded access for individual patients.

There is no obligation for a sponsor to make its drug products available for expanded access; however, as required by the 21st Century Cures Act, or Cures Act, passed in 2016, if a sponsor has a policy regarding how it responds to expanded access requests, it must make that policy publicly available. Sponsors are required to make such policies publicly available upon the earlier of initiation of a Phase 2 or Phase 3 trial; or 15 days after the investigational drug or biologic receives designation as a breakthrough therapy, fast-track product, or regenerative medicine advanced therapy.

In addition, on May 30, 2018, the Right to Try Act, was signed into law. The law, among other things, provides a federal framework for certain patients to access certain investigational new drug products that have completed a Phase I clinical trial and that are undergoing investigation for FDA approval. Under certain circumstances, eligible patients can seek treatment without enrolling in clinical trials and without obtaining FDA permission under the FDA expanded access program. There is no obligation for a drug manufacturer to make its drug products available to eligible patients as a result of the Right to Try Act, but the manufacturer must develop an internal policy and respond to patient requests according to that policy.

Human Clinical Trials in Support of an NDA

Clinical trials involve the administration of the investigational product candidate to human subjects under the supervision of a qualified investigator in accordance with GCP requirements, which include, among other things, the requirement that all research subjects provide their informed consent in writing before their participation in any clinical trial. Clinical trials are conducted under written clinical trial protocols detailing, among other things, the objectives of the study, inclusion and exclusion criteria, the parameters to be used in monitoring safety and the effectiveness criteria to be evaluated.

Human clinical trials are typically conducted in three sequential phases, but the phases may overlap or be combined. Additional studies may also be required after approval.

Phase 1 clinical trials are initially conducted in a limited population to test the product candidate for safety, including adverse effects, dose tolerance, absorption, metabolism, distribution, excretion and pharmacodynamics in healthy humans or in patients. During Phase 1 clinical trials, information about the investigational drug product's pharmacokinetics and pharmacological effects may be obtained to permit the design of well-controlled and scientifically valid Phase 2 clinical trials.

Phase 2 clinical trials are generally conducted in a limited patient population to identify possible adverse effects and safety risks, evaluate the efficacy of the product candidate for specific targeted indications and determine dose tolerance and optimal dosage and dosage schedule. Multiple Phase 2 clinical trials may be conducted by the sponsor to obtain information prior to beginning larger and more costly Phase 3 clinical trials. Phase 2 clinical trials are well controlled, closely monitored and conducted in a limited patient population.

Phase 3 clinical trials proceed if the Phase 2 clinical trials demonstrate that a dose range of the product candidate is potentially effective and has an acceptable safety profile. Phase 3 clinical trials are undertaken within an expanded patient population to further evaluate dosage, provide substantial evidence of clinical efficacy and further test for safety in an expanded and diverse patient population at multiple, geographically dispersed clinical trial sites. A well-controlled, statistically robust Phase 3 clinical trial may be designed to deliver the data that regulatory authorities will use to decide whether or not to approve, and, if approved, how to appropriately label a drug. Such Phase 3 studies are referred to as "pivotal."

In some cases, the FDA may approve an NDA for a product candidate but require the sponsor to conduct additional clinical trials to further assess the product candidate's safety and effectiveness after approval. Such post-approval trials are typically referred to as Phase 4 clinical trials and are conducted either as post-marketing commitments or post-marketing requirements. These studies are used to gain additional experience from the treatment of a larger number of patients in the intended treatment group and to confirm a clinical benefit in the case of drugs approved under accelerated approval regulations. Failure to exhibit due diligence with regard to fulfilling post-marketing commitments or post-marketing requirements could result in withdrawal of approval for products.

A clinical trial may combine the elements of more than one phase and the FDA often requires more than one Phase 3 trial to support marketing approval of a product candidate. A company's designation of a clinical trial as being of a particular phase is not necessarily indicative that the trial will be sufficient to satisfy the FDA requirements of that phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. Generally, pivotal trials are Phase 3 trials, but they may be Phase 2 trials if the design provides a well-controlled and reliable assessment of clinical benefit, particularly in an area of unmet medical need.

Progress reports detailing the status and a brief description of available results of the clinical trials must be submitted at least annually to the FDA. In addition, IND safety reports must be submitted to the FDA for any of the following: serious and unexpected suspected adverse reactions; findings from other studies or animal or *in vitro* testing that suggest a significant risk in humans exposed to the product; and any clinically important increase in the case of a serious suspected adverse reaction over that listed in the protocol or investigator brochure. The FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the clinical data submitted.

Finally, sponsors of clinical trials are required to register and disclose certain clinical trial information on a public registry (clinicaltrials.gov) maintained by the U.S. National Institutes of Health, or NIH. In particular, information related to the product, patient population, phase of investigation, study sites and investigators and other aspects of the clinical trial is made public as part of the registration of the clinical trial. Both the NIH and the FDA have recently signaled the government's willingness to begin enforcing those requirements against non-compliant clinical trial sponsors. The failure to submit clinical trial information to clinicaltrials.gov, as required, is a prohibited act under the FDCA with violations subject to potential civil monetary penalties of up to $10,000 for each day the violation continues.

Concurrent with clinical trials, companies often complete additional animal studies and they must also develop additional information about the chemistry and physical characteristics of the investigational drug as well as finalize a process for manufacturing the product in commercial quantities in accordance with cGMP requirements. The manufacturing process must be capable of consistently producing quality batches of the product candidate and, among other things, must develop methods for testing the identity, strength, quality, purity, and potency of the final drug. Additionally, appropriate packaging must be selected and tested and stability studies must be conducted to demonstrate that the product candidate does not undergo unacceptable deterioration over its shelf life.

Pediatric Studies

Under the Pediatric Research Equity Act of 2003, or PREA, an NDA or supplement thereto must contain data that are adequate to assess the safety and effectiveness of the product for the claimed indications in all relevant pediatric subpopulations and to support dosing and administration for each pediatric subpopulation for which the product is safe and effective. Sponsors must also submit pediatric study plans prior to the assessment data. Those plans must contain an outline of the proposed pediatric study or studies the sponsor plans to conduct, including study objectives and design, any deferral or waiver requests and other information required by regulation. The sponsor, the FDA, and the FDA's internal review committee must then review the information submitted, consult with each other and agree upon a final plan. The FDA or the sponsor may request an amendment to the plan at any time.

For drugs intended to treat a serious or life-threatening disease or condition, the FDA must, upon the request of a sponsor, meet to discuss preparation of the initial pediatric study plan or to discuss deferral or waiver of pediatric assessments. In addition, the FDA will meet early in the development process to discuss pediatric study plans with sponsors,

and the FDA must meet with sponsors by no later than the end-of-phase 1 meeting for serious or life-threatening diseases and by no later than ninety (90) days after the FDA's receipt of the study plan.

The FDA may, on its own initiative or at the request of the sponsor, grant deferrals for submission of some or all pediatric data until after approval of the product for use in adults, or full or partial waivers from the pediatric data requirements. A deferral may be granted for several reasons, including a finding that the product or therapeutic candidate is ready for approval for use in adults before pediatric trials are complete. Unless otherwise required by regulation, the pediatric data requirements do not apply to products with orphan designation, although the FDA has recently taken steps to limit what it considers abuse of this statutory exemption in the PREA.

Rare Pediatric Disease Priority Review Voucher Program

With enactment of the Food and Drug Administration Safety and Innovation Act in 2012, and subsequent passage of the Advancing Hope Act of 2016, Congress authorized the FDA to award priority review vouchers to sponsors of certain rare pediatric disease product applications that meet the criteria specified in the law. This provision is designed to encourage development of new drug and biological products for prevention and treatment of certain rare pediatric diseases. Specifically, under this program, a sponsor who receives an approval for a drug or biologic for a "rare pediatric disease" may qualify for a voucher that can be redeemed to receive a priority review of a subsequent marketing application for a different product. The sponsor of a rare pediatric disease drug product receiving a priority review voucher may transfer (including by sale) the voucher to another sponsor. The voucher may be further transferred any number of times before the voucher is used, as long as the sponsor making the transfer has not yet submitted the application.

For the purposes of this program, a "rare pediatric disease" is a (a) serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years, including age groups often called neonates, infants, children, and adolescents; and (b) rare disease or conditions within the meaning of the Orphan Drug Act. A sponsor may choose to request rare pediatric disease designation, but the designation process is entirely voluntary; requesting designation is not a prerequisite to requesting or receiving a priority review voucher. In addition, sponsors who choose not to submit a rare pediatric disease designation request may nonetheless receive a priority review voucher if they request such a voucher in their original marketing application and meet all of the eligibility criteria.

In December 2016, the Cures Act extended the Rare Pediatric Disease Priority Review Voucher Program, authorizing the FDA to award vouchers through September 30, 2022, limited to drugs with rare pediatric disease designation granted by September 30, 2020. On September 30, 2020, Congress provided a short-term extension of the Priority Review Voucher Program. On December 27, 2020, the Rare Pediatric Disease Priority Review Voucher Program was further extended. Under the current statutory sunset provisions, after September 30, 2024, the FDA may only award a voucher for an approved rare pediatric disease product application if the sponsor has rare pediatric disease designation for the drug, and that designation was granted by September 30, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease priority review vouchers.

Submission and Filing of an NDA

In order to obtain approval to market a drug product in the United States, a marketing application must be submitted to the FDA that provides sufficient data establishing the safety, purity and potency of the proposed drug product for its intended indication. The application includes all relevant data available from pertinent preclinical and clinical trials, together with detailed information relating to the product's chemistry, manufacturing, controls and proposed labeling, among other things. Data can come from company-sponsored clinical trials intended to test the safety and effectiveness of a use of a product, or from a number of alternative sources, including studies initiated by independent investigators. To support marketing approval, the data submitted must be sufficient in quality and quantity to establish the safety, purity and potency of the drug product to the satisfaction of the FDA.

The NDA is a vehicle through which sponsors formally propose that the FDA approve a new product for marketing and sale in the United States for one or more indications. Every new drug product candidate must be the subject of an approved NDA before it may be commercialized in the United States. Under federal law, the submission of most NDAs is subject to an application user fee, which for federal fiscal year 2022 is $3,117,218 for an application requiring clinical data. The sponsor of an approved NDA is also subject to an annual program fee, which for federal fiscal year 2022 is $369,413. Certain exceptions and waivers are available for some of these fees, such as an exception from the application fee for products with orphan designation and a waiver for certain small businesses.

Following submission of an NDA, the FDA conducts a preliminary review of the application within 60 days of receipt and must inform the sponsor at that time or before whether an application is sufficiently complete to permit substantive review. If the FDA determines that the application is incomplete, it will issue a Refuse to File, or RFT, letter and may request additional information and studies. In this event, the application must be resubmitted with the additional information and is subject to review before the FDA accepts it for filing.

Once the submission is accepted for filing, the FDA begins an in-depth substantive review. The FDA has agreed to specified performance goals in the review process of NDAs but the review process and the Prescription Drug User Fee Act, or PDUFA, goal date may be extended by the FDA for three additional months to consider new information or clarification provided by the sponsor to address an outstanding deficiency identified by the FDA following the original submission. Under that agreement, 90% of applications seeking approval of New Molecular Entities, or NMEs, are meant to be reviewed within 10 months from the date on which the FDA accepts the application for filing, and 90% of applications for NMEs that have been designated for "priority review" are meant to be reviewed within six months of the filing date.

In connection with its review of an application, the FDA typically will inspect the facility or facilities where the product is or will be manufactured. These pre-approval inspections may cover all facilities associated with an NDA submission, including component manufacturing, finished product manufacturing and control testing laboratories. The FDA will not approve an application unless it determines that the manufacturing processes and facilities are in compliance with cGMP requirements and adequate to assure consistent production of the product within required specifications. Additionally, before approving an NDA, the FDA will typically inspect one or more clinical sites to assure compliance with GCP and the integrity of the data supporting the application.

In addition, as a condition of approval, the FDA may require a sponsor to develop a REMS. A REMS uses risk-minimization strategies beyond the professional labeling to ensure that the benefits of the product outweigh the potential risks. To determine whether a REMS is needed, the FDA will consider the size of the population likely to use the product, the seriousness of the disease, the expected benefit of the product, the expected duration of treatment, the seriousness of known or potential adverse events and whether the product is a new molecular entity.

The FDA may refer an application for a novel product to an advisory committee or explain why such referral was not made. Typically, an advisory committee is a panel of independent experts, including clinicians and other scientific experts, that reviews, evaluates and provides a recommendation as to whether the application should be approved and under what conditions. The FDA is not bound by the recommendations of an advisory committee, but it considers such recommendations carefully when making decisions.

Fast Track, Breakthrough Therapy, Priority Review and Regenerative Advanced Therapy Designations

The FDA is authorized to designate certain products for expedited review if they are intended to address an unmet medical need in the treatment of a serious or life-threatening disease or condition. These programs are referred to as Fast Track designation, Breakthrough Therapy designation, Priority Review designation and Regenerative Advanced Therapy designation. None of these expedited programs change the standards for approval but they may help expedite the development or approval process of product candidates.

Specifically, the FDA may designate a new product for Fast Track review if it is intended for the treatment of a serious or life-threatening disease or condition and it demonstrates the potential to address unmet medical needs for such a disease or condition. For Fast Track products, sponsors may have greater interaction with the FDA, and the FDA may initiate review of sections of a Fast Track product's NDA before the application is complete. This rolling review may be available if the FDA determines, after preliminary evaluation of clinical data submitted by the sponsor, that a Fast Track product may be effective. The sponsor must also provide, and the FDA must approve, a schedule for the submission of the remaining information, and the sponsor must pay applicable user fees. However, the FDA's time-period goal for reviewing a Fast Track application does not begin until the last section of the application is submitted. In addition, the Fast Track designation may be withdrawn by the FDA if the FDA believes that the designation is no longer supported by data emerging in the clinical trial process.

Second, a new product may be designated as a Breakthrough Therapy if it is intended to treat a serious or life-threatening disease or condition and preliminary clinical evidence indicates that the product may demonstrate substantial improvement over available therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. The FDA may take certain actions with respect to Breakthrough Therapies, including holding meetings with the sponsor throughout the development process; providing timely advice to the product sponsor

regarding development and approval; involving more senior staff in the review process; assigning a cross-disciplinary project lead for the review team and taking other steps to design the clinical trials in an efficient manner.

Third, the FDA may designate a product for Priority Review if it treats a serious condition and, if approved, would provide a significant improvement in safety or effectiveness. The FDA determines, on a case-by-case basis, whether the proposed product represents a significant improvement when compared with other available therapies. Significant improvement may be illustrated by evidence of increased effectiveness in the treatment of a condition, elimination or substantial reduction of a treatment-limiting product reaction, documented enhancement of patient compliance that may lead to improvement in serious outcomes, and evidence of safety and effectiveness in a new subpopulation. A Priority Review designation is intended to direct overall attention and resources to the evaluation of such applications and to shorten the FDA's goal for taking action on a marketing application from ten months to six months.

With passage of the Cures Act in December 2016, Congress authorized the FDA to accelerate review and approval of products designated as Regenerative Advanced Therapies. A product is eligible for this designation if it is a regenerative medicine therapy that is intended to treat, modify, reverse or cure a serious or life-threatening disease or condition and if preliminary clinical evidence indicates that the product has the potential to address unmet medical needs for such disease or condition. The benefits of a Regenerative Advanced Therapy designation include early interactions with the FDA to expedite development and review, benefits available to breakthrough therapies, potential eligibility for Priority Review and accelerated approval based on surrogate or intermediate endpoints.

Accelerated Approval Pathway

The FDA may grant accelerated approval to a product for a serious or life-threatening condition that provides meaningful therapeutic advantage to patients over existing treatments based upon a determination that the product has an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit. The FDA may also grant accelerated approval for such a condition when the product has an effect on an intermediate clinical endpoint that can be measured earlier than an effect on irreversible morbidity or mortality, or IMM, and that is reasonably likely to predict an effect on IMM or other clinical benefit, taking into account the severity, rarity or prevalence of the condition and the availability or lack of alternative treatments. Products granted accelerated approval must meet the same statutory standards for safety and effectiveness as those granted traditional approval.

For the purposes of accelerated approval, a surrogate endpoint is a marker, such as a laboratory measurement, radiographic image, physical sign or other measure that is thought to predict clinical benefit but is not itself a measure of clinical benefit. Surrogate endpoints can often be measured more easily or more rapidly than clinical endpoints. An intermediate clinical endpoint is a measurement of a therapeutic effect that is considered reasonably likely to predict the clinical benefit of a drug, such as an effect on IMM. The FDA has limited experience with accelerated approvals based on intermediate clinical endpoints but has indicated that such endpoints generally may support accelerated approval where the therapeutic effect measured by the endpoint is not itself a clinical benefit and basis for traditional approval, if there is a basis for concluding that the therapeutic effect is reasonably likely to predict the ultimate clinical benefit of a product.

The accelerated approval pathway is most often used in settings in which the course of a disease is long and an extended period of time is required to measure the intended clinical benefit of a product, even if the effect on the surrogate or intermediate clinical endpoint occurs rapidly. Thus, accelerated approval has been used extensively in the development and approval of products for treatment of a variety of cancers in which the goal of therapy is generally to improve survival or decrease morbidity and the duration of the typical disease course requires lengthy and sometimes large trials to demonstrate a clinical or survival benefit. Thus the benefit of accelerated approval derives from the potential to receive approval based on surrogate endpoints sooner than possible for trials with clinical or survival endpoints, rather than deriving from any explicit shortening of the FDA approval timeline, as is the case with priority review.

The accelerated approval pathway is usually contingent on a sponsor's agreement to conduct, in a diligent manner, additional post-approval confirmatory studies to verify and describe the product's clinical benefit. As a result, a product candidate approved on this basis is subject to rigorous post-marketing compliance requirements, including the completion of Phase 4 or post-approval clinical trials to confirm the effect on the clinical endpoint. Failure to conduct required post-approval studies, or to confirm a clinical benefit during post-marketing studies, would allow the FDA to initiate expedited proceedings to withdraw approval of the product. All promotional materials for product candidates approved under accelerated regulations are subject to prior review by the FDA.

The FDA's Decision on an NDA

After evaluating the application and all related information, including the advisory committee recommendations, if any, and inspection reports of manufacturing facilities and clinical trial sites, the FDA will issue either a Complete Response Letter, or CRL, or an approval letter. To reach this determination, the FDA must determine that there is substantial evidence that the drug product is effective and that its expected benefits outweigh its potential risks to patients. This "benefit-risk" assessment is informed by the extensive body of evidence about the product's safety and efficacy in the NDA.

A CRL generally outlines the deficiencies in the submission and may require substantial additional testing or information in order for the FDA to reconsider the application. If and when those deficiencies have been addressed to the FDA's satisfaction in a resubmission of the NDA, the FDA will issue an approval letter. The FDA has committed to reviewing such resubmissions in two or six months depending on the type of information included. Even with submission of this additional information, the FDA ultimately may decide that the application does not satisfy the regulatory criteria for approval. If a CRL is issued, the sponsor will have one year to respond to the deficiencies identified by the FDA, at which time the FDA can deem the application withdrawn or, in its discretion, grant the sponsor an additional six month extension to respond.

An approval letter authorizes commercial marketing of the product with specific prescribing information for specific indications. It may limit the approved indications for use of the product. The agency may also require testing and surveillance programs to monitor the product after commercialization, or impose other conditions, including distribution restrictions or other risk management mechanisms, including a REMS, to help ensure that the benefits of the product outweigh the potential risks. REMS can include medication guides, communication plans for health care professionals, and elements to assure safe use, or ETASU. ETASU can include, but are not limited to, special training or certification for prescribing or dispensing, dispensing only under certain circumstances, special monitoring and the use of patent registries. The FDA may prevent or limit further marketing of a product based on the results of post-market studies or surveillance programs. After approval, many types of changes to the approved product, such as adding new indications, changes and additional labeling claims, are subject to further testing requirements and FDA review and approval.

Post-Approval Regulation

If regulatory approval for marketing of a product or new indication for an existing product is obtained, the sponsor will be required to comply with all regular post-approval regulatory requirements as well as any post-approval requirements that the FDA may have imposed as part of the approval process. The sponsor will be required to report, among other things, certain adverse reactions and manufacturing problems to the FDA, provide updated safety and efficacy information and comply with requirements concerning advertising and promotional labeling requirements. Manufacturers and certain of their subcontractors are required to register their establishments with the FDA and certain state agencies and are subject to periodic unannounced inspections by the FDA and certain state agencies for compliance with ongoing regulatory requirements, including cGMP regulations, which impose certain procedural and documentation requirements upon manufacturers.

A product may also be subject to official lot release, meaning that the manufacturer is required to perform certain tests on each lot of the product before it is released for distribution. If the product is subject to official release, the manufacturer must submit to the FDA samples of each lot, together with a release protocol showing a summary of the history of manufacture of the lot and the results of all of the manufacturer's tests performed on the lot. The FDA may also perform certain confirmatory tests on lots of some products before releasing the lots for distribution. Finally, the FDA will conduct laboratory research related to the safety, purity, potency and effectiveness of pharmaceutical products.

Once an approval is granted, the FDA may withdraw the approval if compliance with regulatory requirements is not maintained or if problems occur after the product reaches the market. Later discovery of previously unknown problems with a product, including adverse events of unanticipated severity or frequency, or with manufacturing processes, or failure to comply with regulatory requirements, may result in revisions to the approved labeling to add new safety information; imposition of post-market studies or clinical trials to assess safety risks; or imposition of distribution or other restrictions under a REMS program. Other potential consequences include, among other things:

- restrictions on the marketing or manufacturing of the product, complete withdrawal of the product from the market or product recalls;
- fines, warning letters or holds on post-approval clinical trials;
- refusal of the FDA to approve pending applications or supplements to approved applications, or suspension or revocation of product license approvals;

- product seizure or detention, or refusal to permit the import or export of products; or
- injunctions or the imposition of civil or criminal penalties.

The FDA strictly regulates the marketing, labeling, advertising and promotion of prescription drug products placed on the market. This regulation includes, among other things, standards and regulations for direct-to-consumer advertising, communications regarding unapproved uses, industry-sponsored scientific and educational activities, and promotional activities involving the Internet and social media. Promotional claims about a drug's safety or effectiveness are prohibited before the drug is approved. After approval, a drug product generally may not be promoted for uses that are not approved by the FDA, as reflected in the product's prescribing information. In the United States, health care professionals are generally permitted to prescribe drugs for such uses not described in the drug's labeling, known as off-label uses, because the FDA does not regulate the practice of medicine. However, FDA regulations impose rigorous restrictions on manufacturers' communications, prohibiting the promotion of off-label uses. It may be permissible, under very specific, narrow conditions, for a manufacturer to engage in nonpromotional, non-misleading communication regarding off-label information, such as distributing scientific or medical journal information as part of bona fide scientific exchange. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product.

If a company is found to have promoted off-label uses, it may become subject to adverse public relations and administrative and judicial enforcement by the FDA, the Department of Justice, or the Office of the Inspector General of the Department of Health and Human Services, or HHS, as well as state authorities. This could subject a company to a range of penalties that could have a significant commercial impact, including civil and criminal fines and agreements that materially restrict the manner in which a company promotes or distributes drug products. The federal government has levied large civil and criminal fines against companies for alleged improper promotion, and has also requested that companies enter into consent decrees or permanent injunctions under which specified promotional conduct is changed or curtailed.

Pediatric Exclusivity

The Best Pharmaceuticals for Children Act provides an incentive of additional marketing exclusivity in the United States to sponsors who voluntarily complete certain pediatric clinical studies. If granted, pediatric exclusivity provides for the attachment of an additional six months of regulatory exclusivity to the term of any patent or existing regulatory exclusivity, including the orphan drug exclusivity. This six-month exclusivity may be granted if an NDA sponsor submits pediatric data that fairly respond to a pediatric written request from the FDA for such data. The data do not need to show the product to be effective in the pediatric population studied; rather, if the clinical trial is deemed to fairly respond to the FDA's request, the additional protection is granted. If reports of requested pediatric studies are submitted to and accepted by the FDA within the statutory time limits, whatever statutory or regulatory periods of exclusivity or patent protection cover the product are extended by six months.

Orphan Drug Designation and Exclusivity

Under the Orphan Drug Act, the FDA may designate a drug product as an "orphan drug" if it is intended to treat a rare disease or condition, generally meaning that it affects fewer than 200,000 individuals in the United States, or more in cases in which there is no reasonable expectation that the cost of developing and making a product available in the United States for treatment of the disease or condition will be recovered from sales of the product. A company must seek orphan drug designation before submitting an NDA for the candidate product. If the request is granted, the FDA will disclose the identity of the therapeutic agent and its potential use. Orphan drug designation does not shorten the PDUFA goal dates for the regulatory review and approval process, although it does convey certain advantages such as tax benefits and exemption from the PDUFA application fee.

If a product with orphan designation receives the first FDA approval for the disease or condition for which it has such designation or for a select indication or use within the rare disease or condition for which it was designated, the product generally will receive orphan drug exclusivity. Orphan drug exclusivity means that the FDA may not approve another sponsor's marketing application for the same drug for the same condition for seven years, except in certain limited circumstances. Orphan exclusivity does not block the approval of a different product for the same rare disease or condition, nor does it block the approval of the same product for different conditions. If a drug designated as an orphan drug ultimately receives marketing approval for an indication broader than what was designated in its orphan drug application, it may not be entitled to exclusivity.

Orphan drug exclusivity will not bar approval of another product under certain circumstances, including if a subsequent product with the same drug for the same condition is shown to be clinically superior to the approved product on the basis of greater efficacy or safety, or providing a major contribution to patient care, or if the company with orphan drug exclusivity is not able to meet market demand. This is the case despite an earlier court opinion holding that the Orphan Drug Act unambiguously required the FDA to recognize orphan drug exclusivity regardless of a showing of clinical superiority.

In September 2021, the Court of Appeals for the 11th Circuit held that, for the purpose of determining the scope of market exclusivity, the term "same disease or condition" in the statute means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." Thus, the court concluded, orphan drug exclusivity applies to the entire designated disease or condition rather than the "indication or use." It is unclear how this court decision will be implemented by the FDA.

Patent Term Restoration and Extension

A patent claiming a new drug product may be eligible for a limited patent term extension under the Hatch-Waxman Act, which permits a patent restoration of up to five years for patent term lost during product development and the FDA regulatory review. The restoration period granted on a patent covering a product is typically one-half the time between the effective date the IND for the clinical investigation and the submission date of an application, plus the time between the submission date of an application and the ultimate approval date. Patent term restoration cannot be used to extend the remaining term of a patent past a total of 14 years from the product's approval date. Only one patent applicable to an approved product is eligible for the extension, and the application for the extension must be submitted prior to the expiration of the patent in question. A patent that covers multiple products for which approval is sought can only be extended in connection with one of the approvals. The United States Patent and Trademark Office reviews and approves the application for any patent term extension or restoration in consultation with the FDA.

Health Care Law and Regulation

Health care providers and third-party payors play a primary role in the recommendation and prescription of drug products that are granted marketing approval. Arrangements with providers, consultants, third-party payors and customers are subject to broadly applicable fraud and abuse, anti-kickback, false claims laws, patient privacy laws, and regulations and other health care laws and regulations that may constrain business and/or financial arrangements. Restrictions under applicable federal and state health care laws and regulations, include the following:

- the federal Anti-Kickback Statute, which prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, paying, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made, in whole or in part, under a federal health care program such as Medicare and Medicaid;
- the federal civil and criminal false claims laws, including the civil False Claims Act, and civil monetary penalties laws, which prohibit individuals or entities from, among other things, knowingly presenting, or causing to be presented, to the federal government, claims for payment that are false, fictitious or fraudulent or knowingly making, using or causing to made or used a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the Foreign Corrupt Practices Act, or FCPA, which prohibits companies and their intermediaries from making, or offering or promising to make, improper payments to non-U.S. officials for the purpose of obtaining or retaining business or otherwise seeking favorable treatment; and
- the federal transparency requirements known as the federal Physician Payments Sunshine Act, which requires certain manufacturers of drugs, devices, biologics and medical supplies to report annually to the Centers for Medicare & Medicaid Services, or CMS, within HHS, information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals, as well as ownership and investment interests held by physicians, other healthcare providers and their immediate family members.

Further, some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government in addition to requiring manufacturers to report information related to payments to physicians and other health care providers or marketing expenditures. Additionally, some state and local laws require the registration of pharmaceutical sales representatives in the jurisdiction. State and foreign laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts.

Pharmaceutical Insurance Coverage and Health Care Reform

In the United States and markets in other countries, patients who are prescribed treatments for their conditions and providers performing the prescribed services generally rely on third-party payors to reimburse all or part of the associated health care costs. Significant uncertainty exists as to the coverage and reimbursement status of products approved by the FDA and other government authorities. Thus, even if a product candidate is approved, sales of the product will depend, in part, on the extent to which third-party payors, including government health programs in the United States such as Medicare and Medicaid, commercial health insurers and managed care organizations, provide coverage and establish adequate reimbursement levels for, the product. The process for determining whether a payor will provide coverage for a product may be separate from the process for setting the price or reimbursement rate that the payor will pay for the product once coverage is approved. Third-party payors are increasingly challenging the prices charged, examining the medical necessity and reviewing the cost-effectiveness of medical products and services and imposing controls to manage costs. Third-party payors may limit coverage to specific products on an approved list, also known as a formulary, which might not include all of the approved products for a particular indication.

In order to secure coverage and reimbursement for any product that might be approved for sale, a company may need to conduct expensive pharmacoeconomic studies in order to demonstrate the medical necessity and cost-effectiveness of the product, in addition to the costs required to obtain FDA or other comparable marketing approvals. Nonetheless, product candidates may not be considered medically necessary or cost effective. A decision by a third-party payor not to cover a product could reduce physician utilization once the product is approved and have a material adverse effect on sales, results of operations and financial condition. Additionally, a payor's decision to provide coverage for a product does not imply that an adequate reimbursement rate will be approved. Further, one payor's determination to provide coverage for a product does not assure that other payors will also provide coverage and reimbursement for the product, and the level of coverage and reimbursement can differ significantly from payor to payor.

The containment of health care costs also has become a priority of federal, state and foreign governments and the prices of products have been a focus in this effort. Governments have shown significant interest in implementing cost-containment programs, including price controls, restrictions on reimbursement and requirements for substitution of generic products. Adoption of price controls and cost-containment measures, and adoption of more restrictive policies in jurisdictions with existing controls and measures, could further limit a company's revenue generated from the sale of any approved products. Coverage policies and third-party reimbursement rates may change at any time. Even if favorable coverage and reimbursement status is attained for one or more products for which a company or its collaborators receive marketing approval, less favorable coverage policies and reimbursement rates may be implemented in the future.

There have been a number of federal and state proposals during the last few years regarding the pricing of pharmaceutical and biopharmaceutical products, limiting coverage and reimbursement for drugs and biologics and other medical products, government control and other changes to the health care system in the United States. In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Affordability Reconciliation Act, or collectively the ACA. In addition, other legislative changes have been proposed and adopted in the United States since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act. These Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been, and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the Tax Cuts and Jobs Act of 2017, or TCJA, which was signed by President Trump on December 22, 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019.

Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA, and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and, on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, CMS issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, HHS and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. A number of states, for example, require drug manufacturers and other entities in the drug supply chain, including health carriers, pharmacy benefit managers, wholesale distributors, to disclose information about pricing of pharmaceuticals. In addition, regional health care authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other health care programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for our product candidates or additional pricing pressures.

Review and Approval of Medicinal Products in the European Union

In order to market any product outside of the United States, a company must also comply with numerous and varying regulatory requirements of other countries and jurisdictions regarding quality, safety and efficacy and governing, among other things, clinical trials, marketing authorization, commercial sales and distribution of products. Whether or not it obtains FDA approval for a product, a sponsor will need to obtain the necessary approvals by the comparable non-U.S. regulatory authorities before it can commence clinical trials or marketing of the product in those countries or jurisdictions. Specifically, the process governing approval of medicinal products in the EU generally follows the same lines as in the United States. It entails satisfactory completion of preclinical studies and adequate and well-controlled clinical trials to establish the safety and efficacy of the product for each proposed indication. It also requires the submission to the relevant competent authorities of a marketing authorization application, or MAA, and granting of a marketing authorization by these authorities as part of a national authorization procedure, or to the EMA as part of a centralized procedure, before the product can be marketed and sold in the EU.

Clinical Trial Approval

On January 31, 2022, the new Clinical Trials Regulation (EU) No 536/2014 became effective in the European Union and replaced the prior Clinical Trials Directive 2001/20/EC. The new regulation aims at simplifying and streamlining the authorization, conduct and transparency of clinical trials in the European Union. Under the new coordinated procedure for the approval of clinical trials, the sponsor of a clinical trial to be conducted in more than one Member State of the European Union, or EU Member State, will only be required to submit a single application for approval. The submission will be made through the Clinical Trials Information System, a new clinical trials portal overseen by the EMA and available to clinical trial sponsors, competent authorities of the EU Member States and the public.

The main characteristics of the regulation include: a streamlined application procedure via a single entry point, the “EU Portal and Database”; a single set of documents to be prepared and submitted for the application as well as simplified reporting procedures for clinical trial sponsors; and a harmonized procedure for the assessment of applications for clinical trials, which is divided in two parts. Part I is assessed by the appointed reporting EU Member State, whose assessment report is submitted for review by the sponsor and all other competent authorities of all EU Member States in which an application for authorization of a clinical trial has been submitted, or Concerned Member States. Part II is assessed separately by each Concerned Member State. Strict deadlines have been established for the assessment of clinical trial applications. The role of the relevant ethics committees in the assessment procedure will continue to be governed by the national law of the Concerned Member State. However, overall related timelines will be defined by the Clinical Trials Regulation.

The new regulation did not change the preexisting requirement that a sponsor must obtain prior approval from the competent national authority of the EU Member State in which the clinical trial is to be conducted. If the clinical trial is conducted in different EU Member States, the competent authorities in each of these EU Member States must provide their approval for the conduct of the clinical trial. Furthermore, the sponsor may only start a clinical trial at a specific study site after the applicable ethics committee has issued a favorable opinion.

As in the United States, parties conducting certain clinical trials must post clinical trial information in the EU at the EudraCT website: https://eudract.ema.europa.eu.

PRIME Designation in the European Union

In March 2016, the European Medicines Agency, or EMA, launched an initiative to facilitate development of product candidates in indications, often rare, for which few or no therapies currently exist. The PRIority MEdicines, or PRIME, scheme is intended to encourage drug development in areas of unmet medical need and provides accelerated assessment of products representing substantial innovation reviewed under the centralized procedure. Products from small- and medium-sized enterprises may qualify for earlier entry into the PRIME scheme than larger companies. Many benefits accrue to sponsors of product candidates with PRIME designation, including but not limited to, early and proactive regulatory dialogue with the EMA, frequent discussions on clinical trial designs and other development program elements, and accelerated marketing authorization application assessment once a dossier has been submitted.

Marketing Authorization

To obtain a marketing authorization for a product under EU regulatory systems, a sponsor must submit an MAA either under a centralized procedure administered by the EMA, or one of the procedures administered by competent authorities in

the EU Member States (decentralized procedure, national procedure or mutual recognition procedure). A marketing authorization may be granted only to a sponsor established in the EU. Regulation (EC) No 1901/2006 provides that prior to obtaining a marketing authorization in the EU, sponsors have to demonstrate compliance with all measures included in an EMA-approved Paediatric Investigation Plan, or PIP, covering all subsets of the pediatric population, unless the EMA has granted (1) a product-specific waiver, (2) a class waiver or (3) a deferral for one or more of the measures included in the PIP.

The centralized procedure provides for the grant of a single marketing authorization by the European Commission that is valid across the European Economic Area (i.e. the EU as well as Iceland, Liechtenstein and Norway). Pursuant to Regulation (EC) No 726/2004, the centralized procedure is compulsory for specific products, including for medicines produced by certain biotechnological processes, products designated as orphan medicinal products, advanced therapy medicinal products and products with a new active substance indicated for the treatment of certain diseases. For products with a new active substance indicated for the treatment of other diseases and products that are highly innovative or for which a centralized process is in the interest of patients, the centralized procedure may be optional. The centralized procedure may at the request of the sponsor also be used in certain other cases. We anticipate that the centralized procedure will be mandatory for the product candidates we are developing.

Under the centralized procedure, the Committee for Human Medicinal Products, or CHMP, is also responsible for conducting the initial assessment of a product and for several post-authorization and maintenance activities, such as the assessment of modifications or extensions to an existing marketing authorization. Under the centralized procedure in the EU, the maximum timeframe for the evaluation of an MAA is 210 days, excluding clock stops, when additional information or written or oral explanation is to be provided by the sponsor in response to questions of the CHMP. Accelerated evaluation might be granted by the CHMP in exceptional cases when a medicinal product is of major interest from the point of view of public health and in particular from the viewpoint of therapeutic innovation. If the CHMP accepts such request, the time limit of 210 days will be reduced to 150 days but it is possible that the CHMP can revert to the standard time limit for the centralized procedure if it considers that it is no longer appropriate to conduct an accelerated assessment. At the end of this period, the CHMP provides a scientific opinion on whether or not a marketing authorization should be granted in relation to a medicinal product. Within 15 calendar days of receipt of a final opinion from the CHMP, the European Commission must prepare a draft decision concerning an application for marketing authorization. This draft decision must take the opinion and any relevant provisions of EU law into account. Before arriving at a final decision on an application for centralized authorization of a medicinal product the European Commission must consult the Standing Committee on Medicinal Products for Human Use. The Standing Committee is composed of representatives of the EU Member States and chaired by a non-voting European Commission representative. The European Parliament also has a related “droit de regard”. The European Parliament’s role is to ensure that the European Commission has not exceeded its powers in deciding to grant or refuse to grant a marketing authorization.

The European Commission may grant a so-called “marketing authorization under exceptional circumstances”. Such authorization is intended for products for which the sponsor can demonstrate that it is unable to provide comprehensive data on the efficacy and safety under normal conditions of use, because the indications for which the product in question is intended are encountered so rarely that the sponsor cannot reasonably be expected to provide comprehensive evidence, or in the present state of scientific knowledge, comprehensive information cannot be provided, or it would be contrary to generally accepted principles of medical ethics to collect such information. Consequently, marketing authorization under exceptional circumstances may be granted subject to certain specific obligations, which may include the following:

- the sponsor must complete an identified program of studies within a time period specified by the competent authority, the results of which form the basis of a reassessment of the benefit/risk profile;
- the medicinal product in question may be supplied on medical prescription only and may in certain cases be administered only under strict medical supervision, possibly in a hospital and in the case of a radiopharmaceutical, by an authorized person; and
- the package leaflet and any medical information must draw the attention of the medical practitioner to the fact that the particulars available concerning the medicinal product in question are as yet inadequate in certain specified respects.

Regulatory Data Protection in the European Union

In the EU, innovative medicinal products approved on the basis of a complete independent data package qualify for eight years of data exclusivity upon marketing authorization and an additional two years of market exclusivity pursuant to Directive 2001/83/EC. Regulation (EC) No 726/2004 repeats this entitlement for medicinal products authorized in accordance the centralized authorization procedure. Data exclusivity prevents sponsors for authorization of generics of these

innovative products from referencing the innovator's data to assess a generic (abridged) application for a period of eight years. During an additional two-year period of market exclusivity, a generic marketing authorization application can be submitted and authorized, and the innovator's data may be referenced, but no generic medicinal product can be placed on the EU market until the expiration of the market exclusivity.

Periods of Authorization and Renewals

A marketing authorization has an initial validity for five years in principle. The marketing authorization may be renewed after five years on the basis of a re-evaluation of the risk-benefit balance by the EMA or by the competent authority of the EU Member State. The European Commission or the competent authorities of the EU Member States may decide, on justified grounds relating to pharmacovigilance, to proceed with one further five-year period of marketing authorization. Once subsequently definitively renewed, the marketing authorization shall be valid for an unlimited period. Any authorization which is not followed by the actual placing of the medicinal product on the EU market (in case of centralized procedure) or on the market of the authorizing EU Member State within three years after authorization ceases to be valid.

Pediatric Studies and Exclusivity

Prior to obtaining a marketing authorization in the EU, sponsors must demonstrate compliance with all measures included in an EMA-approved PIP covering all subsets of the pediatric population, unless the EMA has granted a product-specific waiver, a class waiver, or a deferral for one or more of the measures included in the PIP. The respective requirements for all marketing authorization procedures are laid down in Regulation (EC) No 1901/2006, the so-called Paediatric Regulation. This requirement also applies when a company wants to add a new indication, pharmaceutical form or route of administration for a medicine that is already authorized. The Paediatric Committee of the EMA, or PDCO, may grant deferrals for some medicines, allowing a company to delay development of the medicine for children until there is enough information to demonstrate its effectiveness and safety in adults. The PDCO may also grant waivers when development of a medicine for children is not needed or is not appropriate, such as for diseases that only affect the elderly population. Before an MAA can be filed, or an existing marketing authorization can be amended, the EMA determines that companies actually comply with the agreed studies and measures listed in each relevant PIP. If a sponsor obtains a marketing authorization in all EU Member States, or a marketing authorization granted in the centralized procedure by the European Commission, and the study results for the pediatric population are included in the product information, even when negative, the medicine is then eligible for an additional six-month period of qualifying patent protection through extension of the term of the Supplementary Protection Certificate, or SPC.

Orphan Drug Designation and Exclusivity

Regulation (EC) No. 141/2000, as implemented by Regulation (EC) No. 847/2000 provides that a drug can be designated as an orphan drug by the European Commission if its sponsor can establish: that the product is intended for the diagnosis, prevention or treatment of (1) a life-threatening or chronically debilitating condition affecting not more than five in ten thousand persons in the EU when the application is made, or (2) a life-threatening, seriously debilitating or serious and chronic condition in the EU and that without incentives it is unlikely that the marketing of the drug in the EU would generate sufficient return to justify the necessary investment. For either of these conditions, the sponsor must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the drug will be of significant benefit to those affected by that condition.

Once authorized, orphan medicinal products are entitled to ten years of market exclusivity in all EU Member States and in addition a range of other benefits during the development and regulatory review process including scientific assistance for study protocols, authorization through the centralized marketing authorization procedure covering all member countries and a reduction or elimination of registration and marketing authorization fees. However, marketing authorization may be granted to a similar medicinal product with the same orphan indication during the ten-year period with the consent of the marketing authorization holder for the original orphan medicinal product or if the manufacturer of the original orphan medicinal product is unable to supply sufficient quantities. Marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if it can be demonstrated on the basis of available evidence that the original orphan medicinal product is sufficiently profitable not to justify maintenance of market exclusivity.

Regulatory Requirements After a Marketing Authorization has been Obtained

In case an authorization for a medicinal product in the EU is obtained, the holder of the marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include:

- Compliance with the EU stringent pharmacovigilance or safety reporting rules must be ensured.
- The manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory, must also be conducted in strict compliance with the EU laws, regulations and guidance. These requirements include compliance with EU cGMP standards when manufacturing medicinal products and active pharmaceutical ingredients, including the manufacture of active pharmaceutical ingredients outside of the EU with the intention to import the active pharmaceutical ingredients into the EU
- The marketing and promotion of authorized drugs, including industry-sponsored continuing medical education and advertising directed toward the prescribers of drugs and/or the general public, are strictly regulated in the EU notably under Directive 2001/83EC, as amended, and EU Member State laws. Direct-to-consumer advertising of prescription medicines is prohibited across the EU.

Pricing Decisions for Approved Products

In the EU, pricing and reimbursement schemes vary widely from country to country. Some countries provide that products may be marketed only after a reimbursement price has been agreed. Some countries may require the completion of additional studies that compare the cost-effectiveness of a particular product candidate to currently available therapies or so-called health technology assessments, in order to obtain reimbursement or pricing approval. For example, the EU provides options for its Member States to restrict the range of products for which their national health insurance systems provide reimbursement and to control the prices of medicinal products for human use. Member States may approve a specific price for a product or it may instead adopt a system of direct or indirect controls on the profitability of the company placing the product on the market. Other Member States allow companies to fix their own prices for products, but monitor and control prescription volumes and issue guidance to physicians to limit prescriptions. Recently, many countries in the EU have increased the amount of discounts required on pharmaceuticals and these efforts could continue as countries attempt to manage health care expenditures, especially in light of the severe fiscal and debt crises experienced by many countries in the EU. The downward pressure on health care costs in general, particularly prescription products, has become intense. As a result, increasingly high barriers are being erected to the entry of new products. Political, economic and regulatory developments may further complicate pricing negotiations, and pricing negotiations may continue after reimbursement has been obtained. Reference pricing used by various Member States, and parallel trade, i.e., arbitrage between low-priced and high-priced Member States, can further reduce prices. There can be no assurance that any country that has price controls or reimbursement limitations for pharmaceutical products will allow favorable reimbursement and pricing arrangements for any products, if approved in those countries

Brexit and the Regulatory Framework in the United Kingdom

The United Kingdom's withdrawal from the EU took place on January 31, 2020. The EU and the United Kingdom reached an agreement on their new partnership in the Trade and Cooperation Agreement, or the Agreement, which was applied provisionally beginning on January 1, 2021 and which entered into force on May 1, 2021. The Agreement focuses primarily on free trade by ensuring no tariffs or quotas on trade in goods, including healthcare products such as medicinal products. Thereafter, the EU and the United Kingdom will form two separate markets governed by two distinct regulatory and legal regimes. As such, the Agreement seeks to minimize barriers to trade in goods while accepting that border checks will become inevitable as a consequence that the United Kingdom is no longer part of the single market. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law whereas Northern Ireland continues to be subject to EU rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the United Kingdom the body of EU law governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the EU.

General Data Protection Regulation

The collection, use, disclosure, transfer, or other processing of personal data regarding individuals in the European Union, including personal health data, is subject to the GDPR, which became effective on May 25, 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements

relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States, and permits data protection authorities to impose large penalties for violations of the GDPR, including potential fines of up to €20 million or 4% of annual global revenues, whichever is greater. The GDPR also confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. Compliance with the GDPR will be a rigorous and time-intensive process that may increase the cost of doing business or require companies to change their business practices to ensure full compliance.

Employees and Human Capital Resources

As of December 31, 2021, we had 41 full-time employees, including a total of 5 employees with M.D. or Ph.D. degrees. Of these full-time employees, 29 employees are engaged in research and development. None of our employees are represented by labor unions or covered by collective bargaining agreements. We consider our relationship with our employees to be good.

Our human capital resources objectives include, as applicable, identifying, recruiting, retaining, incentivizing and integrating our existing and additional employees. The principal purposes of our equity incentive plans are to attract, retain and motivate selected employees, consultants and directors through the granting of stock-based compensation awards.

Corporate Information

We were incorporated under the laws of the State of Delaware on January 26, 2016. Our principal executive offices are located at 116 Huntington Avenue, 6th Floor, Boston, Massachusetts 02116, and our telephone number is (617) 206-2020. Our website address is www.imaratx.com. Our website and the information contained on, or that can be accessed through, our website will not be deemed to be incorporated by reference in, and are not considered part of, this Annual Report on Form 10-K.

Item 1A. Risk Factors.

Investing in our common stock involves a high degree of risk. You should carefully consider the risks and uncertainties described below together with all of the other information contained in this Annual Report on Form 10-K, including our consolidated financial statements and the related notes appearing elsewhere in this Annual Report on Form 10-K and in our other filings with the Securities and Exchange Commission, before deciding to invest in our common stock. The risks described below are not the only risks facing our company. The occurrence of any of the following risks, or of additional risks and uncertainties not presently known to us, could cause our business, prospects, operating results and financial condition to suffer materially. In such event, the trading price of our common stock could decline, and you might lose all or part of your investment.

Risks Related to Our Financial Position and Need for Additional Capital

We have incurred significant losses since our inception, and we expect to incur losses over the next several years.

Since inception, we have incurred significant operating losses. Our net loss was $51.4 million for the year ended December 31, 2021 and was $41.4 million for the year ended December 31, 2020. As of December 31, 2021, we had an accumulated deficit of $147.5 million. As noted below, we have identified conditions and events that raise substantial doubt about our ability to continue as a going concern. To date, we have financed our operations primarily through the sale of common stock and the sale of convertible preferred stock. We have devoted substantially all of our financial resources and efforts to research and development, including clinical trials and preclinical studies of tovinontrine (IMR-687). We expect to continue to incur significant expenses and operating losses over the next several years as we continue to develop tovinontrine and any other product candidates we may develop. Our operating expenses and net losses may fluctuate significantly from quarter to quarter and year to year. We anticipate that our expenses will increase substantially as we:

- navigate the impacts of COVID-19 and our response to it;
- continue to advance clinical development of tovinontrine, including our ongoing Ardent Phase 2b clinical trial in patients with sickle cell disease, or SCD, and our Forte Phase 2b clinical trial in patients with β-thalassemia, as well as our open label extension, or OLE, clinical trial in patients with SCD;

- expand our planned research and development efforts for tovinontrine and pursue clinical activities for tovinontrine in heart failure with preserved ejection fraction, or HFpEF;
- continue to incur third-party manufacturing costs to support our clinical trials of tovinontrine and any other product candidates we may develop and, if approved, commercialization of such product candidates;
- seek regulatory and marketing approvals for tovinontrine and any other product candidates we may develop;
- establish a sales, marketing and distribution infrastructure to commercialize tovinontrine and any other product candidates we may develop, in each case if approved;
- commence development activities for any additional product candidates we may develop, including IMR-261;
- acquire or in-license products, product candidates, technologies and/or data referencing rights;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control, manufacturing and other scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company; and
- make any milestone payments to H. Lundbeck A/S, or Lundbeck, under our exclusive license agreement with Lundbeck, or the Lundbeck Agreement, upon the achievement of specified clinical or regulatory milestones.

We have identified conditions and events that raise substantial doubt about our ability to continue as a going concern.

As of December 31, 2021, we had cash, cash equivalents and investments of $90.3 million. We expect these available cash resources will be able to fund our operating expenses and capital expenditure requirements substantially through the first quarter of 2023. We have based this assessment on assumptions that may prove to be wrong, and we could exhaust our available capital resources sooner than we expect. Based on our available cash resources, there is substantial doubt about our ability to continue as a going concern within one year after the date of filing this Annual Report on Form 10-K. If we are unable to obtain additional funding, we will be forced to delay, reduce in scope or eliminate some of our research and development programs, including related clinical trials and operating expenses, potentially delaying the time to market for, or preventing the marketing of, any of our product candidates, which could adversely affect our business prospects and our ability to continue operations, and would have a negative impact on our financial condition and our ability to pursue our business strategies. If we are unable to continue as a going concern, we may have to liquidate our assets and may receive less than the value at which those assets are carried on our audited financial statements, and it is likely that investors will lose all or a part of their investment. The report from our independent registered public accounting firm issued in connection with this annual report on Form 10-K contains, and future reports may contain, statements expressing substantial doubt about our ability to continue as a going concern. If we seek additional financing to fund our business activities in the future and there remains substantial doubt about our ability to continue as a going concern, investors or other financing sources may be unwilling to provide funding to us on commercially reasonable terms, if at all.

We have never generated revenue from product sales and may never achieve or maintain profitability.

To become and remain profitable, we must succeed in developing, and eventually commercializing, a product or products that generate significant revenue. The ability to achieve this success will require us to be effective in a range of challenging activities, including completing preclinical testing and clinical trials of tovinontrine and any other product candidates we may develop, obtaining regulatory approval for these product candidates and manufacturing, marketing and selling any products for which we may obtain regulatory approval. We are only in the preliminary stages of many of these activities. We may never succeed in these activities and, even if we do, may never generate revenues that are significant enough to achieve profitability. Because of the numerous risks and uncertainties associated with pharmaceutical product development, we are unable to accurately predict the timing or amount of increased expenses or when, or if, we will be able to achieve profitability.

Even if we do achieve profitability, we may not be able to sustain or increase profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the value of our company and could impair our ability to raise capital, expand our business, maintain our research and development efforts, diversify our pipeline of product candidates or even continue our operations. A decline in the value of our company could also cause our stockholders to lose all or part of their investment.

We are heavily dependent on the success of tovinontrine.

We currently have no products that are approved for commercial sale and may never be able to develop marketable products. We expect that a substantial portion of our efforts and expenditures over the next several years will be devoted to tovinontrine, which is currently our only product candidate in clinical development. Accordingly, our business currently depends heavily on the successful development, regulatory approval and commercialization of tovinontrine. We cannot be certain that tovinontrine will receive regulatory approval or be successfully commercialized even if we receive regulatory approval. If we were required to discontinue development of tovinontrine or if tovinontrine does not receive regulatory approval or fails to achieve significant market acceptance, we likely would be delayed by many years in our ability to achieve profitability, if ever, and may not be able to generate sufficient revenue to continue our business.

We will need substantial additional funding. If we are unable to raise capital when needed, we could be forced to delay, reduce or eliminate our product development programs or commercialization efforts.

We expect to devote substantial financial resources to our ongoing and planned activities, including our Ardent Phase 2b and OLE clinical trials of tovinontrine in patients with SCD, our Forte Phase 2b clinical trial in patients with β-thalassemia and our planned Phase 2 clinical trial of tovinontrine in HFpEF. We expect our expenses to increase substantially in connection with our ongoing and planned activities, particularly as we advance our preclinical activities and clinical trials of and seek regulatory approval for tovinontrine and other product candidates we may develop. In addition, if we obtain regulatory approval for tovinontrine and any other product candidates we may develop, we expect to incur significant commercialization expenses related to product manufacturing, sales, marketing and distribution.

Identifying potential product candidates and conducting preclinical testing and clinical trials is a time-consuming, expensive and uncertain process that takes years to complete, and we may never generate the necessary data or results required to obtain regulatory approval and achieve product sales. In addition, any product candidates, if approved, may not achieve commercial success. Commercial revenues, if any, will not be derived unless and until we can achieve sales of products, which we do not anticipate for several years, if at all. Accordingly, we will need to obtain substantial additional funding in connection with our continuing operations.

In April 2021, we entered into a sales agreement, or the Sales Agreement, with Cantor Fitzgerald & Co, LLC, as sales agent, providing for the offering, issuance and sale by us of up to an aggregate $75.0 million of our common stock from time to time in “at-the-market” offerings under a shelf registration statement on Form S-3. As of December 31, 2021, we have issued and sold 231,291 shares of common stock under the Sales Agreement, resulting in net proceeds of $1.4 million after deducting commissions and offering expenses. The extent to which we utilize the Sales Agreement as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, general market conditions, the extent to which we are able to secure funds from other sources, and restrictions on our ability to sell common stock pursuant to the Sales Agreement to the extent we are then subject to restrictions on our ability to utilize the Form S-3 shelf registration statement to sell more than one-third of the market value of our public float, meaning the aggregate market value of voting and non-voting common stock held by non-affiliates, in any trailing 12-month period. Accordingly, we may not be able to sell shares under the Sales Agreement at prices or amounts that we deem acceptable, and there can be no assurance that we will sell any further common stock pursuant to the Sales Agreement.

As of December 31, 2021, we had cash, cash equivalents and investments of $90.3 million. We believe that our cash, cash equivalents and investments as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements substantially through the first quarter of 2023. However, we have based this estimate on assumptions that may prove to be wrong, and our operating plan may change as a result of many factors currently unknown to us. As a result, we could deplete our capital resources sooner than we currently expect.

Our future capital requirements will depend on many factors, including:

- the impact of the COVID-19 pandemic and our response to it;
- the time and cost necessary to complete our ongoing Ardent Phase 2b and OLE clinical trials of tovinontrine in patients with SCD, to initiate and complete one or more pivotal clinical trials of tovinontrine in SCD, and to pursue regulatory approvals for tovinontrine in SCD, and the costs of post-marketing studies that could be required by regulatory authorities;
- the time and cost necessary to complete our Forte Phase 2b clinical trial of tovinontrine in patients with β-thalassemia, to initiate and complete one or more pivotal clinical trials of tovinontrine in β-thalassemia, and to

pursue regulatory approvals for tovinontrine in β-thalassemia, and the costs of post-marketing studies that could be required by regulatory authorities;

- the time and cost necessary to complete our planned Phase 2 clinical trial of tovinontrine in patients with HFpEF, to initiate and complete one or more pivotal clinical trials of tovinontrine in HFpEF, and to pursue regulatory approvals for tovinontrine in HFpEF, and the costs of post-marketing studies that could be required by regulatory authorities;
- the costs of obtaining clinical and commercial supplies of tovinontrine and any other product candidates we may develop;
- our ability to successfully commercialize tovinontrine and any other product candidates we may develop;
- the manufacturing, selling and marketing costs associated with tovinontrine and any other product candidates we may develop, including the cost and timing of establishing our sales and marketing capabilities;
- the amount and timing of sales and other revenues from tovinontrine and any other product candidates we may develop, including the sales price and the availability of coverage and adequate third-party reimbursement;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;
- our ability to attract, hire and retain qualified personnel;
- the costs of maintaining, expanding and protecting our intellectual property portfolio; and
- our ability to continue as a going concern.

We will continue to rely on additional financing to achieve our business objectives. Adequate additional financing may not be available to us on acceptable terms, or at all. In addition, we may seek additional capital when market conditions are favorable, or for strategic considerations, even if we believe we have sufficient funds for our current or future operating plans. If adequate funds are not available to us on a timely basis or on terms acceptable to us, we may be required to delay, limit, reduce or terminate preclinical studies, clinical trials or other development activities for one or more product candidates or discovery stage programs or delay, limit, reduce or terminate our establishment of sales and marketing capabilities or other activities that may be necessary to commercialize any product candidates.

Raising additional capital may cause dilution to our stockholders, restrict our operations or require us to relinquish rights to our technologies or product candidates.

Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and marketing, distribution or licensing arrangements. We do not have any committed external source of funds. Based on our available cash resources, there is substantial doubt about our ability to continue as a going concern within one year after the date of filing this Annual Report on Form 10-K, and we expect that we will need to raise additional capital in the near term. To the extent that we raise additional capital through the sale of equity or convertible debt securities, our stockholders' ownership interests will be diluted, and the terms of these securities may include liquidation or other preferences that adversely affect our stockholders' rights as common stockholders. Debt financing and preferred equity financing, if available, may involve agreements that include covenants limiting or restricting our ability to take specific actions, such as incurring additional debt, selling or licensing our assets, making capital expenditures or declaring dividends.

If we raise additional funds through collaborations, strategic alliances or marketing, distribution or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research programs or product candidates or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed or on terms acceptable to us, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Our limited operating history may make it difficult to evaluate the success of our business to date and to assess our future viability.

We commenced activities in 2016 and are a clinical-stage company. Our operations to date have been limited to organizing and staffing our company, business planning, raising capital, developing our technology, undertaking preclinical

studies and clinical trials of tovinontrine and acquiring and commencing preclinical studies for IMR-261. We have not yet demonstrated our ability to successfully develop any product candidate, obtain regulatory approvals, manufacture a commercial scale product or arrange for a third-party to do so on our behalf, or conduct sales and marketing activities necessary for successful product commercialization. Consequently, any predictions about our future success or viability may not be as accurate as they could be if we had a longer operating history or a history of successfully developing and commercializing products.

In addition, as our business grows, we may encounter unforeseen expenses, difficulties, complications, delays and other known and unknown factors. We will need to transition at some point from a company with a research and development focus to a company capable of supporting commercial activities. We may not be successful in such a transition.

We expect our financial condition and operating results to fluctuate significantly from quarter-to-quarter and year-to-year due to a variety of factors, many of which are beyond our control. Accordingly, our stockholders should not rely upon the results of any quarterly or annual periods as indications of future operating performance.

Our ability to use our net operating losses, or NOLs, and research and development tax credit carryforwards to offset future taxable income may be subject to certain limitations.

We have a history of cumulative losses and anticipate that we will continue to incur significant losses in the foreseeable future; thus, we do not know whether or when we will generate taxable income necessary to utilize our NOLs or research and development tax credit carryforwards. As of December 31, 2021, we had federal NOLs of $139.2 million and state NOLs of $129.4 million.

In general, under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, or the Code, and corresponding provisions of state law, a corporation that undergoes an "ownership change," generally defined as a greater than 50 percentage point change (by value) in its equity ownership by certain stockholders over a three year period, is subject to limitations on its ability to utilize its pre-change NOLs and research and development tax credit carryforwards to offset future taxable income. We have not conducted a study to assess whether any such ownership changes have occurred. We may have experienced such ownership changes in the past, including as a result of our public offering of shares of common stock in July 2021, and may experience such ownership changes in the future as a result of subsequent changes in our stock ownership (which may be outside our control). As a result, if, and to the extent that, we earn net taxable income, our ability to use our pre-change NOLs and research and development tax credit carryforwards to offset such taxable income may be subject to limitations.

There is also a risk that due to regulatory changes, such as suspensions on the use of NOLs, or other unforeseen reasons, our existing NOLs could expire or otherwise become unavailable to offset future income tax liabilities. As described below in "Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition," the Tax Cuts and Jobs Act, or the TCJA, as amended by the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, includes changes to U.S. federal tax rates and the rules governing NOL carryforwards that may significantly impact our ability to utilize our NOLs to offset taxable income in the future. Additionally, state NOLs generated in one state cannot be used to offset income generated in another state. For these reasons, even if we attain profitability, we may be unable to use a material portion of our NOLs and other tax attributes.

Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers.

The COVID-19 pandemic and government measures taken in response to it have had a significant impact, both direct and indirect, on businesses and commerce, as worker shortages have occurred; supply chains have been disrupted; facilities and production have been suspended; and demand for certain goods and services, such as medical services and supplies, has spiked, while demand for other goods and services, such as travel, has fallen. The future progression of the pandemic and its effects on our business and operations remain uncertain.

The COVID-19 pandemic has affected our operations to date, including by causing delays in the conduct of our clinical trials. While we have not experienced any significant disruptions with the third parties on which we rely, the COVID-19 pandemic, or the spread of another infectious disease, could also negatively affect the operations of our third-party manufacturers, which could result in disruptions in the supply of tovinontrine or any other product candidates we may develop. In addition, many of our employees are currently working remotely. The COVID-19 pandemic continues to rapidly evolve and could more significantly impact our operations in the future.

We have enrolled and seek to enroll patients in our ongoing clinical trials at sites located both in the United States and internationally. The COVID-19 pandemic has delayed and may continue to delay or otherwise adversely affect these clinical development activities, including our ability to recruit and retain patients in our ongoing clinical trials, as a result of many factors, including:

- diversion of healthcare resources away from the conduct of our clinical trials in order to focus on pandemic concerns, including the availability of necessary materials, the attention of physicians serving as our clinical trial investigators, access to hospitals serving as our clinical trial sites, availability of hospital staff supporting the conduct of our clinical trials and the reluctance of patients enrolled in our clinical trials to visit clinical trial sites;
- potential interruptions in global shipping affecting the transport of clinical trial materials, such as investigational drug product, patient samples and other supplies used in our clinical trials;
- the impact of further limitations on travel that could interrupt key clinical trial activities, such as clinical trial site initiations and monitoring activities, travel by our employees, contractors or patients to clinical trial sites, or the ability of employees at any of our contract manufacturers or contract research organizations, or CROs, to report to work, any of which could delay or adversely impact the conduct or progress of our clinical trials, and limit the amount of clinical data we will be able to report;
- any future interruption of, or delays in receiving, supplies of clinical trial material from our contract manufacturing organizations, or CMOs, due to staffing shortages, production slowdowns or stoppages or disruptions in delivery systems; and
- availability of future capacity at contract manufacturers to produce sufficient drug substance and drug product to meet forecasted clinical trial demand if any of these manufacturers elect or are required to divert attention or resources to the manufacture of other pharmaceutical products.

For example, the COVID-19 pandemic has resulted in disruptions to our clinical trial operations, including some missed and incomplete patient visits in our completed Phase 2a clinical trial of tovinontrine in SCD, delays to some patient visits in our OLE clinical trial in SCD, as well as site activation and enrollment delays and delays in review of our regulatory submissions with respect to our Ardent and Forte Phase 2b clinical trials of tovinontrine in SCD and β-thalassemia. More recently, we have also experienced some disruptions with the supply chain of third-party vendors who assist us in the conduct of our clinical trials. In addition, the COVID-19 pandemic may affect the operations of the U.S. Food and Drug Administration, or FDA, and other health authorities, which could result in delays of regulatory actions related to our programs, including with respect to tovinontrine. Any negative impact that the COVID-19 pandemic has on recruiting or retaining patients in our clinical trials, the ability of our suppliers to provide materials for our product candidates, or the regulatory review process could cause additional delays which could materially and adversely affect our ability to obtain regulatory approval for and to commercialize our product candidates, increase our operating expenses, affect our ability to raise additional capital and have a material adverse effect on our financial results. In addition, if any of our clinical trial patients contract COVID-19, they may have adverse health outcomes that could impact the results of our clinical trials.

Additionally, while the potential economic impact and the duration of the COVID-19 pandemic is difficult to assess or predict, any impact of the COVID-19 pandemic on the global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity.

While we expect the impacts of COVID-19 will continue to have some adverse effect on our business, the extent to which COVID-19 impacts our clinical trials, research and development activities and operations will depend on future developments, which remain uncertain and cannot be predicted with confidence, including the duration of the pandemic, new information which may emerge concerning the severity of COVID-19 and variants of COVID-19, the actions to contain COVID-19 or treat its impact and changes in government spending or priorities, among others. The COVID-19 pandemic is a widespread health crisis that continues to adversely affect the global economy and financial markets of many countries, and any economic downturn could also affect our operations, our ability to conduct our clinical trials, our ability to raise additional funds through public offerings and the volatility of our stock price and trading in our stock. Even after the COVID-19 pandemic has subsided, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

Risks Related to the Discovery, Development and Commercialization of Our Product Candidates

We are heavily dependent on the success of tovinontrine. If we are unable to successfully complete clinical development, obtain regulatory approval for, or commercialize tovinontrine, or experience delays in doing so, our business will be materially harmed.

To date, we have invested a majority of our efforts and financial resources in the preclinical and clinical development of tovinontrine. Our future success is heavily dependent on our ability to successfully develop, obtain regulatory approval for and commercialize tovinontrine. Tovinontrine is currently our only product candidate in clinical development and we are currently testing it as part of our Ardent and Forte Phase 2b clinical trials in SCD and β-thalassemia, our OLE clinical trial in SCD and we plan to initiate a Phase 2 clinical trial of tovinontrine in HFpEF. We cannot be certain that tovinontrine will be successful in clinical trials or receive regulatory approval.

The success of tovinontrine will depend on several factors, including the following:

- our ability to effectively manage any adverse impact of COVID-19;
- successfully completing clinical trials;
- acceptance by the FDA or other regulatory agencies of regulatory filings for tovinontrine;
- expanding and maintaining a workforce of experienced clinical-stage drug development professionals and others to continue to develop tovinontrine;
- obtaining and maintaining intellectual property protection and regulatory exclusivity for tovinontrine;
- making arrangements with third-party manufacturers for, or establishing, commercial manufacturing capabilities;
- establishing sales, marketing and distribution capabilities and successfully launching commercial sales, if and when approved, whether alone or in collaboration with others;
- acceptance of tovinontrine, if and when approved, by patients, the medical community and third-party payors;
- effectively competing with other therapies, including Oxbryta and Adakveo for the treatment of SCD; Zynteglo (currently only approved in Europe and for which FDA approval is currently being sought) and Reblozyl for the treatment of ß-thalassemia; and Entresto and Jardiance for the treatment of HFpEF;
- obtaining and maintaining coverage, adequate pricing and adequate reimbursement from third-party payors, including government payors;
- patients' willingness to pay out-of-pocket for tovinontrine in the absence of coverage and/or adequate reimbursement from third-party payors; and
- maintaining a continued acceptable safety profile following receipt of any regulatory approvals.

Many of these factors are beyond our control, including clinical outcomes, the regulatory review process, potential threats to our intellectual property rights and the manufacturing, marketing and sales efforts of any future collaborator. If we are unable to develop, receive marketing approval for and successfully commercialize tovinontrine, or if we experience delays as a result of any of these factors or otherwise, we may need to spend significant additional time and resources to identify additional product candidates, advance them through preclinical and clinical development and apply for regulatory approvals, which would adversely affect our business, prospects, financial condition and results of operations.

Clinical drug development involves a lengthy and expensive process, with an uncertain outcome. We may incur additional costs or experience delays in completing, or ultimately be unable to complete, the development and commercialization of any product candidates.

The risk of failure for tovinontrine and any other product candidates we may develop is high. It is impossible to predict when or if tovinontrine and any other product candidates we may develop will prove effective or safe in humans or will receive regulatory approval. Before obtaining marketing approval from regulatory authorities for the sale of any product candidate, we must complete preclinical development and then conduct extensive clinical trials to demonstrate the safety and efficacy of such product candidate in humans. We have not yet begun or completed a pivotal clinical trial of tovinontrine or any other product candidate. Clinical trials may fail to demonstrate that tovinontrine and any other product candidates we may develop are safe for humans and effective for indicated uses. Even if the clinical trials are successful, changes in marketing approval policies during the development period, changes in or the enactment or promulgation of additional statutes, regulations or guidance or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application.

Before we can commence clinical trials for a product candidate, we must complete extensive preclinical testing and studies that support our planned investigational new drug applications, or INDs, and other regulatory filings in the United States and abroad. We cannot be certain of the timely completion or outcome of our preclinical testing and studies, and cannot predict if the FDA or other regulatory agencies will accept our proposed clinical programs or if the outcome of our preclinical testing and studies will ultimately support the further development of any product candidates. As a result, we cannot be sure that we will be able to submit INDs or similar applications for our preclinical programs on the timelines we expect, if at all, and we cannot be sure that submission of INDs or similar applications will result in the FDA or other regulatory authorities allowing clinical trials to begin. Furthermore, product candidates are subject to continued preclinical safety studies, which may be conducted concurrent with our clinical testing. The outcomes of these safety studies may delay the launch of or enrollment in future clinical trials and could impact our ability to continue to conduct our clinical trials.

Clinical trials are expensive, difficult to design and implement, can take many years to complete and are uncertain as to outcome. We cannot guarantee that any clinical trials will be conducted as planned or completed on schedule, or at all. A failure of one or more clinical trials can occur at any stage of testing, which may result from a multitude of factors, including, but not limited to, flaws in study design, dose selection issues, placebo effects, patient enrollment criteria and failure to demonstrate favorable safety or efficacy traits.

We may experience numerous unforeseen events during, or as a result of, clinical trials that could delay or prevent our ability to receive marketing approval or commercialize tovinontrine and any other product candidates we may develop, including:

- regulators or institutional review boards, or IRBs, may not authorize us or our investigators to commence a clinical trial or conduct a clinical trial at a prospective trial site;
- we may experience delays in reaching, or fail to reach, agreement on acceptable clinical trial contracts or clinical trial protocols with prospective trial sites;
- regulators may decide the design of our clinical trials is flawed, for example if our trial protocol does not evaluate treatment effects in trial subjects for a sufficient length of time;
- clinical trials of tovinontrine and any other product candidates we may develop may produce negative or inconclusive results, and we may decide, or regulators may require us, to conduct additional clinical trials or abandon product development programs;
- we may be unable to establish clinical endpoints that applicable regulatory authorities would consider clinically meaningful, or, if we seek accelerated approval, biomarker efficacy endpoints that applicable regulatory authorities would consider likely to predict clinical benefit;
- the number of patients required for clinical trials of tovinontrine and any other product candidates we may develop may be larger than we anticipate, enrollment in these clinical trials may be slower than we anticipate or participants may drop out of these clinical trials at a higher rate than we anticipate;
- our third-party contractors may fail to comply with regulatory requirements or meet their contractual obligations to us in a timely manner, or at all;
- we may decide, or regulators or IRBs may require us, to suspend or terminate clinical trials of tovinontrine and any other product candidates we may develop for various reasons, including non-compliance with regulatory requirements or a finding that the participants are being exposed to unacceptable health risks;
- regulators or IRBs may require us to perform additional or unanticipated clinical trials to obtain approval or we may be subject to additional post-marketing testing requirements to maintain regulatory approval;
- regulators may revise the requirements for approving tovinontrine and any other product candidates we may develop, or such requirements may not be as we anticipate;
- the cost of clinical trials of tovinontrine and any other product candidates we may develop may be greater than we anticipate;
- the supply or quality of tovinontrine and any other product candidates we may develop or other materials necessary to conduct clinical trials of such product candidates may be insufficient or inadequate;
- Tovinontrine and any other product candidates we may develop may have undesirable side effects or other unexpected characteristics, causing us or our investigators, regulators or IRBs to suspend or terminate the trials; and
- regulators may withdraw their approval of a product or impose restrictions on its distribution, such as in the form of a risk evaluation and mitigation strategy, or REMS.

We face additional important risks related to the enrollment and completion of our clinical trials of tovinontrine as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers."

If we are required to conduct additional clinical trials or other testing of tovinontrine beyond those that we currently contemplate, if we are unable to successfully complete clinical trials or other testing of tovinontrine or any other product candidates we may develop, if the results of these trials or tests are not positive or are only modestly positive or if there are safety concerns, we may:

- be delayed in obtaining marketing approval for any product candidates;
- not obtain marketing approval at all;
- obtain approval for indications or patient populations that are not as broad as intended or desired;
- obtain approval with labeling or a REMS that includes significant use or distribution restrictions or safety warnings;
- be subject to additional post-marketing testing requirements; or
- have the product removed from the market after obtaining marketing approval.

Our product development costs will also increase if we experience delays in testing or in obtaining marketing approvals. We do not know whether any of our preclinical studies or clinical trials will begin as planned, will need to be restructured or will be completed on schedule, or at all. We may also change the design or protocol of one or more of our clinical trials, including to add additional patients or arms, which could result in increased costs and expenses and/or delays. Significant preclinical study or clinical trial delays also could shorten any periods during which we may have the exclusive right to commercialize any product candidates or allow our competitors to bring products to market before we do and impair our ability to successfully commercialize any product candidates and may harm our business and results of operations.

Because we plan to use a surrogate endpoint for our development of tovinontrine in HFpEF, the FDA or other regulatory authorities may not consider such endpoint to predict or provide clinically meaningful results.

In the second quarter of 2022, we plan to initiate a Phase 2 clinical trial of tovinontrine in HFpEF, in which we plan to evaluate changes in N-terminal pro b-type natriuretic peptide, or NT-proBNP, levels as the primary endpoint. The clinical trial requirements of the FDA and other comparable regulatory agencies and the criteria these regulators use to determine the safety and efficacy of any product candidate vary substantially according to the type, complexity, novelty and intended use and market of the potential product. To date there are only two approved products for HFpEF, and as a result, the design and conduct of clinical trials for a therapeutic product candidate in HFpEF is subject to uncertainties and unknown risks. Even if applicable regulatory authorities do not object to our use of a biomarker endpoint in an earlier stage clinical trial, such regulatory authorities may determine that the biomarker efficacy endpoint is not sufficiently predictive of clinical benefit to support approval. As a result, we expect we may need to consider other endpoints for a pivotal program in HFpEF that has the ability to show clear clinical benefit.

Even if the FDA does find our clinical trial success criteria to be sufficiently validated and clinically meaningful, we may not achieve the pre-specified endpoint to a degree of statistical significance deemed approvable in any pivotal or other clinical trials we may conduct for tovinontrine. Further, even if we do achieve the pre-specified criteria, our trials may produce results that are unpredictable or inconsistent with the results of the more traditional efficacy endpoints in the trial. The FDA also could give overriding weight to other efficacy endpoints over a primary endpoint, even if we achieve statistically significant results on that primary endpoint, if we do not do so on our secondary or other efficacy endpoints. The FDA also weighs the benefits of a product against its risks and the FDA may view the efficacy results in the context of safety as not being supportive of approval. Other regulatory authorities in the European Union and other countries may make similar findings with respect to these endpoints.

The outcome of preclinical studies and earlier-stage clinical trials may not be predictive of the success of later-stage clinical trials.

The outcome of preclinical testing and earlier-stage clinical trials may not be predictive of the success of later-stage clinical trials. Tovinontrine and any other product candidates we may develop may fail to show the desired safety and

efficacy in clinical development despite positive results in preclinical studies or having successfully advanced through initial clinical trials. For example, in our SCD clinical trials, tovinontrine may not be effective at reducing VOCs in the same manner as we have experienced in our Phase 2a clinical trial of tovinontrine or our OLE clinical trial of tovinontrine. Additionally, any other positive results generated in our Phase 2a, OLE or Ardent Phase 2b clinical trial of tovinontrine in adults with SCD would not ensure that we will achieve similar results in larger, pivotal clinical trials or in clinical trials of tovinontrine in adolescent and pediatric populations with SCD. We face similar risks in our development of tovinontrine in areas outside of SCD, including ß-thalassemia and HFpEF, as well as in development of other product candidates we may develop, including IMR-261. Several companies in the pharmaceutical and biotechnology industries have suffered significant setbacks in late-stage clinical trials even after achieving promising results in preclinical testing and earlier-stage clinical trials, and we cannot be certain that we will not face similar setbacks. Moreover, preclinical and clinical data are often susceptible to varying interpretations and analyses, and many companies that have believed their product candidates performed satisfactorily in preclinical studies and clinical trials have nonetheless failed to obtain marketing approval of their products. Furthermore, the failure of any product candidate to demonstrate safety and efficacy in any clinical trial could negatively impact the perception of any other product candidates then under development and/or cause the FDA or other regulatory authorities to require additional testing before approving any other such product candidates.

Interim top-line and preliminary results from our clinical trials that we announce or publish from time to time may change as more patient data become available and are subject to audit and verification procedures, which could result in material changes in the final data.

From time to time, we may publish interim top-line or preliminary results from our clinical trials. Interim results from clinical trials that we may complete are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and more patient data become available. Preliminary or top-line results also remain subject to audit and verification procedures that may result in the final data being materially different from the preliminary data we previously published. As a result, interim and preliminary data should be viewed with caution until the final data are available. Differences between preliminary or interim data and final data could significantly harm our business prospects and may cause the trading price of our common stock to fluctuate significantly.

As an organization, we have never conducted pivotal clinical trials, and we may be unable to do so for tovinontrine or any other product candidates we may develop.

We will need to successfully complete pivotal clinical trials in order to obtain the approval of the FDA, the European Medicines Agency, or EMA, or other regulatory agencies to market tovinontrine or any other product candidate. Carrying out later-stage clinical trials is a complicated process. As an organization, we have not previously conducted any pivotal clinical trials. In order to do so, we will need to expand our clinical development and regulatory capabilities, and we may be unable to recruit qualified personnel. Consequently, we may be unable to successfully and efficiently execute and complete necessary clinical trials in a way that leads to approval of tovinontrine or other product candidates. We may require more time and incur greater costs than our competitors and may not succeed in obtaining regulatory approvals of product candidates that we develop. Failure to commence or complete, or delays in, our planned clinical trials, could prevent us from or delay us in commercializing our product candidates.

If we experience delays or difficulties in the enrollment of patients in clinical trials, our receipt of necessary regulatory approvals could be delayed or prevented.

Identifying and qualifying patients to participate in clinical trials for tovinontrine and any other product candidates we may develop is critical to our success. Successful and timely completion of clinical trials will require that we enroll a sufficient number of patients who remain in the trial until its conclusion. We may not be able to initiate or continue clinical trials for tovinontrine and any other product candidates we may develop if we are unable to locate and enroll a sufficient number of eligible patients to participate in these trials as required by the FDA or similar regulatory authorities outside of the United States. For example, the prevalence of patients with SCD and β-thalassemia in the United States and Europe is estimated to be low. Accordingly, there are limited patient pools from which to draw for clinical trials of tovinontrine for the treatment of SCD and β-thalassemia. We may not be able to identify, recruit, and enroll a sufficient number of patients to complete our clinical trials of tovinontrine because of the perceived risks and benefits of tovinontrine, the availability of competing therapies and clinical trials, the proximity and availability of clinical trial sites for prospective subjects and the subject referral practices of physicians, among other factors.

Patient enrollment is affected by a variety of other factors, including:

- the prevalence and severity of the disease under investigation;
- the eligibility criteria for the trial in question;
- the perceived risks and benefits of the product candidate under trial;
- the requirements of the trial protocols;
- the availability of existing commercially-available treatments for the indications for which we are conducting clinical trials;
- the ability to recruit clinical trial investigators with the appropriate competencies and experience;
- efforts to facilitate timely enrollment in clinical trials;
- the patient referral practices of physicians;
- the ability to monitor patients adequately during and after treatment;
- the proximity and availability of clinical trial sites for prospective patients;
- the conduct of clinical trials by competitors for product candidates that treat the same indications as tovinontrine and any other product candidates we may develop;
- the ability to identify specific patient populations for biomarker-defined trial cohort(s); and
- the cost to, or lack of adequate compensation for, prospective patients.

In addition, the COVID-19 pandemic has impacted, and is likely to continue to directly or indirectly impact the pace of enrollment in our clinical trials as patients may avoid, may not be allowed to, or may not be able to travel to healthcare facilities and physicians' offices unless due to a health emergency.

Our inability to locate and enroll a sufficient number of patients for our clinical trials would result in significant delays, could require us to abandon one or more clinical trials altogether and could delay or prevent our receipt of necessary regulatory approvals. Enrollment delays in our clinical trials may result in increased development costs for tovinontrine and any other product candidates we may develop, which would cause the value of our company to decline and limit our ability to obtain additional financing.

Changes in methods of product candidate manufacturing or formulation may result in additional costs or delay.

As product candidates proceed through preclinical studies to late-stage clinical trials towards potential approval and commercialization, it is common that various aspects of the development program, such as manufacturing methods and formulation, are altered along the way in an effort to optimize processes and results. Such changes carry the risk that they will not achieve these intended objectives. Any of these changes could cause tovinontrine or any other product candidates we may develop to perform differently and affect the results of planned clinical trials or other future clinical trials conducted with the materials manufactured using altered processes. Such changes may also require additional testing, FDA notification or FDA approval. This could delay completion of clinical trials, require the conduct of bridging clinical trials or the repetition of one or more clinical trials, increase clinical trial costs, delay approval of the affected product candidate and jeopardize our ability to commence sales and generate revenue.

If serious adverse events or unacceptable side effects are identified during the development of tovinontrine and any other product candidates we may develop, we may need to abandon or limit our development of those product candidates.

Clinical trials by their nature utilize a sample of the potential patient population. We have only evaluated tovinontrine in a limited number of subjects and our ongoing clinical trials of tovinontrine are being conducted at higher doses than previous clinical trials of tovinontrine. Accordingly, any rare and severe side effects of tovinontrine may be uncovered only in later stages of our current and future clinical development. Many product candidates that initially showed promise in early stage testing have later been found to cause side effects that prevented their further development. If tovinontrine and any other product candidates we may develop are associated with undesirable side effects in clinical trials or have characteristics that are unexpected in clinical trials or preclinical testing, we may need to abandon their development or limit development to more narrow uses or subpopulations in which the side effects or other characteristics are less prevalent, less severe or more

acceptable from a risk-benefit perspective. In pharmaceutical development, many compounds that initially show promise in early-stage or clinical testing are later found to cause side effects that delay or prevent further development of the compound.

Additionally, if results of our clinical trials reveal unacceptable side effects, we, the FDA or similar regulatory authorities outside of the United States, or the IRBs or Ethics Committees at the institutions in which our studies are conducted could suspend or terminate our clinical trials or the FDA or similar foreign regulatory authorities could order us to cease clinical trials or deny approval of tovinontrine and any other product candidates we may develop for any or all targeted indications. Treatment-related side effects could also affect patient recruitment or the ability of enrolled patients to complete any of our clinical trials. If we elect or are forced to suspend or terminate any clinical trial of tovinontrine and any other product candidates we may develop, the commercial prospects of such product candidate will be harmed, and our ability to generate product revenue from such product candidate will be delayed or eliminated. Any of these occurrences could materially harm our business.

We are also developing tovinontrine in combination with other therapies, which exposes us to additional risks.

We are developing tovinontrine both as a monotherapy and in combination with hydroxyurea, a currently approved therapy for SCD, and may develop future product candidates in combination with one or more currently approved therapies. Even if any product candidate we develop were to receive marketing approval or be commercialized for use in combination with other existing therapies, we would continue to be subject to the risks that the FDA or similar regulatory authorities outside of the United States could revoke approval of the therapy used in combination with our product candidate or that safety, efficacy, manufacturing or supply issues could arise with these existing therapies. This could result in our own products being removed from the market or being less successful commercially.

If any product candidate receives marketing approval and we, or others, later discover that the drug is less effective than previously believed or causes undesirable side effects that were not previously identified, our ability to market the drug could be compromised.

We conduct, and intend to conduct in the future, clinical trials of product candidates in carefully defined subsets of patients who have agreed to enter into clinical trials. Consequently, it is possible that our clinical trials may indicate an apparent positive effect of a product candidate that is greater than the actual positive effect, if any, or alternatively fail to identify undesirable side effects. If any product candidate receives regulatory approval, and we, or others, later discover that it is less effective than previously believed, or causes undesirable side effects, a number of potentially significant negative consequences could result, including:

- withdrawal or limitation by regulatory authorities of approvals of such product;
- seizure of the product by regulatory authorities;
- recall of the product;
- restrictions on the marketing of the product or the manufacturing process for any component thereof;
- requirement by regulatory authorities of additional warnings on the label, such as a “black box” warning or contraindication;
- decrease or elimination of third-party reimbursement;
- requirement that we implement a REMS or create a medication guide outlining the risks of such side effects for distribution to patients;
- commitment to expensive post-marketing studies as a prerequisite of approval by regulatory authorities of such product;
- the product may become less competitive;
- initiation of regulatory investigations and government enforcement actions;
- initiation of legal action against us to hold us liable for harm caused to patients; and
- harm to our reputation and resulting harm to physician or patient acceptance of our products.

Any of these events could prevent us from achieving or maintaining market acceptance of a particular product candidate, if approved, and could significantly harm our business, financial condition, and results of operations.

We may not be successful in our efforts to identify or discover additional product candidates and may fail to capitalize on programs or product candidates that may present a greater commercial opportunity or for which there is a greater likelihood of success.

If we do not successfully develop and eventually commercialize products, we will not obtain product revenue in future periods, resulting in significant harm to our financial position and adversely affecting our share price. We are currently conducting our Ardent Phase 2b clinical trial of tovinontrine in patients with SCD, our Forte Phase 2b clinical trial of tovinontrine in patients with β-thalassemia and our OLE clinical trial of tovinontrine in patients with SCD. In addition, we expect to commence clinical development of tovinontrine in HFpEF in the second quarter of 2022. A failure to establish tovinontrine as a viable treatment for SCD, β-thalassemia and/or HFpEF could harm our business prospects. In addition, we may explore tovinontrine in other indications or acquire additional product candidates for development. For example, in 2020 we acquired IMR-261, however we have not yet commenced clinical development of this product candidate and any future development efforts for IMR-261 may not be successful. There can be no assurance that we will be successful in our efforts to identify or acquire additional potential product candidates. Even if we identify or acquire additional product candidates, there can be no assurance that our development efforts will be successful.

Additionally, because we have limited resources, we may forego or delay pursuit of opportunities with certain programs or product candidates or for indications that later prove to have greater commercial potential. For example, we currently intend to focus our capital resources primarily on the development of tovinontrine. However, the development of tovinontrine may ultimately prove to be unsuccessful or less successful than another potential product candidate in our pipeline that we might have chosen to pursue on a more aggressive basis with our capital resources. If we do not accurately evaluate the commercial potential for a particular product candidate, we may relinquish valuable rights to that product candidate through strategic collaboration, licensing or other arrangements in cases in which it would have been more advantageous for us to retain sole development and commercialization rights to such product candidate. Alternatively, we may allocate internal resources to a product candidate in a therapeutic area in which it would have been more advantageous to enter into a partnering arrangement.

We are conducting clinical trials of tovinontrine at clinical trial sites outside the United States, and the FDA may not accept data from trials conducted in such international locations.

In addition to our clinical sites in the United States, we are currently conducting clinical trials of tovinontrine at clinical sites outside of the United States. For example, our Ardent and Forte Phase 2b clinical trials of tovinontrine in SCD and β-thalassemia are currently being conducted at clinical sites in Europe, Asia and Africa. Although the FDA may accept data from clinical trials conducted outside the United States, acceptance of these data is subject to conditions imposed by the FDA. For example, the clinical trial must be well designed and conducted and be performed by qualified investigators in accordance with ethical and Good Clinical Practice, or GCP, principles. The trial population must also adequately represent the U.S. population, and the data must be applicable to the U.S. population and U.S. medical practice in ways that the FDA deems clinically meaningful. In addition, while these clinical trials are subject to the applicable local laws, FDA acceptance of the data will depend on its determination that the trials also complied with all applicable U.S. laws and regulations. If the FDA does not accept the data from any trial conducted or from particular clinical trial sites located outside the United States, it would likely result in the need for additional trials, which would be costly and time-consuming and could delay or permanently halt our development of the applicable product candidates.

Even if any product candidate receives marketing approval, it may fail to achieve the degree of market acceptance by physicians, patients, third-party payors and others in the medical community necessary for commercial success.

If any product candidate receives marketing approval, it may nonetheless fail to gain sufficient market acceptance by physicians, patients, third-party payors and others in the medical community. Sales of medical products depend in part on the willingness of physicians to prescribe the treatment, which is likely to be based on a determination by these physicians that the products are safe, therapeutically effective and cost effective. In addition, the inclusion or exclusion of products from treatment guidelines established by various physician groups and the viewpoints of influential physicians can affect the willingness of other physicians to prescribe the treatment. We cannot predict whether physicians, physicians' organizations, hospitals, other healthcare providers, government agencies or private insurers will determine that our product is safe, therapeutically effective and cost effective as compared with competing treatments. Efforts to educate the medical community and third-party payors on the benefits of tovinontrine and any other product candidates we may develop may require significant resources and may not be successful. If tovinontrine and any other product candidates we may develop do not achieve an adequate level of acceptance, we may not generate significant product revenues and we may not become

profitable. The degree of market acceptance of tovinontrine and any other product candidates we may develop, if approved for commercial sale, will depend on a number of factors, including:

- the efficacy and potential advantages compared to alternative treatments, such as, in the case of tovinontrine, Oxbryta, Adakveo, hydroxyurea, Zynteglo, Reblozyl,Endari and Entresto;
- the effectiveness of sales and marketing efforts;
- the cost of treatment in relation to alternative treatments, including any similar generic treatments;
- the clinical indications for which the product is approved;
- the convenience and ease of administration compared to alternative treatments;
- the willingness of the target patient population to try new therapies and to continue treatment over time and of physicians to prescribe these therapies;
- the strength of marketing and distribution support;
- the timing of market introduction of competitive products;
- the availability of third-party coverage and adequate reimbursement, and patients' willingness to pay out of pocket for required co-payments or in the absence of third-party coverage or adequate reimbursement;
- the prevalence and severity of any side effects; and
- any restrictions on the use of our products, if approved, together with other medications.

If we are unable to establish sales, marketing and distribution capabilities or enter into sales, marketing and distribution agreements with third parties, we may not be successful in commercializing any product candidates if and when they are approved.

We do not have a sales or marketing infrastructure and have no experience in the sale, marketing or distribution of pharmaceutical products. To achieve commercial success for any product for which we have obtained marketing approval, we will need to establish a sales, marketing and distribution organization, either ourselves or through collaborations or other arrangements with third parties.

In the future, we expect that we would begin to build a sales and marketing infrastructure to market tovinontrine and any other product candidates we may develop, if and when approved by the applicable regulatory authority. There are risks involved with establishing our own sales, marketing and distribution capabilities. For example, recruiting and training a sales force is expensive and time-consuming and could delay any product launch. If the commercial launch of a product candidate for which we recruit a sales force and establish marketing capabilities is delayed or does not occur for any reason, we would have prematurely or unnecessarily incurred these commercialization expenses. These efforts may be costly, and our investment would be lost if we cannot retain or reposition our sales and marketing personnel.

Factors that may inhibit our efforts to commercialize our products on our own include:

- our inability to recruit, train and retain adequate numbers of effective sales, marketing, coverage or reimbursement, customer service, medical affairs and other support personnel;
- the inability of sales personnel to educate adequate numbers of physicians on the benefits of any future products;
- the inability of reimbursement professionals to negotiate arrangements for formulary access, reimbursement and other acceptance by payors;
- the inability to price our products at a sufficient price point to ensure an adequate and attractive level of profitability;
- restricted or closed distribution channels that make it difficult to distribute our products to segments of the patient population;
- the lack of complementary products to be offered by sales personnel, which may put us at a competitive disadvantage relative to companies with more extensive product lines; and
- unforeseen costs and expenses associated with creating an independent sales and marketing organization.

If we are unable to establish our own sales, marketing and distribution capabilities and we enter into arrangements with third parties to perform these services, our product revenues and our profitability, if any, are likely to be lower than if we

were to market, sell and distribute any products that we develop ourselves. In addition, we may not be successful in entering into arrangements with third parties to sell, market and distribute any product candidates or may be unable to do so on terms that are acceptable to us. We likely will have little control over such third parties, and any of them may fail to devote the necessary resources and attention to sell and market our products effectively. If we do not establish sales, marketing and distribution capabilities successfully, either on our own or in collaboration with third parties, we will not be successful in commercializing any product candidates.

We face substantial competition, which may result in others discovering, developing or commercializing products before or more successfully than we do.

The development and commercialization of new drug products is highly competitive. We face competition with respect to tovinontrine and will face competition with respect to any product candidates that we may seek to develop or commercialize in the future, from major pharmaceutical companies, specialty pharmaceutical companies and biotechnology companies worldwide. There are a number of large pharmaceutical and biotechnology companies that currently market and sell products or are pursuing the development of products for the treatment of the same disease indications we are pursuing. Some of these competitive products and therapies are based on scientific approaches that are the same as or similar to our approach, and others are based on entirely different approaches. Potential competitors also include academic institutions, government agencies and other public and private research organizations that conduct research, seek patent protection and establish collaborative arrangements for research, development, manufacturing and commercialization.

In the area of SCD, we expect to face competition from voxelotor (marketed as Oxbryta by Global Blood Therapeutics, Inc., or GBT), crizanlizumab (marketed as Adakveo by Novartis AG, or Novartis), HU (marketed under trade names including Droxia by Bristol-Myers Squibb Company and SIKLOS by Addmedica, as well as in generic form) and L-glutamine (marketed as Endari), which are currently the only FDA-approved therapies for the treatment of SCD. In addition, with respect to SCD, we are aware of several product candidates in clinical development, which could be competitive with product candidates that we may successfully develop and commercialize. For example, there are a number of companies in clinical development for gene editing/therapy treatments, including bluebird bio, Inc., Aruvant Sciences, Inc., CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals Incorporated), Sangamo Therapeutics, Inc. (in collaboration with Sanofi), Intellia Therapeutics, Inc. (in collaboration with Novartis), Graphite Bio, Inc. and Editas Medicine, Inc. There are also several companies advancing therapeutic approaches outside of gene editing/therapy, including GBT, Agios Pharmaceuticals, Inc., Forma Therapeutics, Inc., Vifor Pharma Ltd, Novo Nordisk A/S (in collaboration with EpiDestiny, Inc.), Fulcrum Therapeutics, Inc., CSL Ltd. and Pfizer, Inc.

In the area of ß-thalassemia, we expect to face competition from Zynteglo (marketed by bluebird bio, Inc.), which is currently only approved in Europe for the treatment of ß -thalassemia and for which FDA approval is currently being sought, as well as Reblozyl (marketed by Bristol-Myers Squibb Co. and Acceleron Pharma Inc.), which is approved in the United States for the treatment of anemia in adult patients with ß-thalassemia who require regular RBC transfusions. In addition, with respect to ß-thalassemia, we are aware of several product candidates in clinical development, which could be competitive with product candidates that we may successfully develop and commercialize. For example, there are a number of companies in clinical development for gene editing/therapy treatments, including bluebird bio, Inc, CRISPR Therapeutics AG (in collaboration with Vertex Pharmaceuticals Incorporated) and Ionis Pharmaceuticals. There are also several companies advancing therapeutic approaches outside of gene editing/therapy, including Agios Pharmaceuticals, Inc, Forma Therapeutics, Inc., Silence Therapeutics, Inc. and Vifor Pharma Ltd.

In the area of HFpEF, we expect to face competition from Entresto (marketed by Novartis) which is currently the only FDA-approved therapy for HFpEF. We are also aware of several drugs approved for other indications that are likely to seek near-term marketing approval for HFpEF including Jardiance (Eli Lilly & Co.), Farxiga (Astra Zeneca, PLC), Invokana (Johnson & Johnson) and Zynquista (Lexicon Pharmaceuticals, Inc). In addition, Bristol-Myers Squibb Co., Cytokinetics, Inc., Acceleron Pharma, Inc., Palatin Technologies, Inc., Cardurion Pharmaceuticals, Inc. and TransThera Biosciences Co., Ltd., among potentially other companies, are also developing therapeutic approaches for patients with HFpEF.

Our commercial opportunity could be reduced or eliminated if our competitors develop and commercialize products that are safer, more effective, have fewer or less severe side effects, are more convenient or are less expensive than any products that we may develop. Our competitors also may obtain FDA or other regulatory approval for their products more rapidly than we may obtain approval for ours, which could result in our competitors establishing a strong market position before we are able to enter the market. In addition, our ability to compete may be affected in many cases by insurers or other third-party payors seeking to encourage the use of generic products. If any product candidates achieve marketing approval, we expect that they would be priced at a significant premium over competitive generic products.

Many of the companies against which we are competing or against which we may compete in the future have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than we do.

Mergers and acquisitions in the pharmaceutical and biotechnology industries may result in even more resources being concentrated among a smaller number of our competitors. Smaller and other early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large and established companies. These third parties compete with us in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient registration for clinical trials, as well as in acquiring technologies complementary to, or necessary for, our programs.

If the market opportunities for tovinontrine and any other product candidates we may develop are smaller than we believe they are, our revenue may be adversely affected and our business may suffer. Moreover, because the target patient populations we are seeking to treat in SCD and β-thalassemia are relatively small, and the addressable patient population even smaller, we must be able to successfully identify patients and capture a significant market share to achieve profitability and growth.

To date, we have primarily focused our research and product development on treatments for rare inherited genetic disorders of hemoglobin. The prevalence of SCD is approximately 100,000 individuals in the United States and 134,000 individuals in the European Union. Similarly, the prevalence of β-thalassemia globally is estimated to be 288,000 individuals and the aggregate prevalence of β-thalassemia in the European Union and United States is estimated to be 19,000 individuals. Given the small number of patients who have SCD and β-thalassemia, it is critical to our ability to grow and become profitable that we continue to successfully identify patients with these rare diseases. Our projections of both the number of people who have these diseases, as well as the subset of people with these diseases who have the potential to benefit from treatment with tovinontrine and any other product candidates we may develop, are based on our beliefs and estimates. These estimates have been derived from a variety of sources, including the scientific literature, surveys of clinics, patient foundations or market research that we conducted, and may prove to be incorrect or contain errors. New studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. The effort to identify patients with diseases we seek to treat is in early stages, and we cannot accurately predict the number of patients for whom treatment might be possible. Additionally, the potentially addressable patient population for tovinontrine and any other product candidates we may develop may be limited or may not be amenable to treatment with tovinontrine and any other product candidates we may develop, and new patients may become increasingly difficult to identify or gain access to, which would adversely affect our results of operations and our business. Further, even if we obtain significant market share for tovinontrine and any other product candidates we may develop for SCD and β-thalassemia, because the potential target populations are very small, we may never achieve profitability despite obtaining such significant market share.

The target patient populations for SCD and β-thalassemia are relatively small, and there are currently limited standard of care treatments directed at SCD and β-thalassemia. As a result, the pricing and reimbursement of tovinontrine and any other product candidates we may develop, if approved, is uncertain, but must be adequate to support commercial infrastructure. If we are unable to obtain adequate levels of reimbursement, our ability to successfully market and sell tovinontrine and any other product candidates we may develop will be adversely affected.

We rely on CMOs to manufacture tovinontrine and expect to rely on CMOs to manufacture any other product candidates we may develop. If we are unable to enter into such arrangements as expected or if such organizations do not meet our supply requirements, development and/or commercialization of tovinontrine and any other product candidates we may develop may be delayed.

We do not have any manufacturing facilities. We currently rely on a single manufacturer of active pharmaceutical ingredient, or API, for tovinontrine and a different single manufacturer for finished drug product, and we expect to continue to rely on third parties to manufacture clinical supplies of tovinontrine and any other product candidates we may develop and commercial supplies of our products, if and when approved for marketing by applicable regulatory authorities, as well as for packaging, sterilization, storage, distribution and other production logistics. If we are unable to enter into such arrangements on the terms or timeline we expect, development and/or commercialization of tovinontrine and any other product candidates we may develop may be delayed. Reliance on third-party manufacturers may expose us to different risks than if we were to manufacture product candidates ourselves. If these third parties do not successfully carry out their contractual duties, meet expected deadlines or manufacture any product candidates in accordance with regulatory requirements, if there are disagreements between us and such parties or if such parties are unable to expand capacities to support commercialization of any product candidates for which we obtain marketing approval, we may not be able to fulfill, or may be delayed in

producing sufficient product candidates to meet, our supply requirements. These facilities may also be affected by natural disasters, such as floods or fire, or geopolitical developments, or such facilities could face manufacturing issues, such as contamination or regulatory concerns following a regulatory inspection of such facility. In such instances, we may need to locate an appropriate replacement third-party facility and establish a contractual relationship, which may not be readily available or on acceptable terms, which would cause additional delay and increased expense, and may have a material adverse effect on our business.

Our third-party manufacturers are subject to regulatory inspection from time to time, including inspection and approval by the FDA and similar foreign regulators before we can commence the manufacture and sale of any product candidates, and thereafter. Failure by our third-party manufacturers to pass such inspections and otherwise satisfactorily complete the approval regimen with respect to tovinontrine and any other product candidates we may develop may result in regulatory actions such as the issuance of FDA Form 483 notices of observations, warning letters or injunctions or the loss of operating licenses.

We or our third-party manufacturers may also encounter shortages in the raw materials or API necessary to produce tovinontrine and any other product candidates we may develop in the quantities needed for our clinical trials or, if tovinontrine and any other product candidates we may develop are approved, in sufficient quantities for commercialization or to meet an increase in demand, as a result of capacity constraints or delays or disruptions in the market for the raw materials or API, including shortages caused by the purchase of such raw materials or API by our competitors or others. Even if raw materials or API are available, we may be unable to obtain sufficient quantities at an acceptable cost or quality. The failure of us or our third-party manufacturers to obtain the raw materials or API necessary to manufacture sufficient quantities of tovinontrine and any other product candidates we may develop could delay, prevent or impair our development efforts and may have a material adverse effect on our business.

We face additional important risks related to our reliance on CMOs to meet our current and future supply needs of tovinontrine as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers."

Even if we are able to commercialize any product candidates, the products may become subject to unfavorable pricing regulations, third-party coverage or reimbursement practices or healthcare reform initiatives, which could harm our business.

The regulations that govern marketing approvals, pricing, coverage and reimbursement for new drug products vary widely from country to country. Current and future legislation may significantly change the approval requirements in ways that could involve additional costs and cause delays in obtaining approvals. Some countries require approval of the sale price of a drug before it can be marketed. In many countries, the pricing review period begins after marketing or product licensing approval is granted. In some foreign markets, prescription pharmaceutical pricing remains subject to continuing governmental control even after initial approval is granted. As a result, we might obtain marketing approval for a product in a particular country, but then be subject to price regulations that delay our commercial launch of the product, possibly for lengthy time periods, and negatively impact the revenues we are able to generate from the sale of the product in that country. Adverse pricing limitations may hinder our ability to recoup our investment in one or more product candidates, even if any product candidates obtain marketing approval.

Our ability to commercialize any product candidates successfully will depend in part on the extent to which coverage and adequate reimbursement for these products and related treatments will be available from government health administration authorities, private health insurers and other organizations. Government authorities and other third-party payors, such as private health insurers and health maintenance organizations, decide which medications they will pay for and establish reimbursement levels. A primary trend in the U.S. healthcare industry and elsewhere is cost containment. Government authorities and other third-party payors have attempted to control costs by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payors are requiring that drug companies provide them with predetermined discounts from list prices and are challenging the prices charged for medical products. Coverage and reimbursement may not be available for any product that we commercialize and, even if these are available, the level of reimbursement may not be satisfactory. Reimbursement may affect the demand for, or the price of, any product candidate for which we obtain marketing approval. Obtaining and maintaining adequate reimbursement for our products may be difficult. There can be no assurance that any product candidates, even if they are approved for sale in the United States or in other countries, will be considered medically reasonable and necessary for a specific indication or cost-effective by third-party payors. We may be required to conduct expensive pharmacoeconomic studies to justify coverage and reimbursement or the

level of reimbursement relative to other therapies. If coverage and adequate reimbursement are not available, we may not be able to successfully commercialize any product candidate for which we obtain marketing approval.

There may be significant delays in obtaining coverage and reimbursement for newly approved drugs, and coverage may be more limited than the purposes for which the drug is approved by the FDA or similar regulatory authorities outside of the United States. Moreover, eligibility for coverage and reimbursement does not imply that a drug will be paid for in all cases or at a rate that covers our costs, including research, development, manufacture, sale and distribution expenses. Interim reimbursement levels for new drugs, if applicable, may also not be sufficient to cover our costs and may not be made permanent. Reimbursement rates may vary according to the use of the drug and the clinical setting in which it is used, may be based on reimbursement levels already set for lower cost drugs and may be incorporated into existing payments for other services. Net prices for drugs may be reduced by mandatory discounts or rebates required by government healthcare programs or private payors and by any future relaxation of laws that presently restrict imports of drugs from countries where they may be sold at lower prices than in the United States. Further, no uniform policy for coverage and reimbursement exists in the United States. Third-party payors often rely upon Medicare coverage policy and payment limitations in setting their own reimbursement policies, but also have their own methods and process apart from Medicare determinations. As a result, obtaining and maintaining coverage and adequate reimbursement is often time-consuming and costly. Our inability to promptly obtain coverage and adequate reimbursement rates from both government-funded and private payors for any approved products that we develop could have a material adverse effect on our operating results, our ability to raise capital needed to commercialize products and our overall financial condition.

Our future growth depends, in part, on our ability to penetrate foreign markets, where we would be subject to additional regulatory burdens and other risks and uncertainties that, if they materialize, could harm our business.

Our future profitability will depend, in part, on our ability to commercialize tovinontrine and any other product candidates we may develop in markets outside of the United States and the European Union. If we commercialize tovinontrine and any other product candidates we may develop in foreign markets, we will be subject to additional risks and uncertainties, including:

- economic weakness, including inflation, or political instability in particular economies and markets, such as may result in Europe or other geographies as a result of the ongoing conflict between Russia and Ukraine;
- the burden of complying with complex and changing foreign regulatory, tax, accounting and legal requirements, many of which vary between countries;
- different medical practices and customs in foreign countries affecting acceptance in the marketplace;
- tariffs and trade barriers, as well as other governmental controls and trade restrictions;
- other trade protection measures, import or export licensing requirements, economic sanctions or other restrictive actions by U.S. or foreign governments;
- longer accounts receivable collection times;
- longer lead times for shipping;
- compliance with tax, employment, immigration and labor laws for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is common;
- language barriers for technical training;
- reduced protection of intellectual property rights in some foreign countries, and related prevalence of generic alternatives to therapeutics;
- foreign currency exchange rate fluctuations and currency controls;
- differing foreign reimbursement landscapes;
- uncertain and potentially inadequate reimbursement of our products; and
- the interpretation of contractual provisions governed by foreign laws in the event of a contract dispute.

If risks related to any of these uncertainties materializes, it could have a material adverse effect on our business.

Clinical trial and product liability lawsuits against us could divert our resources, could cause us to incur substantial liabilities and could limit commercialization of any products that we may develop.

We face an inherent risk of clinical trial and product liability exposure related to the testing of tovinontrine and any other product candidates we may develop in clinical trials, and we will face an even greater risk if we commercially sell any products that we may develop. While we currently have no products that have been approved for commercial sale, the current and future use of product candidates by us in clinical trials, and the sale of any approved products in the future, may expose us to liability claims. These claims might be made by patients that use the product, healthcare providers, pharmaceutical companies or others selling such products. If we cannot successfully defend ourselves against claims that tovinontrine and any other product candidates or products we may develop caused injuries, we will incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for tovinontrine and any other product candidates or products that we may develop;
- injury to our reputation and significant negative media attention;
- withdrawal of clinical trial participants;
- significant costs to defend any related litigation;
- substantial monetary awards to trial participants or patients;
- loss of revenue;
- reduced resources of our management to pursue our business strategy; and
- the inability to commercialize any products that we may develop.

Although we currently hold clinical trial liability insurance coverage in amounts we believe to be adequate, we may need to increase our insurance coverage as we expand our clinical trials or if we commence commercialization of any product candidates. Insurance coverage is increasingly expensive. We may not be able to maintain insurance coverage at a reasonable cost or in an amount adequate to satisfy any liability that may arise. If a successful clinical trial or product liability claim or series of claims is brought against us for uninsured liabilities or in excess of insured liabilities, our assets may not be sufficient to cover such claims and our business operations could be impaired.

Risks Related to Our Dependence on Third Parties

We rely, and expect to continue to rely, on third parties to conduct our clinical trials, and those third parties may not perform satisfactorily, including failing to meet deadlines for the completion of such trials, which may harm our business.

We currently rely on third-party clinical research organizations to conduct our ongoing Ardent and Forte Phase 2b clinical trials in SCD and in β-thalassemia and expect to rely on a third-party clinical research organization to conduct our planned Phase 2 clinical trial of tovinontrine in HFpEF. We do not plan to independently conduct clinical trials of any other product candidates. We expect to continue to rely on third parties, such as clinical research organizations, clinical data management organizations, medical institutions and clinical investigators, to conduct our clinical trials. These agreements might terminate for a variety of reasons, including a failure to perform by the third parties. If we need to enter into alternative arrangements, our product development activities might be delayed.

Our reliance on these third parties for research and development activities will reduce our control over these activities but will not relieve us of our responsibilities. For example, we will remain responsible for ensuring that each of our clinical trials is conducted in accordance with the general investigational plan and protocols for the trial. Moreover, the FDA requires us to comply with standards, commonly referred to as good clinical practices, or GCPs, for conducting, recording and reporting the results of clinical trials to assure that data and reported results are credible and accurate and that the rights, integrity and confidentiality of trial participants are protected. We also are required to register clinical trials and post the results of completed clinical trials on a government-sponsored database, ClinicalTrials.gov, within specified timeframes. Failure to do so can result in fines, adverse publicity and civil and criminal sanctions.

If these third parties do not successfully carry out their contractual duties, meet expected deadlines or conduct our clinical trials in accordance with regulatory requirements or our stated protocols, we will not be able to obtain, or may be delayed in obtaining, marketing approvals for any product candidates and will not be able to, or may be delayed in our efforts to, successfully develop and commercialize any product candidates. Furthermore, these third parties may also have relationships with other entities, some of which may be our competitors.

We also expect to rely on other third parties to store and distribute drug supplies for our clinical trials. Any performance failure on the part of our distributors could delay clinical development or marketing approval of any product candidates we may successfully develop and commercialization of our products, producing additional losses and depriving us of potential product revenue.

We face additional important risks related to our dependence on third parties as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers."

We contract with a third-party for the manufacture of tovinontrine, plan to contract with third parties for any other product candidates we may develop for preclinical and clinical testing and expect to continue to do so for commercialization. This reliance on third parties entails risks, including that such third parties may not be able to comply with applicable regulatory requirements. Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval.

We rely on a third-party for the manufacture of tovinontrine, and we expect to rely on third parties for the future manufacture of any other product candidates for preclinical and clinical testing. Reliance on third-party manufacturers entails additional risks, including:

- reliance on the third-party for regulatory compliance and quality assurance;
- the possible breach of the manufacturing agreement by the third-party;
- the possible misappropriation of our proprietary information, including our trade secrets and know-how; and
- the possible termination or nonrenewal of the agreement by the third-party at a time that is costly or inconvenient for us.

Third-party manufacturers may not be able to comply with current good manufacturing practices, or cGMP, regulations or similar regulatory requirements outside of the United States. Our failure, or the failure of our third-party manufacturers, to comply with applicable regulations could result in sanctions being imposed on us, including clinical holds, fines, injunctions, civil penalties, delays, suspension or withdrawal of approvals, license revocation, seizures or recalls of product candidates or products, operating restrictions and criminal prosecutions, any of which could significantly and adversely affect supplies of our products.

Tovinontrine and any other product candidates or products that we may develop may compete with other product candidates and products for access to manufacturing facilities. There are a limited number of manufacturers that operate under cGMP regulations and that might be capable of manufacturing for us.

Any performance failure on the part of our existing or future manufacturers could delay clinical development or marketing approval. We do not currently have arrangements in place for redundant supply or a source for bulk drug substance. If any of our future contract manufacturers cannot perform as agreed, we may be required to replace such manufacturers. Although we believe that there are several potential alternative manufacturers who could manufacture tovinontrine and any other product candidates we may develop, we may incur added costs and delays in identifying and qualifying any such replacement.

Our current and anticipated future dependence upon others for the manufacture of tovinontrine and any other product candidates or products we may develop may adversely affect our future profit margins and our ability to commercialize any products that receive marketing approval on a timely and competitive basis.

We face additional important risks related to our reliance on third parties for the manufacture of tovinontrine and other services as a result of the COVID-19 pandemic, which are further described in "—Our business and operations have been and may continue to be adversely affected by the ongoing COVID-19 pandemic, as may the operations of our suppliers and manufacturers and other third-party service providers."

We may enter into collaborations with third parties for the development or commercialization of product candidates. If our collaborations are not successful, we may not be able to capitalize on the market potential of these product candidates and our business could be adversely affected.

While we have retained all rights to and are developing tovinontrine on our own, we may in the future enter into development, distribution or marketing arrangements with third parties with respect to tovinontrine or future product candidates. Our likely collaborators for any sales, marketing, distribution, development, licensing or broader collaboration arrangements include large and mid-size pharmaceutical companies, regional and national pharmaceutical companies and biotechnology companies. We are not currently party to any such arrangement. However, if we do enter into any such arrangements with any third parties in the future, we will likely have limited control over the amount and timing of resources that our collaborators dedicate to the development or commercialization of tovinontrine and any other product candidates we may develop. Our ability to generate revenues from these arrangements will depend on our collaborators' abilities and efforts to successfully perform the functions assigned to them in these arrangements.

Collaborations that we enter into may not be successful, and any success will depend heavily on the efforts and activities of such collaborators. Collaborations pose a number of risks, including the following:

- collaborators have significant discretion in determining the amount and timing of efforts and resources that they will apply to these collaborations;
- collaborators may not perform their obligations as expected;
- collaborators may not pursue commercialization of tovinontrine and any other product candidates we may develop that achieve regulatory approval or may elect not to continue or renew commercialization programs based on results of clinical trials or other studies, changes in the collaborators' strategic focus or available funding, or external factors, such as an acquisition, that may divert resources or create competing priorities;
- collaborators could independently develop, or develop with third parties, products that compete directly or indirectly with any product candidates and products if the collaborators believe that the competitive products are more likely to be successfully developed or can be commercialized under terms that are more economically attractive than ours;
- product candidates discovered in collaboration with us may be viewed by our collaborators as competitive with their own product candidates or products, which may cause collaborators to cease to devote resources to the commercialization of any product candidates;
- a collaborator may fail to comply with applicable regulatory requirements regarding the development, manufacture, distribution or marketing of a product candidate or product;
- disagreements with collaborators, including disagreements over intellectual property or proprietary rights, contract interpretation or the preferred course of development, might cause delays or terminations of the research, development or commercialization of product candidates, might lead to additional responsibilities for us with respect to product candidates, or might result in litigation or arbitration, any of which would be time-consuming and expensive;
- collaborators may not properly obtain, maintain, enforce, defend or protect our intellectual property or proprietary rights or may use our proprietary information in such a way as to potentially lead to disputes or legal proceedings that could jeopardize or invalidate our intellectual property or proprietary information or expose us to potential litigation;
- collaborators may infringe, misappropriate or otherwise violate the intellectual property or proprietary rights of third parties, which may expose us to litigation and potential liability; and
- collaborations may be terminated for the convenience of the collaborator, and, if terminated, we could be required to raise additional capital to pursue further development or commercialization of the applicable product candidates.

Collaboration agreements may not lead to development or commercialization of product candidates in the most efficient manner, or at all. If any collaborations that we enter into do not result in the successful development and commercialization of products or if one of our collaborators terminates its agreement with us, we may not receive any future research funding or milestone or royalty payments under the collaboration. If we do not receive the funding we expect under these agreements, our development of any product candidates could be delayed and we may need additional resources to develop any product candidates. All of the risks relating to product development, regulatory approval and commercialization described in this Annual Report on Form 10-K also apply to the activities of our collaborators.

Additionally, subject to its contractual obligations to us, if a collaborator of ours is involved in a business combination, the collaborator might deemphasize or terminate the development or commercialization of any product candidate licensed to it by us. If one of our collaborators terminates its agreement with us, we may find it more difficult to attract new collaborators and our perception in the business and financial communities could be adversely affected.

If we are not able to establish or maintain collaborations, we may have to alter our development and commercialization plans and our business could be adversely affected.

For some product candidates we may develop, we may decide to collaborate with pharmaceutical or biotechnology companies for the development and potential commercialization of those product candidates. We face significant competition in seeking appropriate collaborators, and a number of more established companies may also be pursuing strategies to license or acquire third-party intellectual property rights that we consider attractive. These established companies may have a competitive advantage over us due to their size, financial resources and greater clinical development and commercialization capabilities. In addition, companies that perceive us to be a competitor may be unwilling to assign or license rights to us. Whether we reach a definitive agreement for a collaboration will depend, among other things, upon our assessment of the collaborator's resources and expertise, the terms and conditions of the proposed collaboration and the proposed collaborator's evaluation of a number of factors. Those factors may include the design or results of clinical trials, the likelihood of approval by the FDA or similar regulatory authorities outside the United States, the potential market for the subject product candidate, the costs and complexities of manufacturing and delivering such product candidate to patients, the potential of competing products, the existence of uncertainty with respect to our ownership of technology, which can exist if there is a challenge to such ownership without regard to the merits of the challenge, and industry and market conditions generally. The collaborator may also consider alternative product candidates or technologies for similar indications that may be available to collaborate on and whether such a collaboration could be more attractive than the one with us for our product candidate. Collaborations are complex and time-consuming to negotiate and document. In addition, there have been a significant number of recent business combinations among large pharmaceutical and biotechnology companies that have resulted in a reduced number of potential future collaborators.

If we are unable to reach agreements with suitable collaborators on a timely basis, on acceptable terms or at all, we may have to curtail the development of a product candidate, reduce or delay its development program or one or more of our other development programs, delay its potential commercialization or reduce the scope of any sales or marketing activities, or increase our expenditures and undertake development or commercialization activities at our own expense. If we elect to fund and undertake development or commercialization activities on our own, we may need to obtain additional expertise and additional capital, which may not be available to us on acceptable terms or at all. If we fail to enter into collaborations and do not have sufficient funds or expertise to undertake the necessary development and commercialization activities, we may not be able to further develop any product candidates or bring them to market.

Risks Related to our Intellectual Property

If we fail to comply with our obligations under our existing license agreements, or under any future intellectual property licenses, or otherwise experience disruptions to our business relationships with our current or any future licensors, we could lose intellectual property rights that are important to our business.

We are party to a license agreement with Lundbeck pursuant to which we have been granted an exclusive worldwide license within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies. The agreement grants us an exclusive license under the licensed technology to, among other things, develop and commercialize any product comprising or containing certain PDE9 inhibitors, including tovinontrine. We are also party to license agreements with the UAB Research Foundation and the University of Pittsburgh with respect to IMR-261. We may enter into additional license agreements in the future. Our current license agreements impose, and we expect that future licenses will impose, specified diligence, milestone payment, royalty and other obligations on us. Furthermore, our licensors have the right to terminate these license agreements if we materially breach the applicable agreement and fail to cure such breach within specified periods or in the event we undergo certain bankruptcy events. In spite of our best efforts, our current or any future licensors might conclude that we have materially breached our license agreements and might therefore terminate the license agreements, thereby removing our ability to develop and commercialize product candidates and technology covered by these license agreements. If these in-licenses are terminated, or if the underlying intellectual property fails to provide the intended exclusivity, competitors would have the freedom to seek regulatory approval of, and to market, products and technologies identical to ours. This could have a material adverse effect on our competitive position, business, financial condition, results of operations and prospects.

Disputes may arise regarding intellectual property subject to a licensing agreement, including:

- the scope of rights granted under the license agreement and other interpretation related issues;
- the extent to which our technology and processes infringe on intellectual property of the licensor that is not subject to the licensing agreement;
- the sublicensing of patent and other rights under our collaborative development relationships;
- our diligence obligations under the license agreement and what activities satisfy those diligence obligations;
- the inventorship and ownership of inventions and know-how resulting from the joint creation or use of intellectual property by our current or future licensors and us and our partners; and
- the priority of invention of patented technology.

In addition, license agreements are complex, and certain provisions in such agreements may be susceptible to multiple interpretations. The resolution of any contract interpretation disagreement that may arise could narrow what we believe to be the scope of our rights to the relevant intellectual property or technology, or increase what we believe to be our financial or other obligations under the relevant agreement, either of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Moreover, if disputes over intellectual property that we have licensed prevent or impair our ability to maintain our current licensing arrangements on commercially acceptable terms, we may be unable to successfully develop and commercialize the affected technology and product candidates, which could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we are unable to obtain, maintain, enforce and protect patent protection for our technology and product candidates or if the scope of the patent protection obtained is not sufficiently broad, our competitors could develop and commercialize technology and products similar or identical to ours, and our ability to successfully develop and commercialize our technology and product candidates may be adversely affected.

Our success depends in large part on our ability to obtain and maintain protection of the intellectual property we may own solely and jointly with others or may license from others, particularly patents, in the United States and other countries with respect to any proprietary technology and product candidates we develop. We seek to protect our proprietary position by filing patent applications in the United States and abroad related to tovinontrine and any other product candidates we may develop that are important to our business and by in-licensing intellectual property related to our technologies and product candidates. If we are unable to obtain or maintain patent protection with respect to any proprietary technology or product candidate, our business, financial condition, results of operations and prospects could be materially harmed.

The patent prosecution process is expensive, time-consuming and complex, and we may not be able to file, prosecute, maintain, defend or license all necessary or desirable patent applications at a reasonable cost or in a timely manner. It is also possible that we will fail to identify patentable aspects of our research and development output before it is too late to obtain patent protection. Moreover, in some circumstances, we may not have the right to control the preparation, filing and prosecution of patent applications, or to maintain, enforce and defend the patents, covering technology that we license from third parties. Therefore, these in-licensed patents and applications may not be prepared, filed, prosecuted, maintained, defended and enforced in a manner consistent with the best interests of our business.

The patent position of pharmaceutical and biotechnology companies generally is highly uncertain, involves complex legal and factual questions and has in recent years been the subject of much litigation. In addition, the scope of patent protection outside of the United States is uncertain and laws of non-U.S. countries may not protect our rights to the same extent as the laws of the United States or vice versa. For example, European patent law restricts the patentability of methods of treatment of the human body more than United States law does. With respect to both owned and in-licensed patent rights, we cannot predict whether the patent applications we and our licensors are currently pursuing will issue as patents in any particular jurisdiction or whether the claims of any issued patents will provide sufficient protection from competitors. Further, we may not be aware of all third-party intellectual property rights potentially relating to tovinontrine and any other product candidates we may develop. In addition, publications of discoveries in the scientific literature often lag behind the actual discoveries, and patent applications in the United States and other jurisdictions are typically not published until 18 months after filing of the priority application, or in some cases not published at all. Therefore, neither we nor our licensors can know with certainty whether either we or our licensors were the first to make the inventions claimed in the patents and patent applications we own or in-license now or in the future, or that either we or our licensors were the first to file for patent protection of such inventions. As a result, the issuance, scope, validity, enforceability and commercial value of our owned and in-licensed patent rights are highly uncertain. Moreover, our owned and in-licensed pending and future patent applications may not result in patents being issued that protect our technology and product candidates, in whole or in part, or

that effectively prevent others from commercializing competitive technologies and products. Changes in either the patent laws or interpretation of the patent laws in the United States and other countries may diminish the value of our patents and our ability to obtain, protect, maintain, defend and enforce our patent rights, narrow the scope of our patent protection and, more generally, could affect the value of, or narrow the scope of, our patent rights.

Currently, we have exclusively licensed one issued U.S. patent directed to methods of treating SCD. In addition, we have pending Patent Cooperation Treaty and U.S. non-provisional applications directed to methods of treating β-thalassemia and HFpEF. In order to continue to pursue protection based on provisional patent applications, we will need to file Patent Cooperation Treaty applications, non-U.S. applications and/or U.S. non-provisional patent applications prior to applicable deadlines. Even then, as highlighted above, patents may never issue from our patent applications, or the scope of any patent may not be sufficient to provide a competitive advantage. With respect to tovinontrine, the last to expire patent covering the composition of matter of tovinontrine licensed from Lundbeck is expected to expire in 2036.

Moreover, we or our licensors may be subject to a third-party preissuance submission of prior art to the United States Patent and Trademark Office, or USPTO, or become involved in opposition, derivation, revocation, reexamination, *inter partes* review, post-grant review or interference proceedings challenging our patent rights or the patent rights of others. An adverse determination in any such submission, proceeding or litigation could reduce the scope of, or invalidate, our patent rights, allow third parties to commercialize our technology or product candidates and compete directly with us, without payment to us, or result in our inability to manufacture or commercialize drugs without infringing third-party patent rights. If the breadth or strength of protection provided by our patents and patent applications is threatened, regardless of the outcome, it could dissuade companies from collaborating with us to license, develop or commercialize current or future product candidates.

Additionally, the coverage claimed in a patent application can be significantly reduced before the patent is issued, and its scope can be reinterpreted after issuance. Even if our owned and in-licensed patent applications issue as patents, they may not issue in a form that will provide us with any meaningful protection, prevent competitors from competing with us or otherwise provide us with any competitive advantage. The issuance of a patent is not conclusive as to its inventorship, scope, validity or enforceability, and our owned and in-licensed patents may be challenged in the courts or patent offices in the United States and abroad. Such challenges may result in loss of exclusivity or freedom to operate or in patent claims being narrowed, invalidated or held unenforceable, in whole or in part, which could limit our ability to stop others from using or commercializing similar or identical technology and products, or limit the duration of the patent protection of our technology and product candidates. Such proceedings also may result in substantial cost and require significant time from our management and employees, even if the eventual outcome is favorable to us. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. Furthermore, our competitors may be able to circumvent our owned or in-licensed patents by developing similar or alternative technologies or products in a non-infringing manner. As a result, our owned and in-licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing technology and products similar or identical to any of our technology and product candidates.

Patent terms may be inadequate to protect our competitive position on any product candidates for an adequate amount of time.

Patents have a limited lifespan. In the United States, if all maintenance fees are timely paid, the natural expiration of a patent is generally 20 years from its earliest U.S. non-provisional filing date. Various extensions may be available, but the life of a patent, and the protection it affords, is limited. Even if patents covering any product candidates are obtained, once the patent life has expired, we may be open to competition from competitive products, including generics or biosimilars. Given the amount of time required for the development, testing and regulatory review of new product candidates, patents protecting such candidates might expire before or shortly after such candidates are commercialized. As a result, our owned and licensed patent portfolio may not provide us with sufficient rights to exclude others from commercializing products similar or identical to ours. For example, the last to expire composition of matter patent covering tovinontrine, licensed from Lundbeck, is expected to expire in 2036. Given the expected expiration date of these patents, and the fact that safe harbor protections in many jurisdictions permit third parties to engage in development, including clinical trials, these patents may not provide us with a meaningful competitive advantage.

If we are unable to obtain licenses from third parties on commercially reasonable terms or fail to comply with our obligations under such agreements, our business could be harmed.

It may be necessary for us to use the patented or proprietary technology of third parties to commercialize our products, in which case we would be required to obtain a license from these third parties. If we are unable to license such technology, or if we are forced to license such technology on unfavorable terms, our business could be materially harmed. If we are unable to obtain a necessary license, we may be unable to develop or commercialize the affected product candidates, which could materially harm our business and the third parties owning such intellectual property rights could seek either an injunction prohibiting our sales or an obligation on our part to pay royalties and/or other forms of compensation. Even if we are able to obtain a license, it may be non-exclusive, thereby giving our competitors access to the same technologies licensed to us.

If we are unable to obtain rights to required third-party intellectual property rights or maintain the existing intellectual property rights we have, we may be required to expend significant time and resources to redesign our technology, product candidates, or the methods for manufacturing them or to develop or license replacement technology, all of which may not be feasible on a technical or commercial basis. If we are unable to do so, we may be unable to develop or commercialize the affected technology and product candidates, which could harm our business, financial condition, results of operations and prospects significantly.

Additionally, if we fail to comply with our obligations under license agreements, our counterparties may have the right to terminate these agreements, in which event we might not be able to develop, manufacture or market, or may be forced to cease developing, manufacturing or marketing, any product that is covered by these agreements or may face other penalties under such agreements. Such an occurrence could materially adversely affect the value of the product candidate being developed under any such agreement. Termination of these agreements or reduction or elimination of our rights under these agreements, or restrictions on our ability to freely assign or sublicense our rights under such agreements when it is in the interest of our business to do so, may result in our having to negotiate new or reinstated agreements with less favorable terms, cause us to lose our rights under these agreements, including our rights to important intellectual property or technology or impede, or delay or prohibit the further development or commercialization of one or more product candidates that rely on such agreements.

If we do not obtain patent term extension in the United States under the Hatch-Waxman Act and in non-U.S. countries under similar legislation, thereby potentially extending the term of our marketing exclusivity for any product candidates we may develop, our business may be materially harmed.

In the United States, the patent term of a patent that covers an FDA-approved drug may be eligible for limited patent term extension, which permits patent term restoration as compensation for the patent term lost during the FDA regulatory review process. The Drug Price Competition and Patent Term Restoration Act of 1984, also known as the Hatch-Waxman Act, permits a patent term extension of up to five years beyond the expiration of the patent. The length of the patent term extension is related to the length of time the drug is under regulatory review. Patent extension cannot extend the remaining term of a patent beyond a total of 14 years from the date of product approval, and only one patent applicable to an approved drug may be extended and only those claims covering the approved drug, a method for using it, or a method for manufacturing it may be extended. Similar provisions are available in Europe and certain other non-United States jurisdictions to extend the term of a patent that covers an approved drug. While, in the future, if and when any product candidates receive FDA approval, we expect to apply for patent term extensions on patents covering those product candidates, there is no guarantee that the applicable authorities will agree with our assessment of whether such extensions should be granted, and even if granted, the length of such extensions. We may not be granted patent term extension either in the United States or in any non-U.S. country because of, for example, failing to exercise due diligence during the testing phase or regulatory review process, failing to apply within applicable deadlines, failing to apply prior to expiration of relevant patents or otherwise failing to satisfy applicable requirements. Moreover, the term of extension, as well as the scope of patent protection during any such extension, afforded by the governmental authority could be less than we request. If we are unable to obtain any patent term extension or the term of any such extension is less than we request, our competitors may obtain approval of competing products following the expiration of our patent rights, and our business, financial condition, results of operations and prospects could be materially harmed.

It is possible that we will not obtain patent term extension under the Hatch-Waxman Act for a U.S. patent covering any of any product candidates that we may identify even where that patent is eligible for patent term extension, or if we obtain such an extension, it may be for a shorter period than we had sought. Further, for our licensed patents, we may not have the right to control prosecution, including filing with the USPTO a petition for patent term extension under the Hatch-Waxman

Act. Thus, if one of our licensed patents is eligible for patent term extension under the Hatch-Waxman Act, we may not be able to control whether a petition to obtain a patent term extension is filed, or obtained, from the USPTO.

Also, there are detailed rules and requirements regarding the patents that may be submitted to the FDA for listing in the Approved Drug Products with Therapeutic Equivalence Evaluations, or the Orange Book. We may be unable to obtain patents covering any product candidates that contain one or more claims that satisfy the requirements for listing in the Orange Book. Even if we submit a patent for listing in the Orange Book, the FDA may decline to list the patent, or a manufacturer of generic drugs may challenge the listing. If a product candidate is approved and a patent covering that product candidate is not listed in the Orange Book, a manufacturer of generic drugs would not have to provide advance notice to us of any abbreviated new drug application filed with the FDA to obtain permission to sell a generic version of such product candidate.

Changes to patent laws in the United States and other jurisdictions could diminish the value of patents in general, thereby impairing our ability to protect our products.

Changes in either the patent laws or interpretation of patent laws in the United States, including patent reform legislation such as the Leahy-Smith America Invents Act, or the Leahy-Smith Act, could increase the uncertainties and costs surrounding the prosecution of our owned and in-licensed patent applications and the maintenance, enforcement or defense of our owned and in-licensed issued patents. The Leahy-Smith Act includes a number of significant changes to United States patent law. These changes include provisions that affect the way patent applications are prosecuted, redefine prior art, provide more efficient and cost-effective avenues for competitors to challenge the validity of patents, and enable third-party submission of prior art to the USPTO during patent prosecution and additional procedures to attack the validity of a patent at USPTO-administered post-grant proceedings, including post-grant review, *inter partes* review, and derivation proceedings. Assuming that other requirements for patentability are met, prior to March 2013, in the United States, the first to invent the claimed invention was entitled to the patent, while outside the United States, the first to file a patent application was entitled to the patent. After March 2013, under the Leahy-Smith Act, the United States transitioned to a first-to-file system in which, assuming that the other statutory requirements for patentability are met, the first inventor to file a patent application will be entitled to the patent on an invention regardless of whether a third-party was the first to invent the claimed invention. As such, the Leahy-Smith Act and its implementation could increase the uncertainties and costs surrounding the prosecution of our patent applications and the enforcement or defense of our issued patents, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects.

In addition, the patent positions of companies in the development and commercialization of biologics and pharmaceuticals are particularly uncertain. Recent U.S. Supreme Court rulings have narrowed the scope of patent protection available in certain circumstances and weakened the rights of patent owners in certain situations. This combination of events has created uncertainty with respect to the validity and enforceability of patents once obtained. Depending on future actions by the U.S. Congress, the federal courts, and the USPTO, the laws and regulations governing patents could change in unpredictable ways that could have a material adverse effect on our patent rights and our ability to protect, defend and enforce our patent rights in the future.

We and our licensors, and any future licensors, may become involved in lawsuits to protect or enforce our patent or other intellectual property rights, which could be expensive, time-consuming and unsuccessful.

Competitors and other third parties may infringe, misappropriate or otherwise violate our or our current and future licensors' issued patents or other intellectual property. As a result, we or any current or future licensor may need to file infringement, misappropriation or other intellectual property related claims, which can be expensive and time-consuming. Any claims we assert against perceived infringers could provoke such parties to assert counterclaims against us alleging that we infringe, misappropriate or otherwise violate their intellectual property. In addition, in a patent infringement proceeding, such parties could counterclaim that the patents we or our licensors have asserted are invalid or unenforceable. In patent litigation in the United States, defendant counterclaims alleging invalidity or unenforceability are commonplace. Grounds for a validity challenge could be an alleged failure to meet any of several statutory requirements, including lack of novelty, obviousness, or non-enablement. Grounds for an unenforceability assertion could be an allegation that someone connected with prosecution of the patent withheld relevant information from the USPTO, or made a misleading statement, during prosecution. Third parties may institute such claims before administrative bodies in the United States or abroad, even outside the context of litigation. Such mechanisms include re-examination, post-grant review, *inter partes* review, interference proceedings, derivation proceedings, and equivalent proceedings in non-U.S. jurisdictions (e.g., opposition proceedings). The outcome following legal assertions of invalidity and unenforceability is unpredictable.

An adverse result in any such proceeding could put one or more of our owned or in-licensed patents at risk of being invalidated or interpreted narrowly and could put any of our owned or in-licensed patent applications at risk of not yielding

an issued patent. A court may also refuse to stop the third-party from using the technology at issue in a proceeding on the grounds that our owned or in-licensed patents do not cover such technology. Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information or trade secrets could be compromised by disclosure during this type of litigation. Any of the foregoing could allow such third parties to develop and commercialize competing technologies and products and have a material adverse impact on our business, financial condition, results of operations and prospects.

Interference or derivation proceedings provoked by third parties, or brought by us or by our licensors, or declared by the USPTO may be necessary to determine the priority of inventions with respect to our patents or patent applications. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms or at all, or if a non-exclusive license is offered and our competitors gain access to the same technology. Our defense of litigation or interference or derivation proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. In addition, the uncertainties associated with litigation could have a material adverse effect on our ability to raise the funds necessary to continue our clinical trials, continue our research programs, license necessary technology from third parties, or enter into development partnerships that would help us bring any product candidates to market.

Third parties may initiate legal proceedings alleging that we are infringing, misappropriating or otherwise violating their intellectual property rights, the outcome of which would be uncertain and could have a material adverse effect on the success of our business.

Our commercial success depends upon our ability and the ability of our collaborators to develop, manufacture, market and sell any product candidates we may develop and use our proprietary technologies without infringing, misappropriating or otherwise violating the intellectual property and proprietary rights of third parties. There is considerable patent and other intellectual property litigation in the pharmaceutical and biotechnology industries. We may become party to, or threatened with, adversarial proceedings or litigation regarding intellectual property rights with respect to our technology and product candidates, including interference proceedings, post grant review, *inter partes* review, and derivation proceedings before the USPTO and similar proceedings in non-U.S. jurisdictions such as oppositions before the European Patent Office. Numerous U.S. and non-U.S. issued patents and pending patent applications, which are owned by third parties, exist in the fields in which we are pursuing development candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our technologies or product candidates that we may identify may be subject to claims of infringement of the patent rights of third parties.

The legal threshold for initiating litigation or contested proceedings is low, so that even lawsuits or proceedings with a low probability of success might be initiated and require significant resources to defend. Litigation and contested proceedings can also be expensive and time-consuming, and our adversaries in these proceedings may have the ability to dedicate substantially greater resources to prosecuting these legal actions than we can. The risks of being involved in such litigation and proceedings may increase if and as any product candidates near commercialization and as we gain the greater visibility associated with being a public company. Third parties may assert infringement claims against us based on existing patents or patents that may be granted in the future, regardless of merit. We may not be aware of all such intellectual property rights potentially relating to our technology and product candidates and their uses, or we may incorrectly conclude that third-party intellectual property is invalid or that our activities and product candidates do not infringe such intellectual property. Thus, we do not know with certainty that our technology and product candidates, or our development and commercialization thereof, do not and will not infringe, misappropriate or otherwise violate any third-party's intellectual property.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations or methods, such as methods of manufacture or methods for treatment, related to the discovery, use or manufacture of the product candidates that we may identify or related to our technologies. Because patent applications can take many years to issue, there may be currently pending patent applications which may later result in issued patents that the product candidates that we may identify may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. Moreover, as noted above, there may be existing patents that we are not aware of or that we have incorrectly concluded are invalid or not infringed by our activities. If any third-party patents were held by a court of competent jurisdiction to cover, for example, the manufacturing process of the product candidates that we may identify, any molecules formed during the manufacturing process or any final product itself, the holders of any such patents may be able to block our ability to commercialize such product candidate unless we obtained a license under the applicable patents, or until such patents expire.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize the product candidates that we may identify. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, pay royalties, redesign our infringing products, be forced to indemnify our customers or collaborators or obtain one or more licenses from third parties, which may be impossible or require substantial time and monetary expenditure.

We may choose to take a license or, if we are found to infringe, misappropriate or otherwise violate a third-party's intellectual property rights, we could also be required to obtain a license from such third-party to continue developing, manufacturing and marketing our technology and product candidates. However, we may not be able to obtain any required license on commercially reasonable terms or at all. Even if we were able to obtain a license, it could be non-exclusive, thereby giving our competitors and other third parties access to the same technologies licensed to us and could require us to make substantial licensing and royalty payments. We could be forced, including by court order, to cease developing, manufacturing and commercializing the infringing technology or product. A finding of infringement could prevent us from commercializing any product candidates or force us to cease some of our business operations, which could materially harm our business. In addition, we may be forced to redesign any product candidates, seek new regulatory approvals and indemnify third parties pursuant to contractual agreements. Claims that we have misappropriated the confidential information or trade secrets of third parties could have a similar material adverse effect on our business, financial condition, results of operations and prospects.

Intellectual property litigation or other legal proceedings relating to intellectual property could cause us to spend substantial resources and distract our personnel from their normal responsibilities.

Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. Such litigation or proceedings could substantially increase our operating losses and reduce the resources available for development activities or any future sales, marketing or distribution activities. We may not have sufficient financial or other resources to conduct such litigation or proceedings adequately. Some of our competitors may be able to sustain the costs of such litigation or proceedings more effectively than we can because of their greater financial resources and may also have an advantage in such proceedings due to their more mature and developed intellectual property portfolios. Uncertainties resulting from the initiation and continuation of intellectual property litigation or other proceedings could compromise our ability to compete in the marketplace.

Obtaining and maintaining patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance, renewal and annuity fees and various other government fees on any issued patent and pending patent application must be paid to the USPTO and non-U.S. patent agencies in several stages or annually over the lifetime of our owned and in-licensed patents and patent applications. The USPTO and various non-U.S. governmental patent agencies also require compliance with a number of procedural, documentary and other similar provisions during the patent application process. In certain circumstances, we may rely on our licensing partners to pay these fees to, or comply with the procedural and documentary rules of, the relevant patent agency. With respect to our patents, we rely on an annuity service, outside firms and outside counsel to remind us of the due dates and to make payment after we instruct them to do so. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which non-compliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. In such an event, potential competitors might be able to enter the market with similar or identical products or technology. If we or our current or future licensors fail to maintain the patents and patent applications covering any product candidates, it may have a material adverse effect on our business, financial condition, results of operations and prospects.

We may not be able to protect our intellectual property and proprietary rights throughout the world.

Filing, prosecuting and defending patents on product candidates in all countries throughout the world would be prohibitively expensive, and the laws of non-U.S. countries may not protect our rights to the same extent as the laws of the United States. In addition, the laws of some non-U.S. countries do not protect intellectual property rights to the same extent as federal and state laws in the United States, and even where such protection is nominally available, judicial and governmental enforcement of such intellectual property rights may be lacking. Consequently, we may not be able to prevent third parties from practicing our inventions in all countries outside the United States, or from selling or importing products made using our inventions in and into the United States or other jurisdictions. Competitors may use our technologies in jurisdictions where we have not obtained patent protection to develop their own products and, further, may export otherwise infringing products to territories where we have patent protection or licenses but enforcement is not as strong as that in the United States. These products may compete with our products, and our patents or other intellectual property rights may not be effective or sufficient to prevent them from competing.

Many companies have encountered significant problems in protecting and defending intellectual property rights in non-U.S. jurisdictions. The legal systems of certain countries do not favor the enforcement of patents, trade secrets, and other intellectual property rights, particularly those relating to biotechnology products, which could make it difficult for us to stop the infringement of our patents or marketing of competing products in violation of our intellectual property and proprietary rights generally. In addition, certain jurisdictions do not protect to the same extent or at all inventions that constitute new methods of treatment.

Proceedings to enforce our intellectual property and proprietary rights in non-U.S. jurisdictions could result in substantial costs and divert our efforts and attention from other aspects of our business, could put our patents at risk of being invalidated or interpreted narrowly, could put our patent applications at risk of not issuing, and could provoke third parties to assert claims against us. We may not prevail in any lawsuits that we initiate, and the damages or other remedies awarded, if any, may not be commercially meaningful. Accordingly, our efforts to enforce our intellectual property and proprietary rights around the world may be inadequate to obtain a significant commercial advantage from the intellectual property that we develop or license.

Many countries have compulsory licensing laws under which a patent owner may be compelled to grant licenses to third parties. In addition, many countries limit the enforceability of patents against government agencies or government contractors. In these countries, the patent owner may have limited remedies, which could materially diminish the value of such patent. If we or any of our current or future licensors is forced to grant a license to third parties with respect to any patents relevant to our business, our competitive position may be impaired, and our business, financial condition, results of operations and prospects may be adversely affected.

We may be subject to claims challenging the inventorship or ownership of our patents and other intellectual property.

We or our licensors may be subject to claims that former employees, collaborators or other third parties have an interest in our owned or in-licensed patents, trade secrets or other intellectual property as an inventor or co-inventor. For example, we or our licensors may have inventorship disputes arise from conflicting obligations of employees, consultants or others who are involved in developing any product candidates. Litigation may be necessary to defend against these and other claims challenging inventorship or our or our licensors' ownership of our owned or in-licensed patents, trade secrets or other intellectual property. If we or our licensors fail in defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights, such as exclusive ownership of, or right to use, intellectual property that is important to any product candidates. Even if we are successful in defending against such claims, litigation could result in substantial costs and be a distraction to management and other employees. Any of the foregoing could have a material adverse effect on our business, financial condition, results of operations and prospects.

We may be subject to claims by third parties asserting that our employees, consultants or contractors have wrongfully used or disclosed confidential information of third parties, or we have wrongfully used or disclosed alleged trade secrets of their current or former employers or claims asserting we have misappropriated their intellectual property, or claiming ownership of what we regard as our own intellectual property.

Certain of our employees, consultants and contractors were previously employed at universities or other pharmaceutical or biotechnology companies, including our competitors or potential competitors. Although we try to ensure that our employees, consultants and contractors do not use the proprietary information or know-how of others in their work for us, we may be subject to claims that these individuals or we have used or disclosed intellectual property, including trade

secrets or other proprietary information, of any such individual's current or former employer. Litigation may be necessary to defend against these claims.

In addition, while it is our policy to require that our employees, consultants and contractors who may be involved in the development of intellectual property to execute agreements assigning such intellectual property to us, we may be unsuccessful in executing such an agreement with each party who in fact develops intellectual property that we regard as our own. Our intellectual property assignment agreements with them may not be self-executing or may be breached, and we may be forced to bring claims against third parties, or defend claims they may bring against us, to determine the ownership of what we regard as our intellectual property. Such claims could have a material adverse effect on our business, financial conditions, results of operations and prospects.

If we fail in prosecuting or defending any such claims, in addition to paying monetary damages, we may lose valuable intellectual property rights or personnel, which could have a material adverse effect on our competitive business position and prospects. Such intellectual property rights could be awarded to a third-party, and we could be required to obtain a license from such third-party to commercialize our technology or products, which license may not be available on commercially reasonable terms, or at all, or such license may be non-exclusive. Even if we are successful in prosecuting or defending against such claims, litigation could result in substantial costs and be a distraction to our management and employees.

If we are unable to protect the confidentiality of our trade secrets, our business and competitive position may be harmed.

In addition to seeking patents for any product candidates, we also rely on trade secrets and confidentiality agreements to protect our unpatented know-how, technology and other proprietary information, to maintain our competitive position. We seek to protect our trade secrets and other proprietary technology, in part, by entering into non-disclosure and confidentiality agreements with parties who have access to them, such as our employees, corporate collaborators, outside scientific collaborators, contract research organizations, contract manufacturers, consultants, advisors and other third parties. We also enter into confidentiality and invention or patent assignment agreements with our employees and consultants, but we cannot guarantee that we have entered into such agreements with each party that may have or has had access to our trade secrets or proprietary technology. Despite these efforts, any of these parties may breach the agreements and disclose our proprietary information, including our trade secrets, and we may not be able to obtain adequate remedies for such breaches. Detecting the disclosure or misappropriation of a trade secret and enforcing a claim that a party illegally disclosed or misappropriated a trade secret is difficult, expensive and time-consuming, and the outcome is unpredictable. In addition, some courts inside and outside of the United States are less willing or unwilling to protect trade secrets. If any of our trade secrets were to be lawfully obtained or independently developed by a competitor or other third-party, we would have no right to prevent them, or those to whom they communicate it, from using that technology or information to compete with us. If any of our trade secrets were to be disclosed to or independently developed by a competitor or other third-party, our competitive position may be materially and adversely harmed.

Intellectual property rights do not necessarily address all potential threats.

The degree of future protection afforded by our intellectual property rights is uncertain because intellectual property rights have limitations and may not adequately protect our business or permit us to maintain our competitive advantage. For example:

- others may be able to make product candidates that are similar to ours but that are not covered by the claims of the patents that we own;
- we, or our license partners or current or future collaborators, might not have been the first to make the inventions covered by the issued patent or pending patent applications that we license or may own in the future;
- we, or our license partners or current or future collaborators, might not have been the first to file patent applications covering certain of our or their inventions;
- others may independently develop similar or alternative technologies or duplicate any of our technologies without infringing our owned or in-licensed intellectual property rights;
- it is possible that our owned and in-licensed pending patent applications or those we may own or in-license in the future will not lead to issued patents;
- issued patents that we hold rights to may be held invalid or unenforceable, including as a result of legal challenges by our competitors;

- our competitors might conduct research and development activities in countries where we do not have patent rights and then use the information learned from such activities to develop competitive products for sale in our major commercial markets;
- we cannot ensure that any of our patents, or any of our pending patent applications, if issued, or those of our licensors, will include claims having a scope sufficient to protect any product candidates;
- we cannot ensure that any patents issued to us or our current or future licensors will provide a basis for an exclusive market for our commercially viable product candidates or will provide us with any competitive advantages;
- we cannot ensure that our commercial activities or product candidates will not infringe upon the patents of others;
- we cannot ensure that we will be able to successfully commercialize any product candidates on a substantial scale, if approved, before the relevant patents that we own or license expire;
- we may not develop additional proprietary technologies that are patentable;
- the patents of others may harm our business; and
- we may choose not to file a patent in order to maintain certain technology as a trade secrets or know-how, and a third-party may subsequently file a patent application covering such technology.

Should any of these events occur, they could have a material adverse effect on our business, financial condition, results of operations and prospects.

Risks Related to Regulatory Approval of Our Product Candidates and Other Legal Compliance Matters

Even if we complete the necessary preclinical studies and clinical trials, the marketing approval process is expensive, time-consuming and uncertain and may prevent us from obtaining approvals for the commercialization of any product candidates. If we are not able to obtain, or if there are delays in obtaining, required regulatory approvals, we will not be able to commercialize any product candidates, and our ability to generate revenue will be materially impaired.

Tovinontrine and any other product candidates we may develop and the activities associated with their development and commercialization, including design, testing, manufacture, packaging, recordkeeping, labeling, storage, approval, advertising, promotion, sale and distribution, export, import and adverse event reporting, are subject to comprehensive regulation by the FDA and other regulatory agencies in the United States and by the EMA and similar regulatory authorities outside of the United States. In addition, regulatory agencies may not approve the labeling claims that are necessary or desirable for the successful commercialization of any such product candidates.

Marketing approval of drugs in the United States requires the submission of a new drug application, or NDA, to the FDA and we are not permitted to market any product candidate in the United States until we obtain approval from the FDA of the NDA for that product. An NDA must be supported by extensive clinical and preclinical data, as well as extensive information regarding pharmacology, toxicology, and chemistry, manufacturing and controls. We have not submitted an application for or received marketing approval for tovinontrine or any other product candidates we may develop in the United States or in any other jurisdiction.

We have only limited experience in filing and supporting the applications necessary to gain marketing approvals and expect to rely on third-party clinical research organizations or other third-party consultants or vendors to assist us in this process. Securing marketing approval requires the submission of extensive preclinical and clinical data and supporting information to regulatory authorities for each therapeutic indication to establish the product candidate’s safety and efficacy. Securing marketing approval also requires the submission of information about the product manufacturing processes to, and inspection of manufacturing facilities by, the regulatory authorities. Our product candidates may not be effective, may be only moderately effective or may prove to have undesirable or unintended side effects, toxicities or other characteristics that may preclude our obtaining marketing approval or prevent or limit commercial use. If any of any product candidates receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The process of obtaining marketing approvals, both in the United States and abroad, is expensive, may take many years, if approval is obtained at all, and can vary substantially based upon a variety of factors, including the type, complexity and novelty of the product candidates involved. Changes in marketing approval policies during the development period, changes in or the enactment of additional statutes or regulations, or changes in regulatory review for each submitted product application may cause delays in the approval or rejection of an application. Regulatory authorities have substantial discretion

in the approval process and may refuse to accept any application or may decide that our data is insufficient for approval and require additional preclinical, clinical or other studies. In addition, varying interpretations of the data obtained from preclinical and clinical testing could delay, limit or prevent marketing approval of a product candidate in various countries. Any marketing approval we ultimately obtain may be limited or subject to restrictions or post-approval commitments that render the approved product not commercially viable.

If we experience delays in obtaining approval or if we fail to obtain approval of tovinontrine and any other product candidates we may develop, the commercial prospects for any product candidates may be harmed and our ability to generate revenues will be materially impaired.

We may not be able to obtain or maintain orphan drug designation or exclusivity for any product candidates and, even if we do, that exclusivity may not prevent the FDA or the EMA from approving other competing products.

We received orphan drug designation for tovinontrine for SCD and β-thalassemia in the United States in February 2017 and June 2020, respectively. We also received orphan drug designation for tovinontrine for SCD in the European Union in August 2020. We may seek orphan drug designation in other indications or for any other product candidates we develop. Regulatory authorities in some jurisdictions, including the United States and the European Union, may designate drugs for relatively small patient populations as orphan drugs. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is a drug intended to treat a rare disease or condition, which is generally defined as a patient population of fewer than 200,000 individuals in the United States.

Generally, if a product with an orphan drug designation subsequently receives the first marketing approval for the indication for which it has such designation, the product is entitled to a period of marketing exclusivity, which precludes the FDA or the EMA from approving another marketing application for the same drug for that time period. The applicable period is seven years in the United States and ten years in the European Union. The exclusivity period in the European Union can be reduced to six years if a drug no longer meets the criteria for orphan drug designation or if the drug is sufficiently profitable so that market exclusivity is no longer justified.

Even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because competing drugs containing a different active ingredient can be approved for the same condition. In addition, even after an orphan drug is approved, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is clinically superior in that it is shown to be safer, more effective or makes a major contribution to patient care. Orphan drug exclusivity may be lost if the FDA or EMA determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug to meet the needs of patients with the rare disease or condition.

On August 3, 2017, the U.S. Congress passed the FDA Reauthorization Act of 2017, or FDARA. FDARA, among other things, codified the FDA's pre-existing regulatory interpretation to require that a drug sponsor demonstrate the clinical superiority of an orphan drug that is otherwise the same as a previously approved drug for the same rare disease in order to receive orphan drug exclusivity. The new legislation reverses prior precedent holding that the Orphan Drug Act unambiguously requires that the FDA recognize the orphan exclusivity period regardless of a showing of clinical superiority.

The FDA may further reevaluate the Orphan Drug Act and its regulations and policies. This may be particularly true in light of a decision from the Court of Appeals for the 11th Circuit in September 2021 finding that, for the purpose of determining the scope of exclusivity, the term "same disease or condition" means the designated "rare disease or condition" and could not be interpreted by the FDA to mean the "indication or use." We do not know if, when or how the FDA may change the orphan drug regulations and policies in the future, and it is uncertain how any changes might affect our business. Depending on what changes the FDA may make to its orphan drug regulations and policies, our business could be adversely impacted.

Although we have obtained Rare Pediatric Disease Designation for tovinontrine for the treatment of SCD and β-thalassemia, we may not be eligible to receive a priority review voucher in the event that FDA approval does not occur prior to September 30, 2026.

The Rare Pediatric Disease Priority Review Voucher Program, or PRV Program, is intended to incentivize pharmaceutical sponsors to develop drugs for rare pediatric diseases. A sponsor who obtains approval of an NDA or BLA for a rare pediatric disease may be eligible for a Priority Review Voucher, or PRV, under this program, which may be redeemed by the owner of such PRV to obtain priority review for a marketing application. A PRV is fully transferrable and can be sold

to any sponsor, who in turn can redeem the PRV for priority review of a marketing application in six months, compared to the standard timeframe of approximately 10 months.

There is no guarantee that, if we ever submit and obtain approval for our product candidates for which we may obtain rare pediatric disease designation in the future, we will receive a rare pediatric disease PRV. In addition to receiving rare pediatric disease designation, in order to receive a rare pediatric disease PRV, the NDA must be granted priority review, rely on clinical data derived from studies examining a pediatric population and dosages of the drug intended for that population, not seek approval for a different adult indication in the original rare pediatric disease product application and be for a drug that does not include a previously approved active ingredient.

Under current statutory sunset provisions, even if a marketing application meets all of these requirements, the FDA may only award a voucher prior to September 30, 2026 and only if the approved product received rare pediatric disease drug product designation prior to September 30, 2024. We cannot be certain that we will receive approval for any of our rare pediatric disease designated products prior to the statutory sunset date, if ever. Moreover, even if we believe that our marketing application meets the other requirements to be eligible to receive a priority review voucher upon approval, the FDA may disagree. Further, if we do not obtain approval of an NDA for tovinontrine for SCD or β-thalassemia by these dates, and if the PRV Program is not further extended by congressional action, we may not receive a PRV.

A Fast Track designation by the FDA may not lead to a faster development or regulatory review or approval process.

We have received Fast Track designation for tovinontrine from the FDA, and we may seek Fast Track designation for other product candidates we may develop. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track designation. The FDA has broad discretion whether or not to grant this designation, so even if we believe a particular product candidate is eligible for this designation, we cannot be certain that the FDA would decide to grant it. Even if we do receive Fast Track designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track designation if it believes that the designation is no longer supported by data from our clinical development program.

Accelerated approval by the FDA, even if granted for any product candidates does not increase the likelihood that any product candidates will ultimately receive full approval.

We may seek approval of tovinontrine and any other product candidates we may develop using the FDA's accelerated approval pathway. A product may be eligible for accelerated approval if it treats a serious or life-threatening condition and generally provides a meaningful advantage over available therapies. In addition, it must demonstrate an effect on a surrogate endpoint that is reasonably likely to predict clinical benefit or on an intermediate clinical endpoint that can be measured earlier than irreversible morbidity or mortality, or IMM, that is reasonably likely to predict an effect on IMM or other clinical benefit. The FDA makes the determination regarding whether to accept a biomarker as a proposed surrogate endpoint.

Prior to seeking such accelerated approval, we will request feedback from the FDA regarding the eligibility of the drug product candidate for accelerated approval and otherwise evaluate our ability to seek and receive such accelerated approval. As a condition of accelerated approval, the FDA will require that a sponsor of a drug or biologic product candidate receiving accelerated approval perform adequate and well-controlled post-marketing clinical trials. These confirmatory trials must be completed with due diligence and we may be required to evaluate different or additional endpoints in these post-marketing confirmatory trials. In addition, the FDA currently requires as a condition for accelerated approval pre-clearance of promotional materials prior to use, which could adversely impact the timing of the commercial launch of the product.

There can be no assurance that the FDA will agree with our surrogate endpoints or intermediate clinical endpoints, or that we will decide to pursue or submit an NDA for accelerated approval or any other form of expedited development, review or approval. Similarly, there can be no assurance that, after feedback from FDA, we will continue to pursue or apply for accelerated approval or any other form of expedited development, review or approval, even if we initially decide to do so. Furthermore, if we decide to submit an application for accelerated approval or under another expedited regulatory designation, there can be no assurance that such submission or application will be accepted or that any expedited review or approval will be granted on a timely basis, or at all.

Moreover, as noted above, for drugs granted accelerated approval, the FDA requires post-marketing trials to confirm the benefit of the drug. These confirmatory trials must be completed with due diligence. We may be required to evaluate additional or different clinical endpoints in these post-marketing confirmatory trials. These confirmatory trials may require enrollment of more patients than we currently anticipate and will result in additional costs, which may be greater than the

estimated costs we currently anticipate. The FDA may withdraw approval of a product candidate approved under the accelerated approval pathway if, for example, the trial required to verify the predicted clinical benefit of our product candidate fails to verify such benefit or does not demonstrate sufficient clinical benefit to justify the risks associated with the drug. The FDA may also withdraw approval if other evidence demonstrates that our product candidate is not shown to be safe or effective under the conditions of use, we fail to conduct any required post approval trial of our product candidate with due diligence or we disseminate false or misleading promotional materials relating to our product candidate.

A failure to obtain accelerated approval or any other form of expedited development, review or approval for tovinontrine and any other product candidates we may develop, or withdrawal of a product candidate, would result in a longer time period for commercialization of such product candidate, could increase the cost of development of such product candidate and could harm our competitive position in the marketplace.

Even if we do receive accelerated approval, we may not ultimately be able to obtain full FDA approval.

Failure to obtain marketing approval in foreign jurisdictions would prevent any product candidates from being marketed abroad.

In order to market and sell our products in the European Union and many other foreign jurisdictions, we or our potential third-party collaborators must obtain separate marketing approvals and comply with numerous and varying regulatory requirements. The approval procedure varies among countries and can involve additional testing. The time required to obtain approval may differ substantially from that required to obtain FDA approval. The regulatory approval process outside of the United States generally includes all of the risks associated with obtaining FDA approval. In addition, in many countries outside of the United States, it is required that the product be approved for reimbursement before the product can be made available for sale in that country. We or our potential third-party collaborators may not obtain approvals from regulatory authorities outside of the United States on a timely basis, if at all. Approval by the FDA does not ensure approval by regulatory authorities in other countries or jurisdictions, and approval by one regulatory authority outside of the United States does not ensure approval by regulatory authorities in other countries or jurisdictions or by the FDA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in other countries. We may not be able to file for marketing approvals and may not receive necessary approvals to commercialize our products in any market.

Additionally, we could face heightened risks with respect to seeking marketing approval in the United Kingdom as a result of the withdrawal of the United Kingdom from the European Union, commonly referred to as Brexit. The United Kingdom is no longer part of the European Single Market and European Union Customs Union. As of January 1, 2021, the Medicines and Healthcare products Regulatory Agency, or the MHRA, became responsible for supervising medicines and medical devices in Great Britain, comprising England, Scotland and Wales under domestic law, whereas Northern Ireland will continue to be subject to European Union rules under the Northern Ireland Protocol. The MHRA will rely on the Human Medicines Regulations 2012 (SI 2012/1916) (as amended), or the HMR, as the basis for regulating medicines. The HMR has incorporated into the domestic law of the United Kingdom the body of European Union law governing medicinal products that pre-existed prior to the United Kingdom's withdrawal from the European Union. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, may force us to restrict or delay efforts to seek regulatory approval in the United Kingdom for our product candidates, which could significantly and materially harm our business.

We expect that we will be subject to additional risks in commercializing any of our product candidates that receive marketing approval outside the United States, including tariffs, trade barriers and regulatory requirements; economic weakness, including inflation, or political instability in particular foreign economies and markets; compliance with tax, employment, immigration and labor laws for employees living or traveling abroad; foreign currency fluctuations, which could result in increased operating expenses and reduced revenue, and other obligations incident to doing business in another country; and workforce uncertainty in countries where labor unrest is more common than in the United States.

We may seek PRIME Designation in the European Union for one or more of our product candidates but we might not receive such designations and, even if we do, such designations may not lead to a faster development or regulatory review or approval process.

In the European Union, we may seek PRIME designation for our product candidates in the future. PRIME is a voluntary program aimed at enhancing the EMA's role to reinforce scientific and regulatory support in order to optimize development and enable accelerated assessment of new medicines that are of major public health interest with the potential to address unmet medical needs. The program focuses on medicines that target conditions for which there exists no satisfactory

method of treatment in the European Union or even if such a method exists, it may offer a major therapeutic advantage over existing treatments. PRIME is limited to medicines under development and not authorized in the European Union and the applicant intends to apply for an initial marketing authorization application through the centralized procedure. To be accepted for PRIME, a product candidate must meet the eligibility criteria in respect of its major public health interest and therapeutic innovation based on information that is capable of substantiating the claims.

The benefits of a PRIME designation include the appointment of a Committee for Human Medicinal Products rapporteur to provide continued support and help to build knowledge ahead of a marketing authorization application, early dialogue and scientific advice at key development milestones, and the potential to qualify products for accelerated review, meaning reduction in the review time for an opinion on approvability to be issued earlier in the application process. PRIME enables an applicant to request parallel EMA scientific advice and health technology assessment advice to facilitate timely market access. Even if we receive PRIME designation for any of our product candidates, the designation may not result in a materially faster development process, review or approval compared to conventional EMA procedures. Further, obtaining PRIME designation does not assure or increase the likelihood of EMA's grant of a marketing authorization.

In light of the large population of patients with SCD and β-thalassemia who reside in foreign countries, our ability to generate meaningful revenues in those jurisdictions may be limited due to the strict price controls and reimbursement limitations imposed by governments outside of the United States.

In some countries, including for example countries in the European Union, the pricing of prescription pharmaceuticals is subject to governmental control. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a drug. To obtain coverage and reimbursement or pricing approval in some countries, we may be required to conduct a clinical trial that compares the cost-effectiveness of our product candidate to other available therapies. If reimbursement of our product candidates is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be harmed, possibly materially, based on the large population of patients with SCD and β-thalassemia who reside in foreign countries.

Inadequate funding for the FDA, the SEC and other government agencies, including from government shut downs, or other disruptions to these agencies' operations, could hinder their ability to hire and retain key leadership and other personnel, prevent new products and services from being developed or commercialized in a timely manner or otherwise prevent those agencies from performing normal business functions on which the operation of our business may rely, which could negatively impact our business.

The ability of the FDA to review and approve new products can be affected by a variety of factors, including government budget and funding levels, ability to hire and retain key personnel and accept the payment of user fees, and statutory, regulatory and policy changes. Average review times at the FDA have fluctuated in recent years as a result. Disruptions at the FDA and other agencies may also slow the time necessary for new product candidates to be reviewed and/or approved by necessary government agencies, which would adversely affect our business. In addition, government funding of the SEC and other government agencies on which our operations may rely, including those that fund research and development activities, is subject to the political process, which is inherently fluid and unpredictable. For example, over the last several years the U.S. government has shut down several times and certain regulatory agencies, such as the FDA and the SEC, have had to furlough critical FDA, SEC and other government employees and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Further, future government shutdowns could impact our ability to access the public markets and obtain necessary capital in order to properly capitalize and continue our operations.

Separately, in response to the COVID-19 pandemic, a number of companies announced receipt of complete response letters due to the FDA's inability to complete required inspections for their applications. As of May 26, 2021, the FDA noted it was continuing to ensure timely reviews of applications for medical products during the ongoing COVID-19 pandemic in line with its user fee performance goals and conducting mission critical domestic and foreign inspections to ensure compliance of manufacturing facilities with FDA quality standards. However, the FDA may not be able to continue its current pace and review timelines could be extended, including where a pre-approval inspection or an inspection of clinical sites is required and due to the ongoing COVID-19 pandemic and travel restrictions, the FDA is unable to complete such required inspections during the review period. Regulatory authorities outside the United States may adopt similar restrictions or other policy measures in response to the COVID-19 pandemic and may experience delays in their regulatory activities.

Accordingly, if a prolonged government shutdown or other disruption occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business. Future shutdowns or other disruptions could also affect other government agencies such as the SEC, which may also impact our business by delaying review of our public filings, to the extent such review is necessary, and our ability to access the public markets.

Any product candidate for which we obtain marketing approval could be subject to post-marketing restrictions or withdrawal from the market and we may be subject to substantial penalties if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, when and if any of them are approved.

Any product candidate for which we obtain marketing approval, along with the manufacturing processes, post-approval clinical data, labeling, advertising and promotional activities for such product, will be subject to continual requirements of and review by the FDA and other regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, cGMP requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, requirements regarding the distribution of samples to physicians and recordkeeping. Even if marketing approval of a product candidate is granted, the approval may be subject to limitations on the indicated uses for which the product may be marketed or to the conditions of approval, including the requirement to implement a REMS. If any product candidate receives marketing approval, the accompanying label may limit the approved use of our drug, which could limit sales of the product.

The FDA may also impose requirements for costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product, including the adoption and implementation of REMS. The FDA and other agencies, including the Department of Justice, or the DOJ, closely regulate and monitor the post-approval marketing and promotion of drugs to ensure, among other things, that they are marketed and distributed only for the approved indications and in accordance with the provisions of the approved labeling. The FDA and other agencies impose and enforce stringent restrictions on manufacturers' communications regarding off-label use, and if we promote our products beyond their approved indications, we may be subject to enforcement action or prosecution arising from off-label promotion. In September 2021, the FDA published final regulations which describe the types of evidence that the agency will consider in determining the intended use of a drug product. Violations of the FDCA and other statutes and regulations relating to the promotion and advertising of prescription drugs may lead to investigations and enforcement actions alleging violations of federal and state healthcare fraud and abuse laws, including the False Claims Act, as well as state consumer protection laws.

In addition, later discovery of previously unknown adverse events or other problems with our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may have various consequences, including:

- suspension of or restrictions on such products, manufacturers or manufacturing processes;
- restrictions and warnings on the labeling or marketing of a product;
- restrictions on product distribution or use;
- requirements to conduct post-marketing studies or clinical trials;
- warning letters or untitled letters;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- fines, restitution or disgorgement of profits or revenues;
- suspension of any ongoing clinical trials;
- suspension or withdrawal of marketing approvals;
- damage to relationships with any potential collaborators;
- unfavorable press coverage and damage to our reputation;
- refusal to permit the import or export of our products;
- product seizure or detention;
- injunctions or the imposition of civil or criminal penalties; or

- litigation involving patients using our products.

In addition, manufacturers of approved products and those manufacturers' facilities are required to comply with extensive FDA requirements, including ensuring that quality control and manufacturing procedures conform to cGMPs applicable to drug manufacturers or quality assurance standards applicable to medical device manufacturers, which include requirements relating to quality control and quality assurance as well as the corresponding maintenance of records and documentation and reporting requirements. We, any contract manufacturers we may engage in the future, our future collaborators and their contract manufacturers will also be subject to other regulatory requirements, including submissions of safety and other post-marketing information and reports, registration and listing requirements, requirements regarding the distribution of samples to clinicians, recordkeeping, and costly post-marketing studies or clinical trials and surveillance to monitor the safety or efficacy of the product such as the requirement to implement a REMS.

Similar restrictions apply to the approval of our products in the European Union. The holder of a marketing authorization is required to comply with a range of requirements applicable to the manufacturing, marketing, promotion and sale of medicinal products. These include: compliance with the European Union's stringent pharmacovigilance or safety reporting rules, which can impose post-authorization studies and additional monitoring obligations; the manufacturing of authorized medicinal products, for which a separate manufacturer's license is mandatory; and the marketing and promotion of authorized drugs, which are strictly regulated in the European Union and are also subject to European Union Member State laws. The failure to comply with these and other European Union requirements can also lead to significant penalties and sanctions.

We may be subject to certain healthcare laws and regulations, which could expose us to criminal sanctions, civil penalties, contractual damages, reputational harm, fines, disgorgement, exclusion from participation in government healthcare programs, curtailment or restricting of our operations, and diminished profits and future earnings.

Healthcare providers, third-party payors and others will play a primary role in the recommendation and prescription of any products for which we obtain marketing approval. Our future arrangements with healthcare providers and third-party payors will expose us to broadly applicable fraud and abuse and other healthcare laws and regulations that may constrain the business or financial arrangements and relationships through which we market, sell and distribute any products for which we obtain marketing approval. Potentially applicable U.S. federal and state healthcare laws and regulations include the following:

- the federal Anti-Kickback Statute, prohibits, among other things, persons and entities from knowingly and willfully soliciting, offering, receiving or providing remuneration, directly or indirectly, in cash or in kind, to induce or reward either the referral of an individual for, or the purchase, order or recommendation of, any good or service, for which payment may be made under a federal healthcare programs such as Medicare and Medicaid;
- The federal false claims laws, including the civil False Claims Act, impose criminal and civil penalties, including those from civil whistleblower or *qui tam* actions against individuals or entities for knowingly presenting, or causing to be presented to the federal government, claims for payment that are false or fraudulent or making a false statement to avoid, decrease or conceal an obligation to pay money to the federal government;
- the federal Health Insurance Portability and Accountability Act of 1996, or HIPAA, imposes criminal and civil liability for executing or attempting to execute a scheme to defraud any healthcare benefit program;
- HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act, or the HITECH Act, also imposes obligations on certain types of individuals and entities, including mandatory contractual terms, with respect to safeguarding the privacy, security and transmission of individually identifiable health information;
- the federal false statements statute prohibits knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false statement in connection with the delivery of or payment for healthcare benefits, items or services;
- the federal Physician Payments Sunshine Act requires certain manufacturers of drugs, devices, biologics, and medical supplies for which payment is available under Medicare, Medicaid, or the Children's Health Insurance Program (with specific exceptions) to report annually to the U.S. Department of Health and Human Services information related to payments and other transfers of value made by that entity to physicians, other healthcare providers and teaching hospitals and ownership and investment interests held by physicians, other healthcare providers and their family members; and
- analogous state laws and regulations, such as state anti- kickback and false claims laws, and transparency laws, may apply to sales or marketing arrangements, and claims involving healthcare items or services reimbursed by

non-governmental third party payors, including private insurers and some state laws require pharmaceutical companies to comply with the pharmaceutical industry's voluntary compliance guidelines and the relevant compliance guidance promulgated by the federal government, in addition to requiring manufacturers to report information related to payments to physicians and other healthcare providers or marketing expenditures. Many state laws also govern the privacy and security of health information in some circumstances, many of which differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. Foreign laws also govern the privacy and security of health information in many circumstances.

The provision of benefits or advantages to physicians to induce or encourage the prescription, recommendation, endorsement, purchase, supply, order or use of medicinal products is prohibited in the European Union. Payments made to physicians in certain European Union Member States must be publicly disclosed. Moreover, agreements with physicians often must be the subject of prior notification and approval by the physician's employer, his or her competent professional organization and/or the regulatory authorities of the individual European Union Member States. These requirements are provided in the national laws, industry codes or professional codes of conduct applicable in the European Union Member States. Failure to comply with these requirements could result in reputational risk, public reprimands, administrative penalties, fines or imprisonment.

Efforts to ensure that our business arrangements with third parties, and our business generally, will comply with applicable healthcare laws and regulations will involve substantial costs. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. If our operations are found to be in violation of any of these laws or any other governmental regulations that may apply to us, we may be subject to significant civil, criminal and administrative penalties, damages, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, disgorgement, contractual damages, and reputational harm, any of which could substantially disrupt our operations. If any of the physicians or other providers or entities with whom we expect to do business is found not to be in compliance with applicable laws, they may be subject to criminal, civil or administrative sanctions, including exclusions from government funded healthcare programs.

Compliance with global privacy and data security requirements could result in additional costs and liabilities to us or inhibit our ability to collect and process data globally, and the failure to comply with such requirements could subject us to significant lawsuits or fines and penalties, which may have a material adverse effect on our business, financial condition or results of operations.

The regulatory framework for the collection, use, safeguarding, sharing, transfer and other processing of information worldwide is rapidly evolving and is likely to remain uncertain for the foreseeable future. Globally, virtually every jurisdiction in which we operate has established its own data security and privacy frameworks with which we must comply. For example, the collection, use, disclosure, transfer, or other processing of personal data regarding data subjects in the European Union, including personal health data, is subject to the European Union General Data Protection Regulation, or the GDPR, which took effect across all member states of the European Economic Area, or EEA, in May 2018. The GDPR is wide-ranging in scope and imposes numerous requirements on companies that process personal data, including requirements relating to processing health and other sensitive data, obtaining consent of the individuals to whom the personal data relates, providing information to individuals regarding data processing activities, implementing safeguards to protect the security and confidentiality of personal data, providing notification of data breaches, and taking certain measures when engaging third-party processors. The GDPR increases our obligations with respect to clinical trials conducted in the EEA by expanding the definition of personal data to include coded data and requiring changes to informed consent practices and more detailed notices for clinical trial subjects and investigators. In addition, the GDPR also imposes strict rules on the transfer of personal data to countries outside the European Union, including the United States and, as a result, increases the scrutiny that such rules should apply to transfers of personal data from clinical trial sites located in the EEA to the United States. The GDPR also permits data protection authorities to require destruction of improperly gathered or used personal information and/or impose substantial fines for violations of the GDPR, which can be up to four percent of global revenues or 20 million Euros, whichever is greater, and confers a private right of action on data subjects and consumer associations to lodge complaints with supervisory authorities, seek judicial remedies, and obtain compensation for damages resulting from violations of the GDPR. In addition, the GDPR provides that European Union member states may make their own further laws and regulations limiting the processing of personal data, including genetic, biometric or health data.

Given the breadth and depth of changes in data protection obligations, complying with the GDPR's requirements is rigorous and time intensive and requires significant resources and an ongoing review of our technologies, systems and practices, as well as those of any third-party collaborators, service providers, contractors or consultants that process or

transfer personal data collected in the European Union. The GDPR and other changes in laws or regulations associated with the enhanced protection of certain types of sensitive data, such as healthcare data or other personal information from our clinical trials, could require us to change our business practices and put in place additional compliance mechanisms, may interrupt or delay our development, regulatory and commercialization activities and increase our cost of doing business, and could lead to government enforcement actions, private litigation and significant fines and penalties against us and could have a material adverse effect on our business, financial condition or results of operations.

Similar privacy and data security requirements are either in place or underway in the United States. There are a broad variety of data protection laws that may be applicable to our activities, and a range of enforcement agencies at both the state and federal levels that can review companies for privacy and data security concerns based on general consumer protection laws. The Federal Trade Commission and state Attorneys General all are aggressive in reviewing privacy and data security protections for consumers. New laws also are being considered at both the state and federal levels. For example, the California Consumer Privacy Act, or CCPA, which became effective on January 1, 2020, is creating similar risks and obligations as those created by GDPR, although the CCPA does exempt certain information collected as part of a clinical trial subject to the Federal Policy for the Protection of Human Subjects (the Common Rule). Many other states have passed similar legislation. A broad range of legislative measures also have been introduced at the federal level. Accordingly, failure to comply with current and any future federal and state laws regarding privacy and security of personal information could expose us to fines and penalties. We also face a threat of consumer class actions related to these laws and the overall protection of personal data. Even if we are not determined to have violated these laws, investigations into these issues typically require the expenditure of significant resources and generate negative publicity, which could harm our reputation and our business.

Current and future legislation may increase the difficulty and cost for us and any future collaborators to obtain reimbursement for any of our candidate products that do receive marketing approval and our ability to generate revenue will be materially impaired.

In the United States and foreign jurisdictions, there have been a number of legislative and regulatory changes and proposed changes regarding the healthcare system that could prevent or delay marketing approval of our product candidates, restrict or regulate post-approval activities and affect our ability to profitably sell any product candidates for which we obtain marketing approval. We expect that current laws, as well as other healthcare reform measures that may be adopted in the future, may result in more rigorous coverage criteria and in additional downward pressure on the price that we, or any collaborators, may receive for any approved products. If reimbursement of our products is unavailable or limited in scope, our business could be materially harmed.

In March 2010, President Obama signed into law the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act of 2010, or collectively the ACA. In addition, other legislative changes have been proposed and adopted since the ACA was enacted. In August 2011, the Budget Control Act of 2011, among other things, created measures for spending reductions by Congress. A Joint Select Committee on Deficit Reduction, tasked with recommending a targeted deficit reduction of at least $1.2 trillion for the years 2013 through 2021, was unable to reach required goals, thereby triggering the legislation's automatic reduction to several government programs. These changes included aggregate reductions to Medicare payments to providers of up to 2% per fiscal year, which went into effect in April 2013 and will remain in effect through 2031 under the CARES Act. These Medicare sequester reductions have been suspended through the end of March 2022. From April 2022 through June 2022 a 1% sequester cut will be in effect, with the full 2% cut resuming thereafter. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. These laws may result in additional reductions in Medicare and other healthcare funding and otherwise affect the prices we may obtain for any of our product candidates for which we may obtain regulatory approval or the frequency with which any such product candidate is prescribed or used.

Since enactment of the ACA, there have been and continue to be, numerous legal challenges and Congressional actions to repeal and replace provisions of the law. For example, with enactment of the TCJA in 2017, Congress repealed the "individual mandate." The repeal of this provision, which requires most Americans to carry a minimal level of health insurance, became effective in 2019. Further, on December 14, 2018, a U.S. District Court judge in the Northern District of Texas ruled that the individual mandate portion of the ACA is an essential and inseverable feature of the ACA and therefore because the mandate was repealed as part of the TCJA, the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court heard this case on November 10, 2020 and on June 17, 2021, dismissed this action after finding that the plaintiffs do not have standing to challenge the constitutionality of the ACA. Litigation and legislation over the ACA are likely to continue, with unpredictable and uncertain results.

The Trump Administration also took executive actions to undermine or delay implementation of the ACA, including directing federal agencies with authorities and responsibilities under the ACA to waive, defer, grant exemptions from, or delay the implementation of any provision of the ACA that would impose a fiscal or regulatory burden on states, individuals, healthcare providers, health insurers, or manufacturers of pharmaceuticals or medical devices. On January 28, 2021, however, President Biden issued a new Executive Order which directs federal agencies to reconsider rules and other policies that limit Americans' access to health care, and consider actions that will protect and strengthen that access. Under this Order, federal agencies are directed to re-examine: policies that undermine protections for people with pre-existing conditions, including complications related to COVID-19; demonstrations and waivers under Medicaid and the ACA that may reduce coverage or undermine the programs, including work requirements; policies that undermine the Health Insurance Marketplace or other markets for health insurance; policies that make it more difficult to enroll in Medicaid and the ACA; and policies that reduce affordability of coverage or financial assistance, including for dependents.

Current and future legislative efforts may limit the costs for our products, if and when they are licensed for marketing, and that could materially impact our ability to generate revenues.

The prices of prescription pharmaceuticals have also been the subject of considerable discussion in the United States. There have been several recent U.S. congressional inquiries, as well as proposed and enacted state and federal legislation designed to, among other things, bring more transparency to pharmaceutical pricing, review the relationship between pricing and manufacturer patient programs, and reduce the costs of pharmaceuticals under Medicare and Medicaid. In 2020, President Trump issued several executive orders intended to lower the costs of prescription products and certain provisions in these orders have been incorporated into regulations. These regulations include an interim final rule implementing a most favored nation model for prices that would tie Medicare Part B payments for certain physician-administered pharmaceuticals to the lowest price paid in other economically advanced countries, effective January 1, 2021. That rule, however, has been subject to a nationwide preliminary injunction and, on December 29, 2021, the Centers for Medicare & Medicaid Services, or CMS, issued a final rule to rescind it. With issuance of this rule, CMS stated that it will explore all options to incorporate value into payments for Medicare Part B pharmaceuticals and improve beneficiaries' access to evidence-based care.

In addition, in October 2020, the Department of Health and Human Services, or HHS, and the FDA published a final rule allowing states and other entities to develop a Section 804 Importation Program, or SIP, to import certain prescription drugs from Canada into the United States. The final rule is currently the subject of ongoing litigation, but at least six states (Vermont, Colorado, Florida, Maine, New Mexico, and New Hampshire) have passed laws allowing for the importation of drugs from Canada with the intent of developing SIPs for review and approval by the FDA. Further, on November 20, 2020, HHS finalized a regulation removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through pharmacy benefit managers, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a new safe harbor for certain fixed fee arrangements between pharmacy benefit managers and manufacturers, the implementation of which have also been delayed by the Biden administration until January 1, 2023.

At the state level, legislatures are increasingly passing legislation and implementing regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. In addition, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. These measures could reduce the ultimate demand for our products, once approved, or put pressure on our product pricing. We expect that additional state and federal healthcare reform measures will be adopted in the future, any of which could limit the amounts that federal and state governments will pay for healthcare products and services, which could result in reduced demand for any product candidates or additional pricing pressures.

Finally, outside the United States, in some nations, including those of the EU, the pricing of prescription pharmaceuticals is subject to governmental control and access. In these countries, pricing negotiations with governmental authorities can take considerable time after the receipt of marketing approval for a product. To obtain reimbursement or pricing approval in some countries, we or our collaborators may be required to conduct a clinical trial that compares the cost-effectiveness of our product to other available therapies. If reimbursement of our products is unavailable or limited in scope or amount, or if pricing is set at unsatisfactory levels, our business could be materially harmed.

If we or any third-party manufacturers we engage now or in the future fail to comply with environmental, health and safety laws and regulations, we could become subject to fines or penalties or incur costs or liabilities that could harm our business.

We and third-party manufacturers we engage now are, and any third-party manufacturers we may engage in the future will be, subject to numerous environmental, health and safety laws and regulations, including those governing laboratory procedures and the handling, use, storage, treatment and disposal of hazardous materials and wastes. Our operations involve

the use of hazardous and flammable materials, including chemicals and biological materials. Our operations also produce hazardous waste products. We generally contract with third parties for the disposal of these materials and wastes. We cannot eliminate the risk of contamination or injury from these materials. In the event of contamination or injury resulting from our use of hazardous materials, we could be held liable for any resulting damages, and any liability could exceed our resources. Liability under certain environmental laws governing the release and cleanup of hazardous materials is joint and several and could be imposed without regard to fault. We also could incur significant costs associated with civil or criminal fines and penalties or become subject to injunctions limiting or prohibiting our activities for failure to comply with such laws and regulations.

Although we maintain general liability insurance as well as workers' compensation insurance to cover us for costs and expenses we may incur due to injuries to our employees resulting from the use of hazardous materials, this insurance may not provide adequate coverage against potential liabilities. We do not maintain insurance for environmental liability or toxic tort claims that may be asserted against us in connection with our storage or disposal of biological, hazardous or radioactive materials.

In addition, we may incur substantial costs in order to comply with current or future environmental, health and safety laws and regulations. These current or future laws and regulations may impair our research, development or production efforts. Our failure to comply with these laws and regulations also may result in substantial fines, penalties or other sanctions.

Further, with respect to the operations of our current and any future third-party contract manufacturers, it is possible that if they fail to operate in compliance with applicable environmental, health and safety laws and regulations or properly dispose of wastes associated with our products, we could be held liable for any resulting damages, suffer reputational harm or experience a disruption in the manufacture and supply of any product candidates or products. In addition, our supply chain may be adversely impacted if any of our third-party contract manufacturers become subject to injunctions or other sanctions as a result of their non-compliance with environmental, health and safety laws and regulations.

We are subject to anti-corruption laws, as well as export control laws, customs laws, sanctions laws and other laws governing our operations. If we fail to comply with these laws, we could be subject to civil or criminal penalties, other remedial measures and legal expenses, be precluded from developing manufacturing and selling certain products outside the United States or be required to develop and implement costly compliance programs, which could adversely affect our business, results of operations and financial condition.

Our operations are subject to anti-corruption laws, including the U.K. Bribery Act 2010, or Bribery Act, the U.S. Foreign Corrupt Practices Act, or FCPA, and other anti-corruption laws that apply in countries where we do business and may do business in the future. The Bribery Act, FCPA and these other laws generally prohibit us, our officers, and our employees and intermediaries from bribing, being bribed or making other prohibited payments to government officials or other persons to obtain or retain business or gain some other business advantage. Compliance with the FCPA, in particular, is expensive and difficult, particularly in countries in which corruption is a recognized problem. In addition, the FCPA presents particular challenges in the pharmaceutical industry, because, in many countries, hospitals are operated by the government, and doctors and other hospital employees are considered foreign officials. Certain payments to hospitals in connection with clinical trials and other work have been deemed to be improper payments to government officials and have led to FCPA enforcement actions.

We may in the future operate in jurisdictions that pose a high risk of potential Bribery Act or FCPA violations, and we may participate in collaborations and relationships with third parties whose actions could potentially subject us to liability under the Bribery Act, FCPA or local anti-corruption laws. In addition, we cannot predict the nature, scope or effect of future regulatory requirements to which our international operations might be subject or the manner in which existing laws might be administered or interpreted. If we expand our operations outside of the United States, we will need to dedicate additional resources to comply with numerous laws and regulations in each jurisdiction in which we plan to operate.

We are also subject to other laws and regulations governing our international operations, including regulations administered by the governments of the United Kingdom and the United States, and authorities in the European Union, including applicable export control regulations, economic sanctions on countries and persons, customs requirements and currency exchange regulations, collectively referred to as the Trade Control laws. In addition, various laws, regulations and executive orders also restrict the use and dissemination outside of the United States, or the sharing with certain non-U.S. nationals, of information classified for national security purposes, as well as certain products and technical data relating to those products. If we expand our presence outside of the United States, it will require us to dedicate additional resources to

comply with these laws, and these laws may preclude us from developing, manufacturing, or selling certain products and product candidates outside of the United States, which could limit our growth potential and increase our development costs.

There is no assurance that we will be completely effective in ensuring our compliance with all applicable anti-corruption laws, including the Bribery Act, the FCPA or other legal requirements, including Trade Control laws. If we are not in compliance with the Bribery Act, the FCPA and other anti-corruption laws or Trade Control laws, we may be subject to criminal and civil penalties, disgorgement and other sanctions and remedial measures, and legal expenses, which could have an adverse impact on our business, financial condition, results of operations and liquidity. The Securities and Exchange Commission, or SEC, also may suspend or bar issuers from trading securities on U.S. exchanges for violations of the FCPA's accounting provisions. Any investigation of any potential violations of the Bribery Act, the FCPA, other anti-corruption laws or Trade Control laws by United Kingdom, U.S. or other authorities could also have an adverse impact on our reputation, our business, results of operations and financial condition.

Our employees, independent contractors, consultants and vendors may engage in misconduct or other improper activities, including non-compliance with regulatory standards and requirements and insider trading, which could cause significant liability for us and harm our reputation.

We are exposed to the risk of fraud or other misconduct by our employees, independent contractors, consultants and vendors. Misconduct by these partners could include intentional failures to comply with FDA regulations or similar regulations of comparable foreign regulatory authorities, provide accurate information to the FDA or similar foreign regulatory authorities, comply with manufacturing standards, comply with federal and state healthcare fraud and abuse laws and regulations and similar laws and regulations established and enforced by comparable foreign regulatory authorities, report financial information or data accurately or disclose unauthorized activities to us. Employee misconduct could also involve the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. This could include violations of HIPAA, other U.S. federal and state law, and requirements of non-U.S. jurisdictions, including the European Union Data Protection Directive. We are also exposed to risks in connection with any insider trading violations by employees or others affiliated with us. It is not always possible to identify and deter employee misconduct, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws, standards, regulations, guidance or codes of conduct. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business and results of operations, including the imposition of significant fines or other sanctions.

Our internal computer systems, or those of our collaborators or other contractors or consultants, may fail or suffer security breaches, which could result in a material disruption of our product development programs.

Our internal computer systems and those of any collaborators, contractors or consultants are vulnerable to damage from computer viruses, unauthorized access, natural disasters, terrorism, war and telecommunication and electrical failures. Such systems are also vulnerable to service interruptions or to security breaches from inadvertent or intentional actions by our employees, third-party vendors and/or business partners, or from cyberattacks by malicious third parties. Cyber incidents are increasing in their frequency, sophistication and intensity, and have become increasingly difficult to detect. For example, we have experienced attempts at phishing and e-mail fraud with the goal of causing payments to be transmitted to an unintended recipient. Cyber incidents could also include the deployment of harmful malware, ransomware, denial-of-service attacks, unauthorized access to or deletion of files, social engineering and other means to affect service reliability and threaten the confidentiality, integrity and availability of information. The risk of cyber incidents could also be increased by cyberwarfare in connection with the ongoing conflict between Russia and Ukraine, including potential proliferation of malware from the conflict into systems unrelated to the conflict.

While we have not experienced any material system failure, accident, cyber incidents or security breach to date, if such an event were to occur and cause interruptions in our operations, it could result in a material disruption of our development programs and our business operations, whether due to a loss of our trade secrets or other proprietary information or other similar disruptions. For example, the loss of clinical trial data from completed or future clinical trials could result in delays in our regulatory approval efforts and significantly increase our costs to recover or reproduce the data. To the extent that any disruption or security breach were to result in a loss of, or damage to, our data or applications, or inappropriate disclosure of confidential or proprietary information, we could incur liability, our competitive position and reputation could be harmed and the further development and commercialization of tovinontrine and any other product candidates we may develop could be delayed.

Risks Related to Employee Matters and Managing Growth

Our future success depends on our ability to retain key executives and to attract, retain and motivate qualified personnel.

We are highly dependent on the research and development, clinical, financial, operational and other business expertise of our executive officers, as well as the other principal members of our management, scientific and clinical teams. Although we have entered into employment offer letters with our executive officers, each of them may terminate their employment with us at any time. We do not maintain "key person" insurance for any of our executives or other employees. Recruiting and retaining qualified scientific, clinical, manufacturing, accounting, legal and sales and marketing personnel will also be critical to our success.

The loss of the services of our executive officers or other key employees could impede the achievement of our research, development and commercialization objectives and seriously harm our ability to successfully implement our business strategy. Furthermore, replacing executive officers and key employees may be difficult and may take an extended period of time because of the limited number of individuals in our industry with the breadth of skills and experience required to successfully develop, gain regulatory approval of and commercialize products. Competition to hire from this limited pool is intense, and we may be unable to hire, train, retain or motivate these key personnel on acceptable terms given the competition among numerous pharmaceutical and biotechnology companies for similar personnel. We also experience competition for the hiring of scientific and clinical personnel from universities and research institutions. In addition, we rely on consultants and advisors, including scientific and clinical advisors, to assist us in formulating our research and development and commercialization strategy. Our consultants and advisors may be employed by employers other than us and may have commitments under consulting or advisory contracts with other entities that may limit their availability to us. Our success also depends on implementing and maintaining internal controls and the accuracy and timeliness of our financial reporting. If we are unable to continue to attract and retain high quality personnel, our ability to pursue our growth strategy will be limited.

We expect to expand our development and regulatory capabilities and potentially implement sales, marketing and distribution capabilities, and as a result, we may encounter difficulties in managing our growth, which could disrupt our operations.

We expect to experience growth in the number of our employees and the scope of our operations, particularly in the areas of drug development, clinical, regulatory affairs and, if any product candidate receives marketing approval, sales, marketing and distribution. To manage our anticipated future growth, we must continue to implement and improve our managerial, operational and financial systems, expand our facilities and continue to recruit and train additional qualified personnel. Due to our limited financial resources and the limited experience of our management team in managing a company with such anticipated growth, we may not be able to effectively manage the expansion of our operations or recruit and train additional qualified personnel. The expansion of our operations may lead to significant costs and may divert our management and business development resources. Any inability to manage growth could delay the execution of our business plans or disrupt our operations.

Risks Related to Our Common Stock and Our Status as a Public Company

An active trading market for our common stock may not continue to develop or be sustained.

Our shares began trading on the Nasdaq Global Select Market on March 12, 2020. Prior to March 12, 2020, there was no public market for our common stock, and we cannot be certain that an active trading market for our shares will continue to develop or be sustained. As a result, it may be difficult for our stockholders to sell their shares without depressing the market price for the shares or at all.

If securities analysts do not publish or cease publishing research or reports or publish misleading, inaccurate or unfavorable research about our business or if they publish negative evaluations of our stock, the price and trading volume of our stock could decline.

The trading market for our common stock relies, in part, on the research and reports that industry or financial analysts publish about us or our business. We do not have control over these analysts. There can be no assurance that existing analysts will continue to cover us or that new analysts will begin to cover us. There is also no assurance that any covering analyst will provide favorable coverage. If one or more of the analysts covering our business downgrade their evaluations of our stock or publish inaccurate or unfavorable research about our business, or provides more favorable relative recommendations about our competitors, the price of our stock could decline. If one or more of these analysts cease to cover our stock, we could lose visibility in the market for our stock, which in turn could cause our stock price and trading volume to decline.

The price of our common stock may be volatile and fluctuate substantially, which could result in substantial losses for our stockholders.

Our stock price is likely to be volatile. The stock market in general and the market for smaller biopharmaceutical companies in particular have experienced extreme volatility that has often been unrelated to the operating performance of particular companies. As a result of this volatility, our stockholders may not be able to sell their common stock at or above the price paid for their shares. The market price for our common stock may be influenced by many factors, including:

- results of or developments in preclinical studies and clinical trials of tovinontrine and any other product candidates we may develop or those of our competitors or potential collaborators;
- timing of the results of our preclinical studies and clinical trials or those of our competitors;
- our success in commercializing any product candidates, if and when approved;
- the success of competitive products or technologies;
- regulatory or legal developments in the United States and other countries;
- developments or disputes concerning patent applications, issued patents or other intellectual property or proprietary rights;
- the recruitment or departure of key personnel;
- the level of expenses related to tovinontrine and any other product candidates we may develop;
- the results of our efforts to discover, develop, acquire or in-license products, product candidates, technologies or data referencing rights, the costs of commercializing any such products and the costs of development of any such product candidates or technologies;
- actual or anticipated changes in estimates as to financial results, development timelines or recommendations by securities analysts;
- variations in our financial results or the financial results of companies that are perceived to be similar to us;
- sales of common stock by us, our executive officers, directors or principal stockholders, or others;
- changes in the structure of healthcare payment systems;
- market conditions in the pharmaceutical and biotechnology sectors;
- general economic, industry and market conditions, including, without limitation, the current adverse impact of the COVID-19 pandemic and political and economic instability caused by the current conflict between Russia and Ukraine and economic sanctions adopted in response to the conflict; and
- the other factors described in this “Risk Factors” section.

In the past, following periods of volatility in the market price of a company’s securities, securities class-action litigation has often been instituted against that company. Any lawsuit to which we are a party, with or without merit, may result in an unfavorable judgment. We also may decide to settle lawsuits on unfavorable terms. Any such negative outcome could result in payments of substantial damages or fines, damage to our reputation or adverse changes to our offerings or business practices. Such litigation may also cause us to incur other substantial costs to defend such claims and divert management’s attention and resources.

Our executive officers, directors and principal stockholders, if they choose to act together, have the ability to control all matters submitted to stockholders for approval.

As of January 15, 2022, our executive officers and directors and our stockholders who owned more than 5% of our outstanding common stock, in the aggregate, beneficially owned shares representing approximately 51% of our common stock. As a result, if these stockholders were to choose to act together, they would be able to control all matters submitted to our stockholders for approval, as well as our management and affairs. For example, these persons, if they choose to act together, would control the election of directors and approval of any merger, consolidation or sale of all or substantially all of our assets.

This concentration of ownership control may:

- delay, defer or prevent a change in control;
- entrench our management and board of directors; or
- delay or prevent a merger, consolidation, takeover or other business combination involving us that other stockholders may desire.

This concentration of ownership may also adversely affect the market price of our common stock.

We have broad discretion in the use of our cash, cash equivalents and investments and may not use them effectively.

Our management has broad discretion in the application of our cash, cash equivalents and investments and could use such funds in ways that do not improve our results of operations or enhance the value of our common stock. The failure by our management to apply these funds effectively could result in financial losses that could cause the price of our common stock to decline and delay the development of tovinontrine and any other product candidates we may develop. Pending their use, we may invest our cash, cash equivalents and investments in a manner that does not produce income or that loses value.

Because we do not anticipate paying any cash dividends on our capital stock in the foreseeable future, capital appreciation, if any, will be the sole source of gain for our stockholders.

We have never declared or paid cash dividends on our capital stock. We currently intend to retain all of our future earnings, if any, to finance the growth and development of our business. As a result, capital appreciation, if any, of our common stock will be the sole source of gain for our stockholders for the foreseeable future.

Sales of a substantial number of shares of our common stock in the public market could cause our stock price to fall, even if our business is doing well.

Sales of a substantial number of shares of our common stock in the public market, or the perception in the market that the holders of a large number of shares intend to sell shares, could reduce the market price of our common stock, impair our ability to raise capital through the sale of additional equity securities, and make it more difficult for our stockholders to sell their common stock at a time and price that they deem appropriate. Persons who were our stockholders prior to our initial public offering continue to hold a substantial number of shares of our common stock. If such persons sell, or indicate an intention to sell, substantial amounts of our common stock in the public market, the trading price of our common stock could decline.

We currently have on file with the SEC a universal shelf registration statement which allows us to offer and sell registered common stock, preferred stock, debt securities, warrants and/or units from time to time pursuant to one or more offerings up to an aggregate of $200 million, at prices and terms to be determined at the time of sale, subject to restrictions that may apply from time to time on our ability to utilize the shelf registration statement to sell more than one-third of the market value of our public float, meaning the aggregate market value of voting and non-voting common stock held by non-affiliates, in any trailing 12-month period. In July 2021, we issued and sold 8,333,333 shares of common stock with aggregate gross proceeds of approximately $50 million under this universal shelf registration statement.

Moreover, holders of an aggregate of 11,005,600 shares of our common stock have rights, subject to specified conditions, to require us to file registration statements covering their shares or to include their shares in registration statements that we may file for ourselves or other stockholders. We have also registered all 3,767,067 shares of common stock that we may issue under our equity compensation plans and such shares can be freely sold in the public market upon issuance, subject to volume limitations applicable to affiliates, vesting arrangements and exercise of options.

We are an "emerging growth company" and a "smaller reporting company," and the reduced disclosure requirements applicable to emerging growth companies and smaller reporting companies may make our common stock less attractive to investors.

We are an "emerging growth company," or EGC, as defined in the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. We may remain an EGC until December 31, 2025, although if the market value of our common stock that is held by non-affiliates exceeds $700.0 million as of any June 30 before that time or if we have annual gross revenues of $1.07 billion or more in any fiscal year, we would cease to be an EGC as of December 31 of the applicable year. We also would cease to be an EGC if we issue more than $1.0 billion of non-convertible debt over a three-year period. For so long as we

remain an EGC, we are permitted and intend to rely on exemptions from certain disclosure requirements that are applicable to other public companies that are not EGCs. These exemptions include:

- being permitted to provide only two years of audited financial statements, in addition to any required unaudited interim financial statements, with correspondingly reduced "Management's Discussion and Analysis of Financial Condition and Results of Operations" disclosure;
- not being required to comply with the auditor attestation requirements in the assessment of our internal control over financial reporting;
- not being required to comply with any requirement that may be adopted by the Public Company Accounting Oversight Board regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements;
- reduced disclosure obligations regarding executive compensation; and
- exemptions from the requirements of holding a nonbinding advisory vote on executive compensation and stockholder approval of any golden parachute payments not previously approved.

We may choose to take advantage of some or all of the available exemptions. We cannot predict whether investors will find our common stock less attractive if we rely on these exemptions. If some investors find our common stock less attractive as a result, there may be a less active trading market for our common stock and our stock price may be more volatile.

In addition, the JOBS Act permits an EGC to take advantage of an extended transition period to comply with new or revised accounting standards applicable to public companies until those standards would otherwise apply to private companies. We have elected to take advantage of such extended transition period, which means that when a standard is issued or revised and it has different application dates for public or private companies, we will adopt the new or revised standard at the time private companies adopt the new or revised standard and will do so until such time that we either (1) irrevocably elect to "opt out" of such extended transition period or (2) no longer qualify as an EGC.

We are also a smaller reporting company, and we will remain a smaller reporting company until the fiscal year following the determination that either (i) our voting and non-voting common shares held by non-affiliates is more than $250 million measured on the last business day of our second fiscal quarter, or (ii) our annual revenues are less than $100 million during the most recently completed fiscal year and our voting and non-voting common shares held by non-affiliates is more than $700 million measured on the last business day of our second fiscal quarter. Similar to emerging growth companies, smaller reporting companies have reduced disclosure obligations, such as an exemption from providing selected financial data and an ability to provide simplified executive compensation information and only two years of audited financial statements.

We have incurred and will continue to incur increased costs as a result of operating as a public company, and our management has devoted and will continued to be required to devote substantial time to new compliance initiatives and corporate governance practices.

As a public company, and particularly after we are no longer an EGC, we will incur significant legal, accounting and other expenses that we did not incur as a private company. The Sarbanes-Oxley Act of 2002, the Dodd-Frank Wall Street Reform and Consumer Protection Act, the listing requirements of the Nasdaq Global Select Market and other applicable securities rules and regulations impose various requirements on public companies, including establishment and maintenance of effective disclosure and financial controls and corporate governance practices. Our management will need to devote a substantial amount of time to these compliance initiatives. Moreover, these rules and regulations will increase our legal and financial compliance costs, particularly as we hire additional financial and accounting employees to meet public company internal control and financial reporting requirements, and will make some activities more time-consuming and costly.

We continue to evaluate these rules and regulations, and cannot predict or estimate the amount of additional costs we may incur or the timing of such costs. These rules and regulations are often subject to varying interpretations, in many cases due to their lack of specificity, and, as a result, their application in practice may evolve over time as new guidance is provided by regulatory and governing bodies. This could result in continuing uncertainty regarding compliance matters and higher costs necessitated by ongoing revisions to disclosure and governance practices.

Pursuant to Section 404 of the Sarbanes-Oxley Act of 2002, or Section 404, we are required to furnish a report by our management on our internal control over financial reporting with our Annual Reports on Form 10-K. However, while we remain an EGC, we will not be required to include an attestation report on internal control over financial reporting issued by our independent registered public accounting firm. To comply with Section 404, we are engaged in a process to document and evaluate our internal control over financial reporting, which is both costly and challenging. In this regard, we will need to continue to dedicate internal resources, including through hiring additional financial and accounting personnel, potentially engage outside consultants and adopt a detailed work plan to assess and document the adequacy of internal control over financial reporting, continue steps to improve control processes as appropriate, validate through testing that controls are functioning as documented and implement a continuous reporting and improvement process for internal control over financial reporting. Despite our efforts, there is a risk that we will not be able to conclude, within the prescribed timeframe or at all, that our internal control over financial reporting is effective as required by Section 404. If we identify one or more material weaknesses in our internal control over financial reporting, it could result in an adverse reaction in the financial markets due to a loss of confidence in the reliability of our financial statements.

If we fail to maintain an effective system of internal control over financial reporting, we may not be able to accurately report our financial results or prevent fraud. As a result, stockholders could lose confidence in our financial and other public reporting, which would harm our business and the trading price of our common stock.

Effective internal controls over financial reporting are necessary for us to provide reliable financial reports and, together with adequate disclosure controls and procedures, are designed to prevent fraud. Any failure to implement required new or improved controls, or difficulties encountered in their implementation could cause us to fail to meet our reporting obligations. In addition, any testing by us conducted in connection with Section 404 of the Sarbanes-Oxley Act of 2002, or any subsequent testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses or that may require prospective or retroactive changes to our financial statements or identify other areas for further attention or improvement. Inferior internal controls could also cause investors to lose confidence in our reported financial information, which could have a negative effect on the trading price of our stock.

We are required to disclose changes made in our internal controls and procedures on a quarterly basis and our management is required to assess the effectiveness of these controls annually. However, for as long as we are an “emerging growth company” under the JOBS Act, our independent registered public accounting firm will not be required to attest to the effectiveness of our internal controls over financial reporting pursuant to Section 404. We could be an “emerging growth company” for up to five years. An independent assessment of the effectiveness of our internal controls over financial reporting could detect problems that our management’s assessment might not. Undetected material weaknesses in our internal controls over financial reporting could lead to financial statement restatements and require us to incur the expense of remediation.

Our disclosure controls and procedures may not prevent or detect all errors or acts of fraud.

As a public company, we are subject to certain reporting requirements of the Exchange Act. Our disclosure controls and procedures are designed to reasonably assure that information required to be disclosed by us in reports we file or submit under the Exchange Act is accumulated and communicated to management, recorded, processed, summarized and reported within the time periods specified in the rules and forms of the SEC. We believe that any disclosure controls and procedures or internal controls and procedures, no matter how well conceived and operated, can provide only reasonable, not absolute, assurance that the objectives of the control system are met. These inherent limitations include the realities that judgments in decision-making can be faulty, and that breakdowns can occur because of simple error or mistake. Additionally, controls can be circumvented by the individual acts of some persons, by collusion of two or more people or by an unauthorized override of the controls. Accordingly, because of the inherent limitations in our control system, misstatements or insufficient disclosures due to error or fraud may occur and not be detected.

Changes in tax laws or in their implementation or interpretation may adversely affect our business and financial condition.

Changes in tax law may adversely affect our business or financial condition. On December 22, 2017, the U.S. government enacted the TCJA, which significantly reformed the Code. The TCJA, as amended by the CARES Act, among other things, contained significant changes to corporate taxation, including a reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, the limitation of the tax deduction for net interest expense to 30% of adjusted taxable income (except for certain small businesses), the limitation of the deduction for NOLs to 80% of current year taxable

income and the elimination of NOL carrybacks, in each case, for NOLs arising in taxable years beginning after December 31, 2017 (though any such NOLs may be carried forward indefinitely and such NOLs arising in taxable years beginning before January 1, 2021 are generally eligible to be carried back up to five years), the imposition of a one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, the elimination of U.S. tax on foreign earnings (subject to certain important exceptions), the allowance of immediate deductions for certain new investments instead of deductions for depreciation expense over time, and the modification or repeal of many business deductions and credits.

In addition to the CARES Act, as part of Congress' response to the COVID-19 pandemic, economic relief legislation has been enacted in 2020 and 2021 containing tax provisions. Regulatory guidance under the TCJA and such additional legislation, is and continues to be forthcoming, and such guidance could ultimately increase or lessen the impact of these laws on our business and financial condition. Also, as a result of the changes in the U.S. presidential administration and control of the U.S. Senate in 2021, additional tax legislation may be enacted; any such additional legislation could have an impact on us. In addition, it is uncertain if and to what extent various states will conform to the TCJA and additional tax legislation.

Provisions in our corporate charter documents and under Delaware law could make an acquisition of our company, which may be beneficial to our stockholders, more difficult and may prevent attempts by our stockholders to replace or remove our current directors and members of management.

Provisions in our certificate of incorporation and our bylaws may discourage, delay or prevent a merger, acquisition or other change in control of our company that stockholders may consider favorable, including transactions in which our stockholders might otherwise receive a premium for their shares. These provisions could also limit the price that investors might be willing to pay in the future for shares of our common stock, thereby depressing the market price of our common stock. In addition, because our board of directors is responsible for appointing the members of our management team, these provisions may frustrate or prevent any attempts by our stockholders to replace or remove our current management by making it more difficult for stockholders to replace members of our board of directors. Among other things, these provisions:

- establish a classified board of directors such that only one of three classes of directors is elected each year;
- allow the authorized number of our directors to be changed only by resolution of our board of directors;
- limit the manner in which stockholders can remove directors from our board of directors;
- establish advance notice requirements for stockholder proposals that can be acted on at stockholder meetings and nominations to our board of directors;
- require that stockholder actions must be effected at a duly called stockholder meeting and prohibit actions by our stockholders by written consent;
- limit who may call stockholder meetings;
- authorize our board of directors to issue preferred stock without stockholder approval, which could be used to institute a "poison pill" that would work to dilute the stock ownership of a potential hostile acquirer, effectively preventing acquisitions that have not been approved by our board of directors; and
- require the approval of the holders of at least 75% of the votes that all our stockholders would be entitled to cast to amend or repeal specified provisions of our certificate of incorporation or bylaws.

Moreover, because we are incorporated in Delaware, we are governed by the provisions of Section 203 of the Delaware General Corporation Law, or the DGCL, which prohibits a person who owns in excess of 15% of our outstanding voting stock from merging or combining with us for a period of three years after the date of the transaction in which the person acquired in excess of 15% of our outstanding voting stock, unless the merger or combination is approved in a prescribed manner.

Our certificate of incorporation designates the state courts in the State of Delaware as the sole and exclusive forum for certain types of actions and proceedings that may be initiated by our stockholders, which could discourage lawsuits against the company and our directors, officers and employees.

Our certificate of incorporation provides that, unless we consent in writing to the selection of an alternative forum, the Court of Chancery of the State of Delaware (or, if the Court of Chancery of the State of Delaware does not have jurisdiction, the federal district court for the District of Delaware) will be the sole and exclusive forum for the following types of proceedings: (1) any derivative action or proceeding brought on our behalf, (2) any action asserting a claim of breach of a fiduciary duty owed by any of our directors, officers, employees or stockholders to our company or our stockholders, (3) any action asserting a claim arising pursuant to any provision of the DGCL or as to which the DGCL confers jurisdiction on the Court of Chancery of the State of Delaware or (4) any action asserting a claim arising pursuant to any provision of our certificate of incorporation or bylaws (in each case, as they may be amended from time to time) or governed by the internal affairs doctrine. These choice of forum provisions will not apply to suits brought to enforce a duty or liability created by the Securities Act, the Exchange Act or any other claim for which federal courts have exclusive jurisdiction.

These exclusive forum provisions may limit the ability of our stockholders to bring a claim in a judicial forum that such stockholders find favorable for disputes with us or our directors, officers or employees, which may discourage such lawsuits against us and our directors, officers and employees. Alternatively, if a court were to find the choice of forum provisions contained in our certificate of incorporation to be inapplicable or unenforceable in an action, we may incur additional costs associated with resolving such action in other jurisdictions, which could materially adversely affect our business, financial condition and operating results.

Item 1B. Unresolved Staff Comments.

Not applicable.

Item 2. Properties.

Our principal facilities consist of office space. Our headquarters consists of approximately 4,210 square feet of office space in Boston, Massachusetts under a lease that we entered into in May 2019. In June 2021, we entered into an amendment to the lease agreement pursuant to which we will lease an additional 5,026 square feet of office space, brining our total leased space to 9,236 square feet. We expect the lease for this additional space to commence by the end of March 2022. The lease covering the entire premises will continue until March 2027, with an option to extend the term for five years through March 2032. In addition, we have a right of first option to lease an additional 2,069 square feet of the premises if such space becomes available during the term of the lease. We believe this office space will be sufficient to meet our needs for the foreseeable future and that suitable additional space will be available as and when needed.

Item 3. Legal Proceedings.

We are not party to any material legal proceedings.

Item 4. Mine Safety Disclosures.

Not applicable.

PART II

Item 5. Market for Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities.

Market Information

Our common stock is publicly traded on The Nasdaq Global Market under the symbol "IMRA."

Holders

As of January 15, 2022, there were approximately 52 holders of record of our common stock. The actual number of stockholders is greater than this number of record holders, and includes stockholders who are beneficial owners, but whose shares are held in street name by brokers and other nominees.

Dividend Policy

We have never declared or paid cash dividends on our common stock. We currently intend to retain all available funds and any future earnings to fund the development and expansion of our business, and we do not anticipate paying any cash dividends in the foreseeable future. Any future determination to declare and pay dividends will be made at the discretion of our board of directors and will depend on then-existing conditions, including our results of operations, financial condition, contractual restrictions, capital requirements, business prospects and other factors our board of directors may deem relevant

Use of Proceeds from Initial Public Offering

On March 16, 2020, we received aggregate net proceeds from our initial public offering of our common stock, or IPO, inclusive of the underwriters' option to purchase additional shares, of approximately $76.5 million, after deducting $6.1 million of underwriting discounts and commissions and $3.9 million of other offering expenses payable by us. The offer and sale of all of the shares of our common stock in our IPO were registered under the Securities Act pursuant to a registration statement on Form S-1 (File No. 333-236465), which was declared effective by the Securities and Exchange Commission on March 11, 2020. We have used approximately $37.7 million of the net proceeds from the IPO as of December 31, 2021. We have invested the unused net proceeds from the offering in money market accounts. There has been no material change in our planned use of the net proceeds from our IPO as described in our final prospectus filed pursuant to Rule 424(b)(4) under the Securities Act with the SEC on March 12, 2020.

Item 6. [Reserved]

Item 7. Management's Discussion and Analysis of Financial Condition and Results of Operations.

You should read the following discussion and analysis of our financial condition and results of operations together with our consolidated financial statements and related notes appearing elsewhere in this Annual Report on Form 10-K. Some of the information contained in this discussion and analysis or set forth elsewhere in this Annual Report on Form 10-K, including information with respect to our plans and strategy for our business and related financing, includes forward-looking statements that involve risks and uncertainties. As a result of many factors, including those factors set forth in the "Risk Factors" section of this Form Annual Report on Form 10-K, our actual results could differ materially from the results described in or implied by the forward-looking statements contained in the following discussion and analysis.

Business Overview

We are a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin, known as hemoglobinopathies, and other serious diseases. Our pipeline is built on the differentiated therapeutic potential of our lead product candidate, tovinontrine (IMR-687), which is an oral, highly selective, potent small molecule inhibitor of phosphodiesterase-9, or PDE9. Tovinontrine is currently in Phase 2b clinical development for the treatment of sickle cell disease, or SCD, and β-thalassemia and we expect to begin clinical development of tovinontrine in heart failure with preserved ejection fraction, or HFpEF, in the second quarter of 2022. We are also advancing IMR-261, an oral activator of nuclear factor erythroid 2–related factor 2, or Nrf2.

Tovinontrine (IMR-687**)**

Our lead candidate, tovinontrine, is a highly selective and potent small molecule inhibitor of PDE9.

SCD Program

We are currently conducting the Ardent Phase 2b clinical trial of tovinontrine, a randomized, double-blind, placebo-controlled trial in approximately 115 adult patients with SCD. We have completed enrollment in the Ardent clinical trial and expect to report interim data from this trial in the first week of April 2022 and final data in the second half of 2022. In November 2021, we made the decision to change the primary endpoint of the Ardent trial to annualized rate of vaso-occlusive crises, or VOCs, following a written recommendation from the FDA. Fetal hemoglobin, or HbF, response, which was previously the primary endpoint, will continue to be evaluated as a key secondary endpoint.

The Ardent trial follows completion of our Phase 2a clinical trial of tovinontrine in SCD, which demonstrated a well-tolerated safety profile for tovinontrine and potential benefits from tovinontrine with respect to VOCs. Changes in SCD-related biomarkers were variable.

We are also conducting a long-term open label extension, or OLE, clinical trial of tovinontrine, which is comprised of patients who completed our Phase 2a clinical trial of tovinontrine. Data from the OLE trial presented at the American Society of Hematology (ASH) Annual Meeting in December 2021 demonstrated a well-tolerated safety profile for tovinontrine, potential benefits from tovinontrine with respect to VOCs and improvements in certain SCD-related biomarkers, including HbF and F-cells, through 12 months of treatment on the OLE trial.

In the second quarter of 2022, we expect to initiate a new, long-term OLE trial of tovinontrine for patients who complete the Ardent Phase 2b clinical trial in SCD. In addition to patients from the Ardent trial, we expect patients from the ongoing Phase 2a OLE trial to roll over into this new OLE trial, resulting in one OLE trial with patients from both the Phase 2a clinical trial and the Ardent Phase 2b clinical trial.

ß-thalassemia Program

We are also conducting the Forte Phase 2b clinical trial of tovinontrine, a randomized, double-blind, placebo-controlled trial in approximately 120 transfusion dependent, or TDT, and non-transfusion dependent, or NTDT, patients with ß-thalassemia. In November 2021, we presented data from a pre-specified interim analysis from the Forte trial in TDT patients. The interim analysis data demonstrated a well-tolerated safety profile for tovinontrine and a trend for reduced transfusion burden in the higher dose cohort. We expect to report additional interim data for TDT and NTDT patients from the Forte trial in the first week of April 2022 and data from the final analysis of the Forte clinical trial in the second half of 2022.

HFpEF Program

In the second quarter of 2022, we expect to dose the first patient in the SP9IN Phase 2 clinical trial of tovinontrine in HFpEF. The SP9IN trial will be a randomized, placebo-controlled trial of approximately 170 patients 45 years of age or older with enriched PDE9 expression and persistent symptoms of HFpEF. The primary endpoint of the trial will be the change in N-terminal pro b-type natriuretic peptide, or NT-proBNP, levels.

IMR-261

We have commenced research activities for IMR-261 (formerly CXA-10), an oral, clinic-ready activator Nrf2. In pre-clinical models of SCD, IMR-261 was observed to activate expression of HbF and reduce VOCs. Furthermore, in a preclinical model of ß-thalassemia, IMR-261 was observed to increase hemoglobin and enhance red blood cell, or RBC, maturation. We have initiated work on drug product manufacturing for IMR-261 as we explore potential clinical development paths in hemoglobinopathies, iron disorders and potentially other areas.

Prior to its acquisition by Imara, IMR-261 was evaluated by Complexa, Inc. in Phase 2 clinical trials in focal segmental glomerulosclerosis, or FSGS, and pulmonary arterial hypertension, or PAH, and independent medical literature suggests potential in a broad array of RBC diseases, including disorders of hemoglobin, and iron overload diseases.

Financial Overview

Since our inception in 2016, our operations have focused on organizing and staffing our company, business planning, raising capital, developing our technology, undertaking preclinical studies and clinical trials of tovinontrine and acquiring and commencing preclinical studies for IMR-261. To date, we have funded our operations primarily through the sale of common stock and the sale of convertible preferred stock.

In February 2020 we effected a 1-for-6.299 reverse stock split of our common stock. All historical share and per share information shown herein and in our consolidated financial statements and related notes have been retroactively adjusted to give effect to the reverse stock split.

On April 1, 2021, we filed a shelf registration statement on Form S-3, or the Shelf, with the SEC in relation to the registration and potential future issuance of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in the aggregate amount of up to $200.0 million. The Shelf was declared effective on April 8, 2021. We also simultaneously entered into a sales agreement, or the Sales Agreement, with Cantor Fitzgerald & Co, LLC, or Cantor, as sales agent, providing for the offering, issuance and sale by us of up to an aggregate $75.0 million of our common stock from time to time in “at-the-market” offerings under the Shelf. As of December 31, 2021, we have issued and sold 231,291 shares of common stock under the Sales Agreement, resulting in net proceeds of $1.4 million after deducting commissions and offering expenses.

On July 16, 2021, we completed a public offering of shares of our common stock and issued and sold 8,333,333 shares of common stock at a public offering price of $6.00 per share, resulting in net proceeds of $46.8 million after deducting underwriting discounts and commissions and estimated offering expenses.

We have incurred significant operating losses since inception. Our losses from operations were $51.4 million and $41.7 million for the years ended December 31, 2021, and 2020, respectively. As of December 31, 2021, we had an accumulated deficit of approximately $147.5 million. We expect to continue to incur significant operating losses for the foreseeable future, as we advance tovinontrine and any product candidates we may develop in the future from discovery through preclinical development and clinical trials and seek regulatory approval of our product candidates. We expect to incur significant expenses related to maintaining and expanding our intellectual property portfolio, hiring additional research and development and business personnel and operating as a public company. In addition, our losses from operations may fluctuate significantly from quarter-to-quarter and year-to-year, depending on the timing of our clinical trials and our expenditures on other research and development activities.

We do not have any products approved for sale. We will not generate revenue from product sales unless and until we successfully complete clinical development and obtain regulatory approval for tovinontrine or any future product candidate. In addition, if we obtain regulatory approval for tovinontrine or any future product candidate and to the extent that we engage in commercialization activities on our own, we expect to incur significant expenses related to developing our commercialization capability to support product sales, marketing, manufacturing, and distribution activities.

As a result, we will need substantial additional funding to support our continuing operations and pursue our growth strategy. Until such time as we can generate significant revenue from product sales, if ever, we expect to finance our operations through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We may be unable to raise additional funds or enter into other arrangements when needed on acceptable terms, or at all. Our failure to raise capital or enter into such agreements as, and when, needed, could have a material adverse effect on our business, results of operations, and financial condition. We will need to generate significant revenue to achieve profitability, and we may never do so.

Because of the numerous risks and uncertainties associated with product development, we are unable to predict the timing or amount of increased expenses or when or if we will be able to achieve or maintain profitability. Even if we are able to generate product sales, we may not become profitable. If we fail to become profitable or are unable to sustain profitability on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce or terminate our operations.

As of December 31, 2021 we had $90.3 million in cash, cash equivalents and investments. We believe that though our cash, cash equivalents and investments as of December 31, 2021 will enable us to fund our operating expenses and capital expenditure requirements substantially through the first quarter of 2023, there is substantial doubt about our ability to continue as a going concern within one year after the issuance date of the consolidated financial statements. See "—Liquidity and Capital Resources."

Impact of COVID-19 Pandemic

In December 2019, a novel strain of coronavirus, called COVID-19, emerged and has now spread globally. The COVID-19 pandemic is ongoing and its impact continues to evolve as of the date of this Annual Report on Form 10-K. We continue to actively monitor the impact of the COVID-19 pandemic on our financial condition, liquidity, operations, suppliers, industry and workforce.

Although we have not experienced any significant adverse impact from the COVID-19 pandemic on our financial condition, results of operations or liquidity as of the date of this Annual Report on Form 10-K, the COVID-19 pandemic has resulted in disruptions to our clinical trial operations, including some missed and incomplete patient visits in our completed Phase 2a clinical trial of tovinontrine in SCD, delays to some patient visits in our OLE clinical trial in SCD, as well as site activation and enrollment delays and delays in review of our regulatory submissions with respect to our Ardent and Forte clinical trials of tovinontrine in SCD and ß-thalassemia. More recently, we have also experienced some disruptions with the supply chain of third-party vendors who assist us in the conduct of our clinical trials. In addition, many of our employees are currently working remotely.

Our financial condition, results of operations and liquidity could be negatively impacted by the COVID-19 pandemic in future periods. The extent to which the COVID-19 pandemic impacts our business will depend on future developments, which remain uncertain and cannot be predicted, including new information that may emerge concerning the continued severity of COVID-19 and variants of COVID-19 and the actions to contain COVID-19 or treat its impact, among others. As the COVID-19 pandemic continues, it may have an adverse effect on our results of future operations, financial position and liquidity, and on our ability to access capital. Even after the COVID-19 pandemic has subsided, we may continue to experience adverse impacts to our business as a result of any economic recession or depression that has occurred or may occur in the future.

Lundbeck License Agreement

In April 2016, we entered into an agreement with H. Lundbeck A/S, or Lundbeck, for a worldwide license under certain patent rights and certain know-how owned or otherwise controlled by Lundbeck within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies, which we refer to as the field. The agreement grants us an exclusive license under the licensed technology, including the right to grant sublicenses with certain restrictions, to research, develop, make, have made, use, sell, have sold, offer to sell, import, export and commercialize any product comprising or containing certain PDE9 inhibitors, in the field. The agreement also grants us a non-exclusive license under the licensed technology to research and develop, and make, have made, use, import and export for purposes of enabling such research and development, enhancements, improvements, modifications or derivatives to licensed products, until but not beyond a specified pre-commercialization developmental stage with respect to each such enhancement, improvement, modification or derivative. Under the agreement, we have made cash payments totaling $1.8 million to date, consisting of an upfront payment and ongoing milestone

payments, and also issued shares of our common stock as described in Note 14 of the notes to our consolidated financial statements in this Annual Report on Form 10-K. We are obligated to make milestone payments to Lundbeck aggregating up to $23.5 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any licensed product and $11.8 million upon the achievement of specified clinical, regulatory and first commercial sale milestones by any IMARA product that is or comprises a PDE9 inhibitor but is not a licensed product, or a PDE9 product, if any. We are obligated to pay tiered royalties of low-to-mid single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of licensed products, and tiered royalties of low single-digit percentages to Lundbeck based on our, and any of our affiliates' and sublicensees', net sales of PDE9 products, if any. See "Business—License and Acquisition Agreements" for a further description of the license agreement with Lundbeck.

Financial Operations Overview

Revenue

We have not generated any revenue since our inception and do not expect to generate any revenue from the sale of products in the near future, if at all. If our development efforts for tovinontrine or additional product candidates that we may develop in the future are successful and result in marketing approval or if we enter into collaboration or license agreements with third parties, we may generate revenue in the future from a combination of product sales or payments from such collaboration or license agreements.

Operating Expenses

Research and Development. Research and development expenses consist primarily of costs incurred in connection with the preclinical and clinical development and manufacture of tovinontrine, and include:

- potential costs related to the impact of the COVID-19 pandemic;
- personnel-related expenses, including salaries, benefits and stock-based compensation expenses, for individuals involved in research and development activities;
- external research and development expenses incurred under agreements with contract research organizations, or CROs, investigative sites, and consultants that conduct our preclinical studies and clinical trials and other scientific development services;
- costs incurred under agreements with contract manufacturing organizations, or CMOs, for developing and manufacturing material for our preclinical studies and clinical trials;
- costs related to compliance with regulatory requirements;
- milestone fees incurred in connection with our current license agreement with Lundbeck; and
- facilities and other allocated expenses, which include direct and allocated expenses for rent, insurance and other operating costs.

We expense research and development costs as incurred. We recognize external development costs based on an evaluation of the progress to completion of specific tasks using information provided to us by our vendors and our clinical investigative sites. Payments for these activities are based on the terms of the individual agreements, which may differ from the pattern of costs incurred, and are reflected in our consolidated financial statements as prepaid expenses or accrued research and development expenses. Nonrefundable advance payments for goods or services to be received in the future for use in research and development activities are deferred and capitalized, even when there is no alternative future use for the research and development. The capitalized amounts are expensed as the related goods are delivered or the services are performed.

A significant portion of our research and development costs have been external costs, which we track after a clinical product candidate has been identified. Our internal research and development costs are primarily personnel-related costs and other indirect costs. Our research and development expenses to-date have primarily been incurred in connection with our development of tovinontrine in SCD and β-thalassemia. We do not intend to track our internal research and development expenses on a program-by-program basis as our personnel are deployed across multiple projects under development.

Research and development activities are central to our business model. Product candidates in later stages of clinical development generally have higher development costs than those in earlier stages of clinical development, primarily due to the increased size and duration of later-stage clinical trials. We expect research and development costs to increase significantly for the foreseeable future as we continue the development of tovinontrine and any product candidates we may

develop in the future. However, we do not believe that it is possible at this time to accurately project total program-specific expenses through commercialization. There are numerous factors associated with the successful commercialization of tovinontrine and any product candidates we may develop in the future, including future trial design and various regulatory requirements, many of which cannot be determined with accuracy at this time based on our stage of development. Additionally, future commercial and regulatory factors beyond our control will impact our clinical development program and plans.

The following table summarizes our research and development expenses for the periods indicated:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Tovinontrine (IMR-687)	$ 29,239	$ 25,902
Personnel expenses (including stock-based compensation)	7,804	5,566
Other expenses	1,399	686
Total research and development expenses	$ 38,442	$ 32,154

The successful development of tovinontrine and any product candidates we may develop in the future is highly uncertain. Therefore, we cannot reasonably estimate or know the nature, timing and estimated costs of the efforts that will be necessary to complete the development and commercialization of tovinontrine or any future product candidates. We are also unable to predict when, if ever, material net cash inflows will commence from the sale of tovinontrine or potential future product candidates, if approved. This is due to the numerous risks and uncertainties associated with developing product candidates, including the uncertainty of:

- the impact of the ongoing COVID-19 pandemic and our response to it;
- the timing and progress of preclinical and clinical development activities;
- the number and scope of preclinical and clinical programs we decide to pursue;
- our ability to maintain our current research and development programs and to establish new ones;
- establishing an appropriate safety profile with investigational new drug application, or IND, enabling studies;
- successful patient enrollment in, and the initiation of, clinical trials;
- the successful completion of clinical trials with safety, tolerability and efficacy profiles that are satisfactory to the U.S. Food and Drug Administration, or FDA, or any comparable foreign regulatory authority;
- the timing, receipt and terms of any regulatory approvals from applicable regulatory authorities;
- our ability to establish new licensing or collaboration arrangements;
- the performance of our future collaborators, if any;
- establishing commercial manufacturing capabilities or making arrangements with third-party manufacturers;
- obtaining, maintaining, defending and enforcing patent claims and other intellectual property rights;
- launching commercial sales of our product candidates, if approved, whether alone or in collaboration with others; and
- maintaining a continued acceptable safety profile of the product candidates following approval.

Any changes in the outcome of any of these variables with respect to the development of tovinontrine or any future product candidates could mean a significant change in the costs and timing associated with the development of these product candidates. For example, if the FDA or another regulatory authority were to delay our planned start of clinical trials or require us to conduct clinical trials or other testing beyond those that we currently expect, or if we experience significant delays in enrollment in any of our planned clinical trials, we could be required to expend significant additional financial resources and time to complete clinical development of that product candidate. We may never obtain regulatory approval for any of our product candidates. Drug commercialization will take several years and millions of dollars in development costs.

General and Administrative. General and administrative expenses consist primarily of personnel-related expenses, including salaries, benefits, and stock-based compensation expenses for personnel in executive, finance, accounting, human

resources and other administrative functions. Other significant general and administrative expenses include legal fees relating to patent, intellectual property and corporate matters, and fees paid for accounting, consulting and other professional services.

We anticipate that our general and administrative expenses will increase in the future as our business expands to support our continued research and development activities, including our future clinical programs. These increases will likely include increased costs related to the hiring of additional personnel and fees to outside consultants, among other expenses. In addition, if we obtain regulatory approval for tovinontrine or any future product candidate and to the extent that we engage in commercialization activities on our own, we expect to incur significant expenses related to building a sales and marketing team to support product sales, marketing and distribution activities.

Total Other Income, Net

Total Other Income, Net. Total other income, net primarily consists of interest earned on our cash, cash equivalents and investments.

Results of Operations

Comparison of the Years Ended December 31, 2021 and 2020

The following table summarizes our results of operations for the years ended December 31, 2021 and 2020:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Operating expenses:		
Research and development	$ 38,442	$ 32,154
General and administrative	13,000	9,544
Total operating expenses	51,442	41,698
Loss from operations	(51,442)	(41,698)
Total other income, net	58	338
Net loss	$ (51,384)	$ (41,360)

Research and Development Expenses

Research and development expenses increased by approximately $6.2 million from $32.2 million for the year ended December 31, 2020 to $38.4 million for the year ended December 31, 2021. The increase in research and development expenses was primarily attributable to the following:

- a $3.3 million increase in costs related to the development and manufacturing of clinical materials, clinical research and oversight of our clinical trials and investigative fees for tovinontrine;
- a $2.2 million increase in personnel-related costs, including a $0.7 million increase in stock-based compensation expense, primarily due to an increase in headcount to support the growth of our research and development efforts; and
- a $0.7 million increase in other research and development operational costs, including professional services, supplies, and travel.

General and Administrative Expenses

General and administrative expenses increased by approximately $3.5 million from $9.5 million for the year ended December 31, 2020 to $13.0 million for the year ended December 31, 2021. The increase in general and administrative expenses was primarily attributable to the following:

- a $2.1 million increase in personnel-related costs, including a $1.0 million increase in stock-based compensation expense, primarily due to an increase headcount;
- a $1.1 million increase in cost associated with directors and officers' insurance premiums due to market conditions and a full year of coverage in 2021;

- a $0.6 million increase in other general and administrative operational costs, including public relations and corporate taxes; and
- a $0.3 million decrease in consulting and professional fees, including legal and accounting fees, due to the hiring of additional full-time employees.

Total Other Income, Net

Total other income, net was $0.3 million for the year ended December 31, 2020, compared to total other income, net of $0.1 million for the year ended December 31, 2021, in each case consisting primarily of interest earned on our cash, cash equivalents and investments.

Liquidity and Capital Resources

Sources of Liquidity

Since our inception, we have incurred significant losses in each period and on an aggregate basis. We have not yet commercialized tovinontrine, which is in clinical development, and we do not expect to generate revenue from sales of tovinontrine or any product candidates we may develop in the future for several years, if at all. Through December 31, 2021, we have funded our operations primarily through the issuance of common stock and convertible preferred stock.

In February 2020, we raised $17.1 million in gross proceeds from the sale of 1,562,994 shares of Series B preferred stock upon a waiver of specified milestone conditions from the holders of a majority of the shares then held by the holders of Series B preferred stock.

In March 2020, we completed an IPO of our common stock and issued and sold 4,700,000 shares of common stock at a public offering price of $16.00 per share, resulting in gross proceeds of $75.2 million. In April 2020, the underwriters exercised their option in full to purchase 705,000 additional shares of common stock for aggregate gross proceeds of $11.3 million. Inclusive of the underwriters' option to purchase additional shares, we received approximately $76.5 million in net proceeds from the IPO after deducting $10.0 million of underwriting discounts and commissions and offering expenses.

On April 1, 2021, we filed the Shelf with the SEC in relation to the registration and potential future issuance of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in the aggregate amount of up to $200.0 million. The Shelf was declared effective on April 8, 2021.We also simultaneously entered into the Sales Agreement with Cantor, as sales agent, providing for the offering, issuance and sale by us of up to an aggregate $75.0 million of our common stock from time to time in "at-the-market" offerings under the Shelf. As of December 31, 2021, we have issued and sold 231,291 shares of common stock under the Sales Agreement, resulting in net proceeds of $1.4 million after deducting commissions and offering expenses. The extent to which we utilize the Sales Agreement as a source of funding will depend on a number of factors, including the prevailing market price of our common stock, general market conditions, the extent to which we are able to secure funds from other sources, and restrictions on our ability to sell common stock pursuant to the Sales Agreement to the extent we are then subject to restrictions on our ability to utilize the Form S-3 shelf registration statement to sell more than one-third of the market value of our public float, meaning the aggregate market value of voting and non-voting common stock held by non-affiliates, in any trailing 12-month period. Accordingly, we may not be able to sell shares under the Sales Agreement at prices or amounts that we deem acceptable, and there can be no assurance that we will sell any further common stock pursuant to the Sales Agreement.

On July 16, 2021, we completed a public offering of shares of our common stock and issued and sold 8,333,333 shares of common stock at a public offering price of $6.00 per share, resulting in net proceeds of $46.8 million after deducting underwriting discounts and commissions and estimated offering expenses.

As of December 31, 2021, we had $90.3 million in cash, cash equivalents and investments. Based on our recurring losses and negative cash flows from operations since inception, expectation of continuing operating losses and negative cash flows from operations for the foreseeable future, and the need to raise additional capital to finance our future operations, we have concluded that there is substantial doubt about our ability to continue as a going concern for at least twelve months from the date of filing this Annual Report on Form 10-K. See Note 1 of the notes to our annual consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a further discussion of our liquidity and the conditions and events that raise substantial doubt regarding our ability to continue as a going concern.

While we do not currently expect that the COVID-19 pandemic will have a material adverse impact on our short-term or long-term liquidity, the impact of the COVID-19 pandemic on the global financial markets may reduce our ability to access capital, which could negatively impact our short-term and long-term liquidity. See "—Impact of COVID-19 Pandemic."

Cash Flows

The following table provides information regarding our cash flows for the periods indicated:

	Year Ended December 31,	
	2021	2020
	(in thousands)	
Net cash used in operating activities	$ (46,771)	$ (37,398)
Net cash used in investing activities	(1,632)	(16,721)
Net cash provided by financing activities	49,101	96,881
Net increase (decrease) in cash, cash equivalents, and restricted cash	$ 698	$ 42,762

Net Cash Used in Operating Activities

Net cash used in operating activities for the year ended December 31, 2021 was $46.8 million primarily due to our net loss of $51.4 million, partially offset by stock-based compensation expense of $3.8 million, depreciation expense of $0.1 million, amortization of $0.2 million on our short-term investments, and net cash inflows from the change in operating assets and liabilities of $0.5 million.

Net cash used in operating activities for the year ended December 31, 2020 was $37.4 million primarily due to our net loss of $41.4 million, partially offset by stock-based compensation expense of $2.2 million, depreciation expense of $0.1 million, amortization of $0.1 million on our short-term investments, and net cash inflows from the change in operating assets and liabilities of $1.7 million.

Net Cash Used in Investing Activities

Net cash used in investing activities for the year ended December 31, 2021 was $1.6 million primarily due to purchases of marketable securities of $47.6 million, partially offset by proceeds from sales and maturities of short-term investments of $45.9 million.

Net cash used in investing activities for the year ended December 31, 2020 was $16.7 million primarily due to purchases of marketable securities of $64.2 million, partially offset by proceeds from sales and maturities of short-term investments of $47.5 million.

Net Cash Provided by Financing Activities

Net cash provided by financing activities for the year ended December 31, 2021 was $49.1 million, primarily due to $46.8 million of net proceeds after deducting underwriting discounts and commissions and payment of issuance costs from our July 2021 offering, $1.4 million of net proceeds after deducting underwriting discounts and commissions and payment of issuance costs from the sale of common stock under the Sales Agreement with Cantor, and $0.9 million of proceeds received from the exercise of stock options.

Net cash provided by financing activities for the year ended December 31, 2020 was $96.9 million, primarily due to $80.4 million of net proceeds received from our IPO, after deducting underwriting discounts and commissions, $17.1 million of cash inflow resulting from sale of Series B Preferred Stock in February 2020, and $1.0 million of proceeds from stock option exercises. The proceeds from our IPO were partially offset by payments of $1.7 million of issuance costs.

Funding Requirements

We expect our expenses to increase substantially in connection with our ongoing research and development activities, particularly as we continue research and development, initiate clinical trials, and seek marketing approval for tovinontrine and any of our future product candidates. In addition, we expect to incur additional costs associated with operating as a public company. Our expenses will also increase if, and as, we:

- navigate the impacts of COVID-19 and our response to it;
- continue to advance clinical development of tovinontrine, including our ongoing Ardent and Forte Phase 2b clinical trials of tovinontrine in patients with SCD and β-thalassemia and our OLE clinical trial in patients with SCD;

- expand our planned research and development efforts for tovinontrine and pursue clinical activities for tovinontrine in HFpEF;
- continue to incur third-party manufacturing costs to support our clinical trials of tovinontrine and any other product candidates we may develop and, if approved, commercialization of such product candidates;
- seek regulatory and marketing approvals for tovinontrine and any other product candidates we may develop;
- establish a sales, marketing and distribution infrastructure to commercialize tovinontrine and any other product candidates we may develop, in each case if approved;
- commence development activities for any additional product candidates we may identify, including IMR-681;
- acquire or in-license products, product candidates, technologies and/or data referencing rights;
- maintain, expand, enforce, defend and protect our intellectual property;
- hire additional clinical, quality control, manufacturing and other scientific personnel;
- add operational, financial and management information systems and personnel, including personnel to support our product development and planned future commercialization efforts and our operations as a public company; and
- make any milestone payments to Lundbeck under our exclusive license agreement with Lundbeck, upon the achievement of specified clinical or regulatory milestones.

Based on our current operating plan, we expect that our existing cash, cash equivalents and investments will enable us to fund our operating expenses and capital expenditure requirements substantially through the first quarter of 2023. We have concluded that there is substantial doubt about our ability to continue as a going concern for at least twelve months from the date of filing this Annual Report on Form 10-K. However, we have based this estimate on assumptions that may prove to be wrong and we could exhaust our capital resources sooner than we expect.

Because of the numerous risks and uncertainties associated with research, development and commercialization of product candidates, we are unable to estimate the exact amount of our working capital requirements. Our future funding requirements will depend on many factors, including:

- the impact of the COVID-19 pandemic and our response to it;
- the time and cost necessary to complete our ongoing Ardent and OLE clinical trials of tovinontrine in patients with SCD, to initiate and complete one or more pivotal clinical trials of tovinontrine in SCD, and to pursue regulatory approvals for tovinontrine in SCD, and the costs of post-marketing studies that could be required by regulatory authorities;
- the time and cost necessary to complete our Forte clinical trial of tovinontrine in patients with β-thalassemia, to initiate and complete one or more pivotal clinical trials of tovinontrine in β-thalassemia, and to pursue regulatory approvals for tovinontrine in β-thalassemia, and the costs of post-marketing studies that could be required by regulatory authorities;
- our ability to advance tovinontrine in HFpEF into and through clinical development, and the timing and scope of these development activities;
- the costs of obtaining clinical and commercial supplies of tovinontrine and any other product candidates we may identify and develop;
- our ability to successfully commercialize tovinontrine and any other product candidates we may identify and develop;
- the manufacturing, selling and marketing costs associated with tovinontrine and any other product candidates we may identify and develop, including the cost and timing of establishing our sales and marketing capabilities;
- the amount and timing of sales and other revenues from tovinontrine and any other product candidates we may identify and develop, including the sales price and the availability of coverage and adequate third-party reimbursement;
- the time and cost necessary to respond to technological and market developments;
- the extent to which we may acquire or in-license other product candidates and technologies;

- our ability to attract, hire and retain qualified personnel; and
- the costs of maintaining, expanding and protecting our intellectual property portfolio.

A change in the outcome of any of these or other variables with respect to the development of tovinontrine or any product candidate we may develop in the future could significantly change the costs and timing associated with the development of that product candidate. Further, our operating plans may change in the future, and we may need additional funds to meet operational needs and capital requirements associated with such operating plans. Until such time, if ever, as we can generate substantial product revenues, we expect to finance our cash needs through a combination of equity offerings, debt financings, collaborations, strategic alliances and licensing arrangements. We currently have no credit facility or committed sources of capital. Based on our available cash resources, there is substantial doubt about our ability to continue as a going concern within one year after the date of filing this Annual Report on Form 10-K, and we expect that we will need to raise additional capital in the near term. To the extent that we raise additional capital through the sale of equity or convertible debt securities, the ownership interests of our existing stockholders may be diluted, and the terms of these securities may include liquidation or other preferences that could adversely affect the rights of such stockholders. Additional debt financing, if available, may involve agreements that include restrictive covenants that limit our ability to take specific actions, such as incurring additional debt, making capital expenditures or declaring dividends, that could adversely impact our ability to conduct our business.

If we raise additional funds through collaborations, strategic alliances or licensing arrangements with third parties, we may have to relinquish valuable rights to our technologies, future revenue streams, research program or product candidates, or grant licenses on terms that may not be favorable to us. If we are unable to raise additional funds through equity or debt financings when needed, we may be required to delay, limit, reduce or terminate our product development or future commercialization efforts or grant rights to develop and market product candidates that we would otherwise prefer to develop and market ourselves.

Contractual Obligations

In the normal course of business**,** we enter into agreements that contain contractual obligations, of which the most significant to date include our facility lease and our licensing agreement with Lundbeck.

In May 2019, we entered into a lease agreement for 4,210 square feet of office space located in Boston, Massachusetts. In June 2021, we entered into an amendment to the lease agreement pursuant to which we will lease an additional 5,026 square feet of office space, brining our total leased space to 9,236 square feet. We expect the lease for this additional space to commence by the end of March 2022. As of commencement of the additional lease space, the remaining required payments for our operating lease, not including the optional extension period, will be approximately $3.2 million. For further information regarding our operating lease agreement, please see Note 8 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

Our license agreement with Lundbeck, as well as certain other agreements, requires us to pay third parties upon achievement of certain development, regulatory or commercial milestones. Amounts related to contingent payments are not considered contractual obligations as they are contingent on the successful achievement of certain development, regulatory and commercial milestones that may not be achieved. We have not included payments contingent upon the achievement of certain development, regulatory or commercial milestones on our consolidated balance sheets. For further information regarding certain of our license agreements and amounts that could become payable in the future under those agreements, please see Note 7 to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K.

In addition, we are party to certain agreements with contract research organizations for clinical trials and clinical supply manufacturing and with vendors for preclinical research studies and other services and products for operating purposes. Such contracts are generally cancellable

by us for convenience with a specified amount of notice. We may be subject to certain termination fees or wind-down costs upon termination of these agreements. The exact amount of such costs are generally not fixed or estimable.

Critical Accounting Policies and Estimates

This management’s discussion and analysis is based on our consolidated financial statements, which have been prepared in accordance with U.S. generally accepted accounting principles. The preparation of these consolidated financial statements requires us to make judgments and estimates that affect the reported amounts of assets and liabilities, the

disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reported periods. We base our estimates on historical experience, known trends and events, and various other factors that we believe to be reasonable under the circumstances. Actual results may differ from these estimates under different assumptions or conditions. On an ongoing basis, we evaluate our judgments and estimates in light of changes in circumstances, facts, and experience. The effects of material revisions in estimates, if any, will be reflected in the consolidated financial statements prospectively from the date of change in estimates.

While our critical accounting policies are described in more detail in the notes to our consolidated financial statements appearing elsewhere in this Annual Report on Form 10-K, we believe the following accounting policies used in the preparation of our consolidated financial statements require the most significant judgments and estimates. See Note 2 of the notes to our annual consolidated financial statements included elsewhere in this Annual Report on Form 10-K for a description of our other significant accounting policies.

Accrued Research and Development Expenses

As part of the process of preparing our consolidated financial statements, we are required to estimate our accrued third-party research and development expenses as of each balance sheet date. This process involves reviewing open contracts and purchase orders, communicating with our personnel to identify services that have been performed on our behalf, and estimating the level of service performed and the associated cost incurred for the service when we have not yet been invoiced or otherwise notified of the actual cost. The majority of our service providers invoice us monthly in arrears for services performed or when contractual milestones are met. We make estimates of our accrued expenses as of each balance sheet date based on facts and circumstances known to us at that time. We periodically confirm the accuracy of our estimates with the service providers and make adjustments if necessary. The significant estimates in our accrued research and development expenses include the costs incurred for services performed by our vendors in connection with research and development activities for which we have not yet been invoiced.

We base our expenses related to research and development activities on our estimates of the services received and efforts expended pursuant to quotes and contracts with vendors that conduct research and development on our behalf. The financial terms of these agreements are subject to negotiation, vary from contract to contract and may result in uneven payment flows. There may be instances in which payments made to our vendors will exceed the level of services provided and result in a prepayment of the research and development expense. In accruing service fees, we estimate the time period over which services will be performed and the level of effort to be expended in each period. If the actual timing of the performance of services or the level of effort varies from our estimate, we adjust the accrual or prepaid balance accordingly. Non-refundable advance payments for goods and services that will be used in future research and development activities are expensed when the activity has been performed or when the goods have been received rather than when the payment is made.

Although we do not expect our estimates to be materially different from amounts incurred, if our estimates of the status and timing of services performed differ from the actual status and timing of services performed, it could result in us reporting amounts that are too high or too low in any particular period. To date, there have been no material differences between our estimates of such expenses and the amounts incurred.

Stock-Based Compensation

We measure stock-based compensation issued to employees and non-employees based on the grant date fair value of the stock-based awards and recognize stock-based compensation expense on a straight-line basis over the requisite service period of the awards, which is generally the vesting period of the respective award. We have also granted stock-based awards with performance-based vesting conditions. We recognize compensation expense for awards with performance-based vesting conditions over the remaining service period using the accelerated attribution method when the performance condition is deemed to be probable. We account for forfeitures as they occur.

We classify stock-based compensation expense in our consolidated statements of operations in the same manner in which the award recipient’s salary and related costs are classified or in which the award recipient’s service payments are classified. In future periods, we expect stock-based compensation expense to increase, due in part to our existing unrecognized stock-based compensation expense and as we grant additional stock-based awards to continue to attract and retain our employees.

We determine the fair value of stock-based awards based on the fair value of our common stock on the date of grant. The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected

term of the option, the risk-free interest rate for a period that approximates the expected term of the option, and our expected dividend yield. Given our limited trading history as a public company, we determine the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies. We expect to continue to do so until we have adequate historical data regarding the volatility of our own traded stock price. The expected term of our stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Prior to our IPO, the expected term of our stock options granted to non-employees also used the "simplified" method. Following our IPO, the expected term of options granted to non-employees is determined by contractual term. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. We have not paid, and do not anticipate paying, dividends on our common stock; therefore, the expected dividend yield is assumed to be zero.

As there was no public market for our common stock prior to our IPO, the estimated fair value of our common stock for awards made prior to the IPO was approved by our board of directors, with input from management, as of the date of each award grant, considering our most recently available independent third-party valuations of common stock and utilizing the valuation of our company's enterprise value determined utilizing various methods including the back-solve method, option pricing model, or OPM, or a hybrid of the probability-weighted expected return method, or PWERM, and the OPM. The total enterprise value was then allocated to the various outstanding equity instruments, including the underlying common stock, utilizing the option-pricing model. We believed the assumptions underlying these valuations represented our best estimates. The independent third-party valuations were performed in accordance with the guidance outlined in the American Institute of Certified Public Accountants' Accounting and Valuation Guide, *Valuation of Privately-Held-Company Equity Securities Issued as Compensation*.

Following our IPO, we have determined the fair value of our common stock based on the quoted market price of our common stock on the Nasdaq Global Select Market.

Emerging Growth Company Status

We are an "emerging growth company," or EGC, under the Jumpstart Our Business Startups Act of 2012, or the JOBS Act. Section 107 of the JOBS Act provides that an EGC can take advantage of the extended transition period provided in Section 7(a)(2)(B) of the Securities Act of 1933, as amended, for complying with new or revised accounting standards. Thus, an EGC can delay the adoption of certain accounting standards until those standards would otherwise apply to private companies. We have elected to avail ourselves of delayed adoption of new or revised accounting standards and, therefore, we will be subject to the same requirements to adopt new or revised accounting standards as private entities.

As an EGC, we may take advantage of certain exemptions and reduced reporting requirements under the JOBS Act. Subject to certain conditions, as an EGC:

- we may present only two years of audited financial statements and only two years of related Management's Discussion and Analysis of Financial Condition and Results of Operations within registration statements;
- we may avail ourselves of the exemption from providing an auditor's attestation report on our system of internal controls over financial reporting pursuant to Section 404(b) of the Sarbanes-Oxley Act;
- we may avail ourselves of the exemption from complying with any requirement that may be adopted by the Public Company Accounting Oversight Board, or PCAOB, regarding mandatory audit firm rotation or a supplement to the auditor's report providing additional information about the audit and the financial statements, known as the auditor discussion and analysis;
- we may provide reduced disclosure about our executive compensation arrangements; and
- we may not require nonbinding advisory votes on executive compensation or stockholder approval of any golden parachute payments.

We will remain an EGC until the earliest of (i) December 31, 2025, (ii) the last day of the fiscal year in which we have total annual gross revenues of $1.07 billion or more, (iii) the date on which we have issued more than $1.0 billion in non-convertible debt during the previous rolling three-year period, or (iv) the date on which we are deemed to be a large accelerated filer under the Securities Exchange Act of 1934, as amended.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk.

Our primary exposure to market risk is interest rate sensitivity, which is affected by changes in the general level of U.S. interest rates, particularly because our cash equivalents are in the form of money market funds that are invested in U.S. Treasury securities. We also hold investments in corporate debt securities and commercial paper. As of December 31, 2021, we had cash, cash equivalents and investments of $90.3 million. Interest income is sensitive to changes in the general level of interest rates; however, due to the short-term maturities of our cash equivalents and the low risk profile of our investments, an immediate 10% change in interest rates would not have a material effect on the fair market value of our investment portfolio.

We are not currently exposed to significant market risk related to changes in foreign currency exchange rates; however, we have contracted with and may continue to contract with foreign vendors that are located in Europe and Asia, who we may pay in local currency. Our operations may be subject to fluctuations in foreign currency exchange rates in the future.

Item 8. Financial Statements and Supplementary Data.

Our consolidated financial statements, together with the report of our independent registered public accounting firm, are presented beginning on page F-1 of this Annual Report on Form 10-K.

Item 9. Changes in and Disagreements With Accountants on Accounting and Financial Disclosure.

None.

Item 9A. Controls and Procedures.

Evaluation of Disclosure Controls and Procedures

Our management, with the participation of our Chief Executive Officer and Chief Financial Officer and Chief Operating Officer (our principal executive officer and principal financial officer, respectively), evaluated the effectiveness of our disclosure controls and procedures as of December 31, 2021. The term "disclosure controls and procedures," as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, or the Exchange Act, means controls and other procedures of a company that are designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is recorded, processed, summarized and reported, within the time periods specified in the SEC's rules and forms. Disclosure controls and procedures include, without limitation, controls and procedures designed to ensure that information required to be disclosed by a company in the reports that it files or submits under the Exchange Act is accumulated and communicated to the company's management, including its principal executive and principal financial officers, or persons performing similar functions, as appropriate to allow timely decisions regarding required disclosure. Our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving their objectives and our management necessarily applies its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Based on the evaluation of our disclosure controls and procedures as of December 31, 2021, our Chief Executive Officer and Chief Financial Officer and Chief Operating Officer concluded that, as of such date, our disclosure controls and procedures were effective at the reasonable assurance level.

Management's Report on Internal Control Over Financial Reporting

Our management is responsible for establishing and maintaining adequate internal control over financial reporting as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act. Our internal control system was designed to provide reasonable assurance to our management and our board of directors regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles. All internal control systems, no matter how well designed have inherent limitations. Therefore, even those systems determined to be effective can provide only reasonable assurance with respect to financial statement preparation and presentation. Our management assessed the effectiveness of our internal control over financial reporting as of December 31, 2021. In making this assessment, our management used the criteria set forth in Internal Control-Integrated Framework issued by the Committee of Sponsoring Organizations of the Treadway Commission in 2013 (COSO criteria). Based on this assessment, management concluded that our internal control over financial reporting was effective as of December 31, 2021. This Annual Report on Form 10-K does not include an attestation report of our independent registered public accounting firm because we are exempt from this requirement pursuant to rules of the Securities and Exchange Commission.

Changes in Internal Control over Financial Reporting

During the year ended December 31, 2021, we implemented certain internal controls in connection with our adoption of ASC 842. There were no other changes in our internal control over financial reporting during the year ended December 31, 2021 that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

Item 9B. Other Information.

None.

Item 9C. Disclosure Regarding Foreign Jurisdictions that Prevent Inspections.

Not applicable.

PART III

Item 10. Directors, Executive Officers and Corporate Governance.

Executive Officers and Directors

The following table sets forth the name, age as of January 31, 2022, and position of each of our executive officers and directors. There are no family relationships among any of our directors or executive officers.

Name	Age	Position
Executive Officers		
Rahul D. Ballal, Ph.D.	44	President and Chief Executive Officer, Director
Michael P. Gray	51	Chief Financial Officer, Chief Operating Officer
Kenneth Attie, M.D.	64	Senior Vice President, Chief Medical Officer
Non-Employee Directors		
David M. Mott(1) (2) (3)	56	Chairman of the Board of Directors
David Bonita, M.D.(2)	46	Director
Mark Chin(1) (2)	40	Director
Edward R. Conner, MD (3)	49	Director
Barbara J. Dalton, Ph.D.(3)	68	Director
Carl Goldfischer, M.D.(1)	63	Director
Laura Williams, M.D., MPH(2)	59	Director

(1) Member of the audit committee.
(2) Member of the compensation committee.
(3) Member of the nominating and corporate governance committee.

Executive Officers

Rahul D. Ballal, Ph.D. has served as our President and Chief Executive Officer and as a member of our board of directors since June 2018. Prior to joining us, Dr. Ballal served as Chief Business Officer of Northern Biologics Inc., a biotechnology company, from May 2016 to June 2018, and as an Entrepreneur-in-Residence at Versant Ventures Management LLC, a life sciences venture capital firm, from May 2016 to June 2018. Previously, Dr. Ballal was Vice President, Business Development at Flexion Therapeutics, Inc., or Flexion, a public biopharmaceutical company, from March 2011 to May 2016. Prior to Flexion, he held a venture fellowship position at Novartis Venture Funds, a venture capital fund, as part of the Kauffman Fellowship, from June 2010 to June 2012, and overlapped in business development at the Broad Institute of Massachusetts Institute of Technology, a biomedical and genomic research center, from September 2009 to March 2011. Dr. Ballal was also the founder and CEO of Redmind LLC, a venture backed data analytics startup that was sold to Ikimbo Inc. in June 2002. Dr. Ballal received his Ph.D. in biochemistry and molecular biology from Georgetown University, his M.S. in biotechnology from Johns Hopkins University and his B.A. in biology from Brown University. We believe Dr. Ballal is qualified to serve on our board of directors based on his broad experience in the life sciences industry, including in various investment, operating and leadership roles.

Michael P. Gray has served as our Chief Financial Officer and Chief Operating Officer since April 2019. Prior to joining us, Mr. Gray held various leadership positions at Arsanis, Inc., now X4 Pharmaceuticals, Inc., a public biopharmaceutical company, including President and Chief Executive Officer from November 2018 to March 2019, Chief Financial Officer from March 2016 to March 2019, Chief Operating Officer from September 2017 to November 2018, and Chief Business Officer from March 2016 to September 2017. Mr. Gray also served in various leadership positions from January 1998 through February 2016 at Curis Inc., or Curis, a public oncology drug development company. He served as Curis' Chief Financial Officer and Chief Business Officer from February 2014 to February 2016 and as its Chief Financial Officer and Chief Operating Officer from December 2006 to February 2014. From December 2003 until December 2006, Mr. Gray served as Curis' Vice President of Finance and Chief Financial Officer and from August 2000 until December 2003, served as its Senior Director of Finance and Controller. Previously, Mr. Gray held positions including Controller at Reprogenesis Inc., a biotechnology company focused on the development of cell therapy drug candidates, and as an audit professional for the accounting and consulting firm of Ernst & Young, LLP. Mr. Gray served on the board of directors of Therapeutics Acquisition Corporation, a special purpose acquisition corporation, from May 2020 to July 2021, when it

completed its merger with POINT Biopharma, Inc. Mr. Gray received his M.B.A. in corporate finance and entrepreneurial management from the F.W. Olin Graduate School of Business at Babson College and a B.S. in accounting from Bryant University.

Kenneth Attie, M.D. has served as our Senior Vice President and Chief Medical Officer since January 2021. Prior to joining us, Dr. Attie served as Vice President of Medical Research at Acceleron Pharma Inc., a biopharmaceutical company, from November 2009 to January 2021. Prior to Acceleron, Dr. Attie held clinical development and medical affairs leadership roles of increasing responsibility at Altus Pharmaceuticals Inc., a biopharmaceutical company, from 2007 to 2009, Insmed, Inc., a biopharmaceutical company, from 2005 to 2007, and Genentech, Inc, a biotechnology company, from 1988 to 2000. Dr. Attie received his B.A. in music from the University of Michigan and his M.D. from the New York University School of Medicine.

Non-Employee Directors

David M. Mott has served as a member of our board of directors since January 2016. Mr. Mott has been a private investor through Mott Family Capital since February 2020 and previously served as a General Partner at New Enterprise Associates, Inc., or New Enterprise Associates, a venture capital firm and, with its affiliates, a holder of more than 5% of our voting securities, from September 2008 to February 2020, where he led the healthcare investing practice. From 1992 until 2008, Mr. Mott worked at MedImmune, Inc., or MedImmune, a biotechnology company and subsidiary of AstraZeneca plc, or AstraZeneca, a public global, science-led biopharmaceutical company, and served in numerous roles during his tenure, including most recently as Chief Executive Officer from October 2000 to July 2008. During that time, Mr. Mott also served as Executive Vice President of AstraZeneca from June 2007 to July 2008 following AstraZeneca's acquisition of MedImmune in June 2007. Mr. Mott has served on the board of directors of several public companies, including Epizyme, Inc., or Epizyme, a public biopharmaceutical company, since 2009, Ardelyx, Inc., a public specialized biopharmaceutical company, since 2009, Adaptimmune Therapeutics plc, a public clinical-stage biopharmaceutical company, since September 2014, Mersana Therapeutics, Inc., a public life sciences company, since July 2012 and Novavax, Inc., a public late-stage biotechnology company, since June 2020, and previously served on the board of Nightstar Therapeutics plc, a public gene therapy company, from November 2015 to June 2019, Clementia Pharmaceuticals, Inc., a clinical-stage company, from June 2015 to February 2018, and Tesaro, Inc., an oncology-focused company, from May 2010 to January 2019. Mr. Mott received his B.A. in economics and government from Dartmouth College. We believe Mr. Mott is qualified to serve on our board of directors based on his experience as an executive officer at MedImmune and his role on several public boards of directors as well as his leadership position in healthcare investing.

David Bonita, M.D. has served as a member of our board of directors since March 2019. Since February 2020, Dr. Bonita has been a member of OrbiMed Advisors LLC, or OrbiMed, an investment firm and, with its affiliates, a holder of more than 5% of our voting securities, where he previously served as a private equity partner from June 2013 to February 2020. From June 2004 to June 2013, Dr. Bonita held other positions at OrbiMed. Dr. Bonita has also served as Secretary for Auraeda, Inc. since October 2021. Dr. Bonita has served on the board of directors of Tricida, Inc., a pharmaceutical company, since January 2014, Acutus Medical Inc, an arrhythmia management company, since March 2016, Ikena Oncology, Inc, an oncology company, since March 2016, Prelude Therapeutics, Inc., an oncology company, since July 2016, and Repare Therapeutics Inc., a cancer-focused biotechnology company, since September 2019. Dr. Bonita also previously served on the boards of directors of Clementia Pharmaceuticals Inc., a public pharmaceutical company, from April 2013 to April 2019, Loxo Oncology, Inc., a public biopharmaceutical company, from October 2013 to December 2017, Si-Bone, Inc., a public medical device company, from April 2014 to June 2019, and ViewRay Inc., a public medical device company from January 2008 to June 2018. Dr. Bonita currently serves, and has previously served, on the boards of directors of numerous private companies. Dr. Bonita worked as a corporate finance analyst in the healthcare investment banking groups of Morgan Stanley and UBS. He has published scientific articles in peer-reviewed journals based on signal transduction research performed at Harvard Medical School. He received his B.A. in biology from Harvard University and his joint M.D./M.B.A. from Columbia University. We believe that Dr. Bonita is qualified to serve on our board of directors based on his roles on several public and private boards of directors as well as his extensive experience in investing in healthcare companies.

Mark Chin has served as a member of our board of directors since March 2019. Mr. Chin has served as a Managing Director at Arix Bioscience plc, a life science investment company and, with its affiliates, a holder of more than 5% of our voting securities, since July 2021 and served as an Investment Director at Arix from August 2016 to April 2020. From September 2012 to July 2016, Mr. Chin served as a Principal at Longitude Capital Management Co. LLC, a healthcare venture capital firm. From January 2011 to September 2012, Mr. Chin served as a Consultant with the Boston Consulting Group, a global management consulting firm. Mr. Chin has served on the board of Harpoon Therapeutics Inc., a public clinical-stage immunotherapy company, since May 2017, and Iterum Therapeutics plc, a public clinical-stage pharmaceutical company, since May 2017. Mr. Chin earned his B.S. in management science from the University of California, San Diego,

his M.B.A. from the Wharton School at the University of Pennsylvania and his M.S. in biotechnology from the University of Pennsylvania. We believe Mr. Chin is qualified to serve on our board of directors based on his roles on several public and private boards of directors and his extensive experience in investing in healthcare companies as well as his consulting experience.

Edward R. Conner, M.D. has served as a member of our board of directors since April 2020. Since July 2021, Dr. Conner has served as Chief Medical Officer at Locanabio, Inc., a gene therapy company. From May 2019 to July 2021, Dr. Conner served as Senior Vice President and Chief Medical Officer at Audentes Therapeutics, Inc., an Astellas company and a genetic medicines company. From November 2016 to May 2019, he served as Senior Vice President and Chief Medical Officer at Sangamo Therapeutics, Inc., a biotechnology company. Dr. Conner served as Vice President, Clinical Development at Ultragenyx Pharmaceutical Inc., a pharmaceutical company, from January 2015 to October 2016, and in senior clinical and medical leadership positions at BioMarin Pharmaceutical Inc., a pharmaceutical company and at Genentech, Inc., a biotechnology company, prior to that. Dr. Conner earned his B.S. in Biology from Duke University and his M.D. from the University of California, San Francisco. We believe Dr. Conner is qualified to serve on our board of directors based on his significant industry experience leading medical and clinical development operations.

Barbara J. Dalton, Ph.D. has served as a member of our board of directors since January 2016. Dr. Dalton has served as the Vice President of Venture Capital for Pfizer Ventures, the venture capital group of Pfizer Inc. and, with its affiliates, a holder of more than 5% of our voting securities, since she joined Pfizer in 2007. She serves on the board of Artios Ltd., Priovant Therapeutics, Inc., Ixchelsis Ltd, AMRA Medical and Second Genome, which are all private independent biopharmaceutical companies. Barbara also serves on several other Pfizer Venture Investments portfolio companies as a board observer. Dr. Dalton began her pharmaceutical career as a Research Scientist in Immunology at SmithKline Beecham Ltd. (formerly SmithKline and French Laboratories), a pharmaceutical company that merged with Glaxo Holdings to become GSK, and joined their venture capital group, SR One, Ltd., in the early 1990s. She was also a founding member and Partner with EuclidSR Partners LP, a private venture capital firm, where SmithKline was a leading limited partner. She received her Ph.D. in microbiology and immunology from The Medical College of Pennsylvania (now the Drexel University College of Medicine) and received her B.S. in General Science from Pennsylvania State University. We believe Dr. Dalton is qualified to serve on our board of directors based on her research background, her past role on several public and private boards of directors, as well as her extensive experience in venture investing in healthcare companies.

Carl Goldfischer, M.D. has served as a member of our board of directors since January 2016. Dr. Goldfischer has served as an Investment Partner, Managing Director, member of the board of directors and member of the executive committee of Bay City Capital LLC, or Bay City Capital, a life sciences investment firm, since January 2000. Prior to joining Bay City Capital, Dr. Goldfischer was Chief Financial Officer and VP of Finance and Strategic Planning of ImClone Systems Inc., a biopharmaceutical company. Dr. Goldfischer has served on the board of directors of Epizyme, Inc., a public biopharmaceutical company, since September 2009. He has previously served on the board of directors of EnteroMedics Inc., now ReShape Lifesciences Inc., a public medical device company, from 2004 to September 2017, MAP Pharmaceuticals, Inc., a biopharmaceutical company, from 2004 to 2011 and Poniard Pharmaceuticals, Inc., a public biopharmaceutical company, from 2000 to 2012. Dr. Goldfischer received his B.A. in Liberal Arts from Sarah Lawrence College and his M.D. with honors in scientific research from Albert Einstein College of Medicine at Yeshiva University. We believe Dr. Goldfischer is qualified to serve on our board of directors based on his experience as chief financial officer at ImClone Systems and his role on several public and private boards of directors as well as his experience in investing in healthcare companies.

Laura Williams, M.D., MPH, has served as a member of our board of directors since June 2021. Since October 2021, Dr. Williams has served as the Chief Medical Officer at Ardelyx, Inc., a biopharmaceutical company, and she served as Senior Vice President, Global Therapeutic Strategies and Patient Advocacy for Ardelyx from November 2020 to October 2021. Prior to Ardelyx, she served as Senior Vice President and Head of Clinical Development and Biostatistics at AMAG Pharmaceuticals, Inc., a pharmaceutical company, from September 2017 until January 2020. From September 2016 to August 2017, Dr. Williams served as Vice President of Clinical Development at Myovant Sciences Ltd., a healthcare company. From 1998 to July 2016, Dr. Williams served in roles of increasing responsibility at Abbott Laboratories and AbbVie, Inc. Dr. Williams received her B.S. from Mississippi State University, her M.D. from the University of Iowa and MPH in Epidemiology from the University of Washington. We believe Dr. Williams is qualified to serve on our board of directors based on her significant strategic and clinical development experience, as well her experience with patient advocacy.

Delinquent Section 16(a) Reports

Section 16(a) of the Exchange Act requires directors, officers and persons who are beneficial owners of more than 10% of our common stock to file with the SEC reports of their ownership of our securities and of changes in that ownership.

To our knowledge, based upon a review of copies of reports filed with the SEC with respect to the fiscal year ended December 31, 2021 and written representations by our directors and officers that no other reports were required with respect to their transactions, all reports required to be filed under Section 16(a) by our directors and officers and persons who were beneficial owners of more than 10% of our common stock were timely filed, except that Mark Chin filed one late Form 4 with respect to one transaction.

Code of Business Conduct and Ethics

We have adopted a written code of business conduct and ethics that applies to our directors, officers and employees, including our principal executive officer, principal financial officer, principal accounting officer or controller, or persons performing similar functions. We have posted a current copy of the code on the "Corporate Governance" section of the "Investors" section of our website, www.imaratx.com. In addition, we intend to post on our website all disclosures that are required by law or Nasdaq listing standards concerning any amendments to, or waivers from, any provision of the code.

Audit Committee

The members of our audit committee are Mark Chin, Carl Goldfischer and David Mott. Dr. Goldfischer is the chair of the audit committee. Our audit committee's responsibilities include:

- appointing, approving the compensation of, and assessing the independence of our registered public accounting firm;
- overseeing the work of our independent registered public accounting firm, including through the receipt and consideration of reports from that firm;
- reviewing and discussing with management and our independent registered public accounting firm our annual and quarterly financial statements and related disclosures;
- monitoring our internal control over financial reporting, disclosure controls and procedures and code of business conduct and ethics;
- overseeing our internal audit function;
- overseeing our risk assessment and risk management policies;
- establishing policies regarding hiring employees from our independent registered public accounting firm and procedures for the receipt and retention of accounting related complaints and concerns;
- meeting independently with our internal auditing staff, if any, our independent registered public accounting firm and management;
- reviewing and approving or ratifying any related person transactions; and
- preparing the audit committee report required by Securities and Exchange Commission, or SEC, rules.

All audit and non-audit services, other than *de minimis* non-audit services, to be provided to us by our independent registered public accounting firm must be approved in advance by our audit committee.

Our board of directors has determined that Dr. Goldfischer is an "audit committee financial expert" as defined in applicable SEC rules. The composition of our audit committee satisfies the member independence requirements under current Nasdaq and SEC rules and regulations. Our board of directors has also determined that each member of our audit committee can read and understand fundamental financial statements, in accordance with applicable requirements. In arriving at these determinations, the board of directors has examined each audit committee member's scope of experience and the nature of their employment in the corporate finance sector.

Item 11. Executive Compensation.

The following discussion relates to the compensation of our President and Chief Executive Officer, Rahul D. Ballal, Ph.D., our Chief Financial Officer and Chief Operating Officer, Michael P. Gray, and our Chief Medical Officer, Kenneth Attie, M.D., for the years ended December 31, 2021 and 2020. These three individuals are collectively referred to in this Annual Report on Form 10-K as our named executive officers.

We continuously review all elements of our executive compensation program, including the function and design of our equity incentive programs, to ensure that our program is competitive with the companies with which we compete for executive talent and that it is appropriate for a public company of our size and stage of development.

Summary Compensation Table

The following table sets forth information regarding compensation awarded to, earned by or paid to each of our named executive officers for the years ended December 31, 2021 and 2020.

Name and Principal Position	Year	Salary ($)	Bonus ($)(1)	Option awards ($)(2)	All other compensation ($)	Total ($)
Rahul D. Ballal, Ph.D.(3)	2021	517,729	232,978	1,189,482	1,090(4)	1,941,279
President and Chief Executive Officer	2020	436,687	177,289	—	2,620(5)	616,596
Michael Gray	2021	454,454	172,692	575,168	1,090(6)	1,203,404
Chief Financial Officer and Chief Operating Officer	2020	392,740	134,263	—	2,620(7)	529,623
Kenneth Attie (8)	2021	400,750	179,500	1,040,600	1,090(9)	1,621,940
Chief Medical Officer						

(1) Amounts represent a cash bonus award to our named executive officers under our discretionary annual cash bonus program and with respect to Dr. Attie, also includes a $50,000 signing bonus paid to Dr. Attie in connection with the commencement of his employment.
(2) The amounts reported in the "Option awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of Financial Accounting Standards Board Accounting Standards Codification, or ASC, Topic 718. See Note 11 of the notes to our consolidated financial statements in this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the named executive officer upon the vesting of the stock options, the exercise of the stock options or the sale of the common stock underlying such stock options.
(3) Dr. Ballal also serves as a member of our board of directors but does not receive any additional compensation for his service as a director.
(4) Amount represents compensation of $1,090 from premiums paid on behalf of Dr. Ballal for life insurance.
(5) Amount represents compensation of $1,090 from premiums paid on behalf of Dr. Ballal for life insurance and $1,530 in reimbursements for monthly parking costs.
(6) Amount represents compensation of $1,090 from premiums paid on behalf of Mr. Gray for life insurance.
(7) Amount represents compensation of $1,090 from premiums paid on behalf of Mr. Gray for life insurance and $1,530 in reimbursements for monthly parking costs.
(8) Dr. Attie commenced employment with us on January 19, 2021.
(9) Amount represents compensation of $1,090 from premiums paid on behalf of Dr. Attie for life insurance.

Narrative to Summary Compensation Table

Base Salary. In 2021, we paid Dr. Ballal an annualized base salary of $437,750 until February 1, 2021, when his annualized base salary was increased to $525,000. In 2021, we paid Mr. Gray an annualized base salary of $393,444, until February 1, 2021, when his annualized base salary was increased to $460,000. In 2021, we paid Dr. Attie an annualized base salary of $420,000, which was pro-rated to reflect the number of days he served with our company following his hire in January 2021. We use base salaries to recognize the experience, skills, knowledge and responsibilities required of all our employees, including our named executive officers. None of our named executive officers are currently party to an employment agreement or other agreement or arrangement that provides for automatic or scheduled increases in base salary.

Annual Bonus. Our board of directors may, in its discretion, award bonuses to our executive officers, including our named executive officers, from time to time. Our letter agreements with Dr. Ballal, Mr. Gray and Dr. Attie provide that they will be eligible for an annual discretionary bonus up to a specified percentage of their salaries based upon our achievements and their performance, as determined by our board of directors. Performance-based bonuses, which are calculated as a percentage of base salary, are designed to motivate our employees to achieve annual goals based on our strategic, financial and operating performance objectives. From time to time, our board of directors has approved discretionary annual cash bonuses to our named executive officers with respect to their prior year performance. In 2020, Dr. Ballal was eligible to receive a discretionary bonus of up to 45% of his annualized base salary. In 2021, Dr. Ballal's annual discretionary bonus

eligibility was increased up to 50% of his annualized base salary. We paid Dr. Ballal a discretionary bonus of $177,289 with respect to 2020 and $232,978 with respect to 2021. In 2020, Mr. Gray was eligible to receive a discretionary bonus of up to 35% of his annualized base salary. In 2021, Mr. Gray's annual discretionary bonus eligibility was increased up to 40% of his annualized base salary. We paid Mr. Gray a discretionary bonus of $134,263 with respect to 2020 and $172,692 with respect to 2021. In 2021, Dr. Attie was eligible to receive a discretionary bonus of up to 35% of his annualized base salary, pro-rated to reflect the number of days he served with our company following his hire in January 2021. We paid Dr. Attie a discretionary bonus of $129,500 with respect to 2021. We also paid Dr. Attie a $50,000 signing bonus in 2021 in connection with his commencement of employment.

Equity Incentives. Although we do not have a formal policy with respect to the grant of equity incentive awards to our executive officers, or any formal equity ownership guidelines applicable to them, we believe that equity grants provide our executives with a strong link to our long-term performance, create an ownership culture and help to align the interests of our executives and our stockholders. In addition, we believe that equity grants with a time-based vesting feature promote executive retention because this feature incentivizes our executive officers to remain in our employment during the vesting period. Accordingly, our board of directors periodically reviews the equity incentive compensation of our executive officers, including our named executive officers, and from time to time may grant equity incentive awards to them.

We granted an option to purchase 133,350 shares of our common stock to Dr. Ballal in January 2021. The shares underlying the option vest and become exercisable over four years, with 25% of the shares vesting on the first anniversary of the date of grant, and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Ballal's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

We granted an option to purchase 60,800 shares of our common stock to Mr. Gray in January 2021. The shares underlying the option vest and become exercisable over four years, with 25% of the shares vesting on the first anniversary of the date of grant, and the remaining shares vesting in equal quarterly installments thereafter, subject to Mr. Gray's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Mr. Gray's employment within twelve months following a change in control.

We granted an option to purchase 110,000 shares of our common stock to Dr. Attie in January 2021 in connection with his commencement of employment. The shares underlying the option vest and become exercisable over four years, with 25% of the shares vesting on the first anniversary of the date of grant, and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Attie's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Attie's employment within twelve months following a change in control.

We did not grant equity incentive awards to any of our named executive officers during 2020.

Prior to the completion of our initial public offering in March 2020, our executives were eligible to participate in our 2016 Stock Incentive Plan, as amended, or the 2016 Plan. Our employees and executives are now eligible to receive stock options and other stock-based awards pursuant to our 2020 Equity Incentive Plan, or the 2020 Plan.

We have used stock options and other stock-based awards to compensate our executive officers in the form of initial grants in connection with the commencement of employment and also at various times, often but not necessarily annually, if we have performed as expected or better than expected. The award of stock options and other stock-based awards to our executive officers have historically been made by our board of directors or compensation committee. None of our executive officers is currently party to an employment agreement that provides for automatic award of stock options or other stock-based awards. We have granted stock options and other stock-based awards to our executive officers with time-based and performance-based vesting. The options that we have granted to our executive officers typically vest as to 25% of the shares underlying the award on the first anniversary of the grant date and in equal quarterly installments for three years thereafter. We have also granted performance-based awards tied to the achievement of milestones. Vesting rights cease upon termination of employment and exercise rights for stock options cease shortly after termination, except that vesting is fully accelerated upon certain terminations in connection with a change of control and exercisability is extended in the case of death or disability. Prior to the exercise of a stock option, the holder has no rights as a stockholder with respect to the shares subject to such option, including no voting rights and no right to receive dividends or dividend equivalents.

We have historically awarded stock options and other stock-based awards with exercise prices or purchase prices, as applicable, that are equal to the fair market value of our common stock on the date of grant as determined by our board of directors.

Outstanding Equity Awards at Fiscal Year-End

The following table sets forth information regarding all outstanding stock options held by each of our named executive officers as of December 31, 2021.

Name	Number of securities underlying unexercised options (#) exercisable	Number of securities underlying unexercised options (#) unexercisable	Option exercise price ($)	Option expiration date
Rahul D. Ballal	230,374	33,625(1)	3.15	10/18/2028
	220,885	100,403(2)	4.92	5/15/2029
	43,813	56,332(3)	4.92	5/15/2029
	—	133,350(4)	13.05	1/27/2031
Michael Gray	138,943	84,116(5)	4.92	5/15/2029
	16,648	21,407(6)	4.92	5/15/2029
	—	60,800(7)	13.83	1/25/2031
Kenneth Attie	—	110,000(8)	13.83	1/25/2031

(1) This option was granted on October 19, 2018, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares having vested on the first anniversary of the date of grant and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Ballal's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

(2) This option was granted on May 16, 2019, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares having vested on the first anniversary of the date of grant and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Ballal's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

(3) This option was granted on May 16, 2019, and 25% of the shares underlying the option vested on February 25, 2021, the first anniversary of the closing of the second tranche of our series B preferred stock financing, with the remaining shares vesting in quarterly installments for three years thereafter. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

(4) This option was granted on January 28, 2021, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares having vested on the first anniversary of the date of grant and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Ballal's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Ballal's employment within twelve months following a change in control.

(5) This option was granted on May 16, 2019, and the shares underlying the option vest and become exercisable over four years with 25% of the shares having vested on the first anniversary of the date of grant and the remaining shares vesting in equal quarterly installments thereafter, subject to Mr. Gray's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Mr. Gray's employment within twelve months following a change in control.

(6) This option was granted on May 16, 2019, and 25% of the shares underlying the option vested on February 25, 2021, the first anniversary of the closing of the second tranche of our series B preferred stock financing, with the remaining shares vesting in quarterly installments for three years thereafter. The vesting of this stock option will be fully accelerated upon a qualifying termination of Mr. Gray's employment within twelve months following a change in control

(7) This option was granted on January 26, 2021, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares having vested on the first anniversary of the date of grant and the remaining shares vesting in equal quarterly installments thereafter, subject to Mr. Gray's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Mr. Gray's employment within twelve months following a change in control.

(8) This option was granted on January 26, 2021, and the shares underlying the option vest and become exercisable over four years, with 25% of the shares having vested on the first anniversary of the date of grant and the remaining shares vesting in equal quarterly installments thereafter, subject to Dr. Attie's continuous service with us. The vesting of this stock option will be fully accelerated upon a qualifying termination of Dr. Attie's employment within twelve months following a change in control.

Employment Agreements

Letter Agreement with Rahul D. Ballal, Ph.D.

In connection with our initial hiring of Dr. Ballal as our President and Chief Executive Officer, we entered into a letter agreement with him dated April 17, 2018, which was amended and restated on August 12, 2019 and September 23, 2019, and further amended on November 5, 2021. We refer to the current letter agreement, as amended, as the Ballal letter agreement. Under the Ballal letter agreement, Dr. Ballal is an at-will employee, and his employment with us can be terminated by Dr. Ballal or us at any time and for any reason. Pursuant to the Ballal letter agreement, Dr. Ballal's current annualized base salary is $550,000, and he is eligible to receive an annual discretionary bonus of up to 50% of his annualized base salary. We will also reimburse all of Dr. Ballal's monthly parking costs at a designated parking garage lot or his commuting costs for public transportation.

Under the Ballal letter agreement, Dr. Ballal is entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, in the event of the termination of his

employment by us without cause or by him for good reason, each as defined in the Ballal letter agreement, to (i) continue receiving his then-current annual base salary for a period of twelve months following the date his employment with us is terminated, and (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to twelve months following the date that his employment with us is terminated.

In the event that Dr. Ballal's employment is terminated by us without cause or by Dr. Ballal with good reason within twelve months following a change of control, each as defined in the Ballal letter agreement, Dr. Ballal will be entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, to (i) continue receiving his then-current annual base salary for a period of eighteen months following the date his employment with us is terminated, (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to eighteen months following the date that his employment with us is terminated and (iii) one hundred and fifty percent of his annual bonus target amount for the year in which the termination occurs, payable as a lump sum. In addition, under the terms of the Ballal letter agreement or the applicable option agreements, Dr. Ballal will be entitled to full acceleration of vesting on all outstanding options as of the date of his termination. Under the Ballal letter agreement, if payments and benefits payable to Dr. Ballal in connection with a change in control are subject to Section 4999 of the Code, then such payments and benefits will either be paid in full or be reduced so that the Section 4999 excise tax does not apply, whichever results in the better after-tax result for Dr. Ballal.

Letter Agreement with Michael P. Gray

In connection with our initial hiring of Mr. Gray as our Chief Financial Officer and Chief Operating Officer, we entered into a letter agreement with him dated February 26, 2019, which was amended and restated on June 27, 2019 and September 23, 2019 and further amended on November 5, 2021. We refer to the current letter agreement, as amended, as the Gray letter agreement. Under the Gray letter agreement, Mr. Gray is an at-will employee, and his employment with us can be terminated by Mr. Gray or us at any time and for any reason. Pursuant to the Gray letter agreement, Mr. Gray's current annualized base salary is $480,700, and he is eligible to receive an annual discretionary bonus of up to 40% of his annualized base salary. We will also reimburse all of Mr. Gray's monthly parking costs at a designated parking garage lot or his commuting costs for public transportation.

Under the Gray letter agreement, Mr. Gray is entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, in the event of the termination of his employment by us without cause or by him for good reason, each as defined in the Gray letter agreement, to (i) continue receiving his then-current annual base salary for a period of nine months following the date his employment with us is terminated, and (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to nine months following the date that his employment with us is terminated.

In the event that Mr. Gray's employment is terminated by us without cause or by Mr. Gray with good reason within twelve months following a change of control, each as defined in the Gray letter agreement, Mr. Gray will be entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, to (i) continue receiving his then-current annual base salary for a period of twelve months following the date his employment with us is terminated, (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to twelve months following the date that his employment with us is terminated and (iii) one hundred percent of his annual bonus target amount for the year in which the termination occurs, payable as a lump sum. In addition, under the terms of the Gray letter agreement or the applicable option agreements, Mr. Gray will be entitled to full acceleration of vesting on all outstanding options as of the date of his termination. Under the Gray letter agreement, if payments and benefits payable to Mr. Gray in connection with a change in control are subject to Section 4999 of the Code, then such payments and benefits will either be paid in full or be reduced so that the Section 4999 excise tax does not apply, whichever results in the better after-tax result for Mr. Gray.

The severance payments that Mr. Gray is eligible to receive under the Gray letter agreement will be reduced, but not below $1,000, by the amount of garden leave pay received by Mr. Gray under the restrictive covenant agreement he entered into with us described further under "Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreements" below.

Letter Agreement with Kenneth Attie, M.D.

In connection with our initial hiring of Dr. Attie as our Chief Medical Officer, we entered into a letter agreement with him dated December 4, 2020, which was amended on November 5, 2021. We refer to this letter agreement as the Attie letter agreement Under the Attie letter agreement, Dr. Attie is an at-will employee, and his employment with us can be terminated by Dr. Attie or us at any time and for any reason. Pursuant to the Attie letter agreement, Dr. Attie's annualized base salary is

$436,800, and he is eligible to receive an annual discretionary bonus of up to 35% of his annualized base salary. We will also reimburse all of Dr. Attie's monthly parking costs at a designated parking garage lot or his commuting costs for public transportation.

Under the Attie letter agreement, Dr. Attie is entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, in the event of the termination of his employment by us without cause or by him for good reason, each as defined in the Attie letter agreement, to (i) continue receiving his then-current annual base salary for a period of nine months following the date his employment with us is terminated, and (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to nine months following the date that his employment with us is terminated.

In the event that Dr. Attie's employment is terminated by us without cause or by Dr. Attie with good reason within twelve months following a change of control, each as defined in the Attie letter agreement, Dr. Attie will be entitled, subject to his execution and nonrevocation of a release of claims in our favor and his continued compliance with certain restrictive covenants, to (i) continue receiving his then-current annual base salary for a period of twelve months following the date his employment with us is terminated, (ii) reimbursement of COBRA premiums for health benefit coverage for a period of up to twelve months following the date that his employment with us is terminated and (iii) one hundred percent of his annual bonus target amount for the year in which the termination occurs, payable as a lump sum. In addition, Dr. Attie will be entitled to full acceleration of vesting of the option to purchase 110,000 shares of our common stock granted to Dr. Attie in January 2021 in connection with the commencement of his employment. Under the Attie letter agreement, if payments and benefits payable to Dr. Attie in connection with a change in control are subject to Section 4999 of the Code, then such payments and benefits will either be paid in full or be reduced so that the Section 4999 excise tax does not apply, whichever results in the better after-tax result for Dr. Attie.

The severance payments that Dr. Attie is eligible to receive under the Attie letter agreement will be reduced, but not below $1,000, by the amount of garden leave pay received by Dr. Attie under the restrictive covenant agreement he entered into with us described further under "Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreements" below.

Employee Non-Competition, Non-Solicitation, Confidentiality and Assignment Agreements

Each of our executive officers has entered into a standard form of agreement with respect to non-competition, non-solicitation, confidential information and assignment of inventions. Under this agreement, each executive officer has agreed not to compete with us during his employment and for a period ranging from six months to one year after the termination of his employment, not to solicit our employees, consultants, clients or customers during his employment and for a period ranging from six months to one year after the termination of his employment, and to protect our confidential and proprietary information indefinitely. In addition, under this agreement, each executive officer has agreed that we own all inventions that are developed by such executive officer during his employment with us that are related to our business or research and development conducted or planned to be conducted by us at the time such development is created. Each executive officer also agreed to provide us with a non-exclusive, royalty-free, perpetual license to use any prior inventions that such executive officer incorporates into inventions assigned to us under this agreement.

401(k) Plan

We maintain a defined contribution employee retirement plan for our employees, including our named executive officers. The plan is intended to qualify as a tax-qualified 401(k) plan so that contributions to the 401(k) plan, and income earned on such contributions, are not taxable to participants until withdrawn or distributed from the 401(k) plan (except in the case of contributions under the 401(k) plan designated as Roth contributions). Under the 401(k) plan, each employee is fully vested in his or her deferred salary contributions and any qualified nonelective contributions made by us. Employee contributions are held and invested by the plan's trustee as directed by participants. The 401(k) plan provides us with the discretion to match employee contributions.

Limitation of Liability and Indemnification

Our certificate of incorporation limits the personal liability of directors for breach of fiduciary duty to the maximum extent permitted by the Delaware General Corporation Law, or the DGCL, and provides that no director will have personal liability to us or to our stockholders for monetary damages for breach of fiduciary duty as a director. However, these provisions do not eliminate or limit the liability of any of our directors:

- for any breach of the director's duty of loyalty to us or our stockholders;
- for acts or omissions not in good faith or that involve intentional misconduct or a knowing violation of law;

- for voting for or assenting to unlawful payments of dividends, stock repurchases or other distributions; or
- for any transaction from which the director derived an improper personal benefit.

Any amendment to or repeal of these provisions will not eliminate or reduce the effect of these provisions in respect of any act, omission or claim that occurred or arose prior to such amendment or repeal. If the DGCL is amended to provide for further limitations on the personal liability of directors of corporations, then the personal liability of our directors will be further limited to the greatest extent permitted by the DGCL.

In addition, our certificate of incorporation provides that we must indemnify our directors and officers and we must advance expenses, including attorneys' fees, to our directors and officers in connection with legal proceedings, subject to very limited exceptions.

We maintain a general liability insurance policy that covers specified liabilities of our directors and officers arising out of claims based on acts or omissions in their capacities as directors or officers. In addition, we have entered into indemnification agreements with all of our directors and executive officers. These indemnification agreements may require us, among other things, to indemnify each such executive officer or director for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our executive officers or directors.

Some of our non-employee directors may, through their relationships with their employers, be insured or indemnified against specified liabilities incurred in their capacities as members of our board of directors.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, executive officers or persons controlling us, in the opinion of the SEC, such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

Rule 10b5-1 Plans

Our directors and executive officers may adopt written plans, known as Rule 10b5-1 plans, in which they will contract with a broker to buy or sell shares of our common stock on a periodic basis. Under a Rule 10b5-1 plan, a broker executes trades pursuant to parameters established by the director or officer when entering into the plan, without further direction from the director or officer. In addition, our directors and executive officers may buy or sell additional shares outside of a Rule 10b5-1 plan when they are not in possession of material, nonpublic information.

Director Compensation

The table below shows all compensation to our non-employee directors during the year ended December 31, 2021.

Name	Fees earned or paid in cash ($)	Option awards ($)(1)(2)	Total ($)
David M. Mott	79,938	40,649	120,587
Carl Goldfischer, M.D.	50,000	40,649	90,649
Barbara J. Dalton, Ph.D.	41,517	40,649	82,166
Sara Nayeem, M.D.(3)	37,188	40,649	77,837
David Bonita, M.D.	40,000	40,649	80,649
Mark Chin	45,028	40,649	85,677
Edward R. Conner	39,000	40,649	79,649
Laura Williams. M.D., MPH(4)	20,222	85,402	105,624
Mette Kristine Agger(5)	21,261	—	21,261

(1) The amounts reported in the "Option awards" column reflect the aggregate fair value of stock-based compensation awarded during the year computed in accordance with the provisions of ASC 718. See Note 11 of the notes to our consolidated financial statements in this Annual Report on Form 10-K regarding assumptions underlying the valuation of equity awards. These amounts reflect the accounting cost for these stock options and do not reflect the actual economic value that may be realized by the directors upon the vesting of the stock options, the exercise of the stock options or the sale of the common underlying such stock options.
(2) As of December 31, 2021, the aggregate number of shares of our common stock subject to outstanding option awards for each non-employee director was as follows: Mr. Mott, 23,185 shares; Ms. Agger, 0 shares; Dr. Goldfischer, 23,185 shares; Dr. Dalton, 23,185 shares; Dr. Nayeem, 5,151 shares; Dr. Bonita, 23,185 shares; Mr. Chin, 23,185 shares; Mr. Conner, 23,185 shares; and Dr. Williams, 15,457 shares.
(3) Dr. Nayeem resigned from our board effective November 15, 2021.
(4) Dr. Williams was elected to our board on June 29, 2021.

(5) Ms. Agger earned $21,261 in fees related to her service as a director of the company which Ms. Agger decided to voluntarily forego. Ms. Agger did not stand for re-election to our board at our 2021 annual meeting of stockholders and served as a member of our board until June 29, 2021.

Dr. Ballal, one of our directors who also serves as our President and Chief Executive Officer, does not receive any additional compensation for his service as director. Dr. Ballal is one of our named executive officers and, accordingly, the compensation that we pay to Dr. Ballal is discussed under "—Summary Compensation Table" and "—Narrative to Summary Compensation Table."

In October 2019, our board of directors approved a director compensation program that became effective on March 11, 2020, and which was amended on December 22, 2021. Under this director compensation program, we pay our non-employee directors a cash retainer for service on the board of directors and for service on each committee on which the director is a member. The chairman of the board and the chairman of each committee will receive higher retainers for such service. These fees are payable in arrears in four equal quarterly installments on the last day of each quarter, provided that the amount of such payment will be prorated for any portion of such quarter that the director is not serving on our board of directors, on such committee or in such position. The fees paid to non-employee directors for service on the board of directors and for service on each committee of the board of directors on which the director is a member are as follows:

	Member Annual Fee	Chairman Incremental Annual Fee	
Board of Directors	$ 35,000	$ 30,000	(1)
Audit Committee	$ 7,500	$ 15,000	
Compensation Committee	$ 5,000	$ 10,000	
Nominating and Corporate Governance Committee	$ 4,000	$ 8,000	

(1) $15,000 for a lead independent director, if any.

Notwithstanding the foregoing, each of our non-employee directors may elect, no later than December 31 of each year, to receive his or her annual base fees for service on the board of directors in the form of an option to purchase our common stock, which option will be granted on January 2 of the following year, have a Black-Scholes value equal to the annual base board of directors fees that are anticipated to be payable to the director for the entire calendar year, have an exercise price equal to the closing price of our common stock on the date of grant of the award, vest in four equal quarterly installments on the last day of each quarter, subject to the director's continued service as a director through each applicable vesting date (with such vesting prorated for any portion of the quarter that the director is not serving on our board of directors) and have a term of ten years from the date of grant. No such election may be made with respect to fees for serving as chairman (or lead independent director) of the board of directors, or as a member or chairman of a committee of our board of directors.

We also reimburse our non-employee directors for reasonable travel and other expenses incurred in connection with attending meetings of our board of directors and any committee of our board of directors on which he or she serves.

In addition, under our director compensation program, each non-employee director receives under the 2020 Plan, upon his or her initial election or appointment to our board of directors, or in the case of our directors serving at the time of our initial public offering, received upon completion of our initial public offering, an option to purchase 17,000 shares of our common stock. Each of these options vest as to 33.3333% of the shares underlying such award on each of the first, second and third anniversaries of the date of grant of the award, subject to the non-employee director's continued service as a director, employee or consultant. Further, on the dates of each of our annual meetings of stockholders, each non-employee director that has served on our board of directors will receive, under the 2020 Plan, an option to purchase 8,500 shares of our common stock, provided that for a non-employee director who was initially elected to our board of directors within the 12 months preceding the annual meeting of stockholders, the number of shares subject to such option will be pro-rated on a monthly basis for time in service. Each of these options will vest on the twelve-month anniversary of the date of the date of grant of the award (or, if earlier, the date of the next annual meeting of stockholders following the date of grant of the award), subject to the non-employee director's continued service as a director, employee or consultant. All options issued to our non-employee directors under our director compensation program are issued at exercise prices equal to the fair market value of our common stock on the date of grant, will have a term of ten years and will become exercisable in full upon a change in control of our company.

Item 12. Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters.

The following table sets forth information with respect to the beneficial ownership of our common stock as of January 15, 2022 by:

- each of our directors;
- each of our named executive officers;
- all of our directors and executive officers as a group; and
- each person, or group of affiliated persons, who is known by us to beneficially own more than 5% of our common stock.

Beneficial ownership is determined in accordance with the rules and regulations of the SEC and includes voting or investment power with respect to our common stock. Shares of our common stock that an individual has a right to acquire within 60 days after January 15, 2022 are considered outstanding and beneficially owned by the person holding such right for the purpose of calculating the percentage ownership of that person but not for the purpose of calculating the percentage ownership of any other person, except with respect to the percentage ownership of all directors and executive officers. Except as otherwise noted, the persons and entities in this table have sole voting and investing power with respect to all of the shares of our common stock beneficially owned by them, subject to community property laws, where applicable. Except as otherwise set forth below, the address of each beneficial owner is c/o IMARA Inc., 116 Huntington Avenue, 6th Floor, Boston, Massachusetts 02116.

Name of Beneficial Owner	Shares Beneficially Owned	Percentage of Shares Beneficially Owned (%)
OrbiMed Private Investments VII, LP(1)	4,386,568	16.7%
Entities affiliated with New Enterprise Associates 14, L.P.(2)	3,305,601	12.6%
Arix Bioscience Holdings Limited(3)	2,344,072	8.9%
FMR LLC(4)	2,010,154	7.6%
Entities affiliated with Pfizer Ventures (US) LLC(5)	1,557,722	5.9%
Lundbeckfond Invest A/S(6)	1,432,722	5.5%
Directors and Named Executive Officers:		
David Bonita, Ph.D.(1)(8)	4,396,872	16.7%
Mark Chin(3)(8)	2,354,376	9.0%
Edward R. Connor(7)	5,151	*
Barbara J. Dalton, Ph.D.(5)(8)	1,568,026	6.0%
Carl Goldfischer, M.D.(8)(9)	713,684	2.7%
David M. Mott(8)	10,304	*
Laura Williams, M.D., MPH	—	*
Rahul D. Ballal, Ph.D.(10)	572,170	2.1%
Michael P. Gray(11)	188,901	*
Kenneth Attie, M.D.(12)	27,500	*
All current executive officers and directors as a group(10 persons)(13)	9,836,984	37.4%

* Less than one percent.

(1) Consists of (i) 4,199,068 shares of common stock held by OrbiMed Private Investments VII, LP, or OPI VII and (ii) 187,500 shares of common stock held by The Biotech Growth Trust PLC, or BIOG. OrbiMed Capital GP VII LLC, or GP VII, is the general partner of OPI VII and OrbiMed Advisors LLC, or OrbiMed Advisors, is the managing member of GP VII. By virtue of such relationships, GP VII and OrbiMed Advisors may be deemed to have voting and investment power with respect to the shares held by OPI VII and as a result may be deemed to have beneficial ownership of such shares. David Bonita, M.D., an employee of OrbiMed Advisors, is a member of our Board of Directors. OrbiMed Advisors exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and W. Carter Neild. Each of GP VII, OrbiMed Advisors, and David Bonita M.D. disclaims beneficial ownership of the shares held by OPI VII, except to the extent of its or his pecuniary interest therein if any. OrbiMed Capital LLC, or OrbiMed Capital, is the sole portfolio manager of BIOG. OrbiMed Capital disclaims any beneficial ownership over the shares. OrbiMed Capital exercises this investment and voting power through a management committee comprised of Carl L. Gordon, Sven H. Borho and W. Carter Neild. OrbiMed Capital disclaims beneficial ownership of the shares held by BIOG, except to the extent of its or his pecuniary interest therein if any. The business address for OPI VII and BIOG is c/o OrbiMed Advisors LLC, 601 Lexington Avenue 54th Floor, New York, NY 10022.

(2) Based solely on a Form 4 filed with the SEC on January 25, 2022. The securities are directly held by New Enterprise Associates 14, L.P., or NEA 14, and are indirectly held by NEA Partners 14, L.P., or NEA Partners 14, the sole general partner of NEA 14, NEA 14 GP, LTD, or NEA 14 LTD, the sole general partner of NEA Partners 14 and each of the individual directors of NEA 14 LTD (NEA Partners 14, NEA 14 LTD and the individual

directors of NEA 14 LTD, or collectively the Indirect Reporting Persons. The individual directors are Forest Baskett, Anthony A. Florence, Jr., Patrick J. Kerins, Scott D. Sandell and Peter Sonsini. The Indirect Reporting Persons disclaim beneficial ownership of such portion of the NEA 14 securities in which the Indirect Reporting Persons have no pecuniary interest. The address for NEA is 1954 Greenspring Drive, Suite 600, Timonium, MD 21093.

(3) Based solely on a Schedule 13D/A filed with the SEC on July 20, 2021. Consists of 2,344,072 shares of common stock held by Arix Bioscience Holdings Limited, or Arix Ltd. Arix Bioscience Plc, or Arix Plc, is the sole owner and parent of Arix Ltd. and may be deemed to indirectly beneficially own the shares held by Arix Ltd. Mark Chin, a Managing Director at Arix Plc, is a member of our Board of Directors. The address for Arix Ltd. and Arix Plc is 20 Berkeley Square, London, W1J 6EQ, United Kingdom.

(4) Based solely on a Schedule 13G/A filed with the SEC on February 9, 2022. Consists of 2,010,154 shares of common stock held by FMR LLC. Members of the Johnson family, including Abigail P. Johnson, are the predominant owners, directly or through trusts, of Series B voting common shares of FMR LLC, representing 49% of the voting power of FMR LLC. The Johnson family group and all other Series B shareholders have entered into a shareholders' voting agreement under which all Series B voting common shares will be voted in accordance with the majority vote of Series B voting common shares. Accordingly, through their ownership of voting common shares and the execution of the shareholders' voting agreement, members of the Johnson family may be deemed, under the Investment Company Act of 1940, to form a controlling group with respect to FMR LLC. Neither FMR LLC nor Abigail P. Johnson has the sole power to vote or direct the voting of the shares owned directly by the various investment companies registered under the Investment Company Act, or Fidelity Funds, advised by Fidelity Management & Research Company LLC, or FMR Co. LLC, a wholly owned subsidiary of FMR LLC, which power resides with the Fidelity Funds' Boards of Trustees. FMR Co. LLC carries out the voting of the shares under written guidelines established by the Fidelity Funds' Boards of Trustees. The address of FMR LLC is 245 Summer Street, Boston, Massachusetts 02210.

(5) Based solely on a Schedule 13G filed with the SEC on March 26, 2020. Consists of (i) 1,481,719 shares of common stock held by Pfizer Ventures (US) LLC, or Pfizer Ventures, and (ii) 76,003 shares of common stock held by Pfizer Inc., or Pfizer. Pfizer Ventures is a wholly-owned subsidiary of Pfizer and Pfizer may be deemed to beneficially own the shares directly owned by Pfizer Ventures. Barbara Dalton, the Vice President of Venture Capital at Pfizer Ventures, is a member of our Board of Directors. The address of Pfizer and Pfizer Ventures is 235 East 42nd Street, New York, New York 10017.

(6) Consists of 1,432,722 shares of common stock held by Lundbeckfond Invest A/S, or Lunbeckfonden. The board of directors of Lundbeckfonden consists of Jørgen Huno Rasmussen, Steffen Kragh, Lars Holmqvist, Susanne Krüger Kjær, Michael Kjær, Peter Schütze, Gunhild Waldemar, Ludovic Tranholm Otterbein, Vagn Flink Møller Pedersen, Henrik Villsen Andersen and Peter Adler Würtzen. No individual member of the Lunbeckfonden board of directors is deemed to hold any beneficial ownership or reportable pecuniary interest in the shares held by Lunbeckfonden. The board of directors of Lunbeckfonden and Lene Skole, the chief executive officer of Lunbeckfonden, may be deemed to share voting and investment authority over the shares held by Lundbeckfonden. The address of Lundbeckfonden and the above-mentioned persons is Scherfigsvej 7, DK-2100 Copenhagen, Denmark.

(7) Consists of 5,151 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2022 or will become exercisable within 60 days after such date.

(8) Includes 10,304 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2022 or will become exercisable within 60 days after such date.

(9) Consists of (i) 690,232 shares of common stock held by Bay City Capital Fund V, L.P., or Bay City Capital Fund V, and (ii) 13,148 shares of common stock held by Bay City Capital Fund V Co-Investment Fund, L.P., or Bay City Capital Fund V Co-Investment. Bay City Capital Management V, or GP V, is the General Partner of Bay City Capital Fund V and Bay City Capital Fund V Co-Investment, or collectively, BCC V. Bay City Capital LLC, or BCC LLC, is the Manager of GP V. BCC V has shared voting and dispositive power with respect to the shares held by BCC V. GP V has sole voting and dispositive power with respect to the shares held by BCC V. GP V disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. BCC LLC has sole voting and dispositive power with respect to the shares held by BCC V. BCC LLC disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. Carl Goldfischer and Fred Craves are managing directors of BCC LLC and have voting and dispositive power with respect to shares held by Bay City Capital Funds. Dr. Goldfischer disclaims beneficial ownership of these shares, except to the extent of its pecuniary interest therein. The address for Bay City Capital Fund V is 750 Battery Street, Suite 400, San Francisco, CA 94111.

(10) Includes 571,561 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2022 or will become exercisable within 60 days after such date.

(11) Includes 187,189 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2022 or will become exercisable within 60 days after such date.

(12) Consists of 27,500 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2022 or will become exercisable within 60 days after such date.

(13) Consists of 8,994,063 shares of common stock and 842,921 shares of common stock issuable upon the exercise of options that are exercisable as of January 15, 2022 or will become exercisable within 60 days after such date.

Securities Authorized for Issuance under Equity Compensation Plans

The following table contains information about our equity compensation plans as of December 31, 2021:

Plan Category	Number of securities to be issued upon exercise of outstanding options, warrants and rights	Weighted-average exercise price of outstanding options, warrants and rights	Number of securities remaining available for future issuance under equity compensation plans (excluding securities reflected in column (a))
Equity compensation plans approved by security holders			
2016 Stock Incentive Plan	1,068,045	$ 4.51	—
2020 Equity Incentive Plan (1)	1,304,979	13.82	1,216,532
2020 Employee Stock Purchase Plan (2)	—	—	175,667
Equity compensation plans not approved by security holders	—	—	—
Total	2,373,024	$ 9.63	1,392,199

(1) Our 2020 Equity Incentive Plan, or 2020 Plan, has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2020 Plan to be added on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing for each fiscal year until, and including, the fiscal year ending December 31, 2030, equal to the least of (i) 4% of the outstanding shares on such date and (ii) an amount determined by our board of directors. On January 1, 2022, a further 1,051,490 shares were reserved for future issuance under the 2020 Plan pursuant to this provision.

(2) Our 2020 Employee Stock Purchase Plan, or 2020 ESPP, has an evergreen provision that allows for an annual increase in the number of shares available for issuance under the 2020 Plan to be added on the first day of each fiscal year, commencing on January 1, 2021 and ending on January 1, 2031, equal to the least of (i) 386,432 shares of common stock, (ii) 1% of the outstanding shares on such date and (iii) an amount determined by the Board. On January 1, 2022, 262,872 additional shares were reserved for issuance under the 2020 ESPP pursuant to this provision.

Item 13. Certain Relationships and Related Transactions, and Director Independence.

Since January 1, 2020, we have engaged in the following transactions in which the amounts involved exceeded $120,000 and any of our directors, executive officers, or holders of more than 5% of our capital stock, or any member of the immediate family of, or person sharing the household with, the foregoing persons, had or will have a direct or indirect material interest. We believe that all of these transactions were on terms as favorable as could have been obtained from unrelated third parties.

Lundbeck Exclusive License Agreement

In April 2016, we entered into an exclusive license agreement with H. Lundbeck A/S, or Lundbeck, pursuant to which Lundbeck granted us a worldwide license under certain patent rights and certain know-how owned or otherwise controlled by Lundbeck within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or diseases or disorders, including those directly or indirectly related to hemoglobinopathies. As partial consideration for the licenses granted under the agreement, we issued 167,523 shares of our common stock to Lundbeck in April 2016. We issued 127,002 shares of our common stock to Lundbeck in December 2016 and 148,746 shares of our common stock in August 2017 as a result of antidilution provisions contained in the exclusive license agreement triggered by subsequent closings of our series A preferred stock, described below. In addition, pursuant to this exclusive license agreement, we have made cash payments to Lundbeck of $1.8 million to date consisting of an upfront payment and ongoing milestone payments. See “Business—License and Acquisition Agreements” for additional information regarding the exclusive license agreement. Mette Kirstine Agger, who was a member of our board of directors until June 29, 2021, is the Managing Partner of Lundbeckfond Invest A/S, the majority stockholder of Lundbeck. Lundbeckfond Invest A/S owns more than 5% of our capital stock.

Series B Preferred Stock Financing

In February 2020, we issued and sold an aggregate of 9,845,348 shares of series B preferred stock, at a price per share of $1.7419 in cash, for an aggregate purchase price of $17.1 million.

The following table sets forth the aggregate number of shares of series B preferred stock that we issued and sold to our directors and 5% stockholders and their affiliates and the aggregate purchase price for such shares:

Purchaser(1)	Shares of Series B Preferred Stock	Aggregate Purchase Price
New Enterprise Associates 14, L.P.(2)	1,687,778	$ 2,939,941
OrbiMed Private Investments VII, LP(3)	3,013,888	5,249,892
Arix Bioscience Holdings Limited(4)	1,578,683	2,749,908
Entities affiliated with RA Capital Healthcare Fund, L.P.(5)	1,567,222	2,729,944
Pfizer Ventures (US) LLC(6)	568,333	989,979
Lundbeckfond Invest A/S(7)	568,333	989,979
Entities affiliated with Bay City Capital(8)	258,333	449,990

(1) See Part III, Item 12. "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of this Annual Report on Form 10-K for additional information about shares held by certain of these entities.
(2) David M. Mott, the chairman of our board of directors, was a general partner of New Enterprise Associates, and Sara Nayeem, M.D., who was a member of our board of directors until November 15, 2021, was a partner at New Enterprise Associates until February 2021.
(3) David Bonita, M.D., a member of our board of directors, is a General Partner of OrbiMed Advisors.
(4) Mark Chin, a member of our board of directors, is a Managing Director at Arix Bioscience.
(5) RA Capital Healthcare Fund, L.P. was a 5% stockholder at the time of the transaction.
(6) Barbara J. Dalton, Ph.D., a member of our board of directors, is Vice President of Venture Capital of Pfizer, Inc., an affiliate of Pfizer Ventures (US) LLC.
(7) Mette Kirstine Agger, who was a member of our board of directors until June 29, 2021, is a Managing Partner of Lundbeckfonden Ventures.
(8) Carl Goldfischer, M.D., a member of our board of directors, is a Managing Director of Bay City Capital.

The series B preferred stock converted into common stock on a 6.299-for-1 basis upon the closing of our initial public offering on March 16, 2020.

Initial Public Offering

In March 2020, we closed our initial public offering, pursuant to which we issued and sold 4,700,000 shares of our common stock. In April 2020, we issued and sold an additional 705,000 shares of common stock pursuant to the full exercise of the underwriters' over-allotment option. The following table sets forth the aggregate number of shares of our common stock that we issued and sold to our directors and 5% stockholders and their affiliates and the aggregate purchase price for such shares. Such purchases were made through the underwriters at the initial public offering price of $16.00 per share.

Purchaser(1)	Shares of Common Stock	Aggregate Purchase Price
New Enterprise Associates 14, L.P.(2)	475,000	$ 7,600,000
OrbiMed Private Investments VII, LP(3)	1,125,000	18,000,000
Arix Bioscience Holdings Limited(4)	187,500	3,000,000
Entities affiliated with RA Capital Healthcare Fund, L.P.(5)	625,000	10,000,000
Pfizer Ventures (US) LLC(6)	312,500	5,000,000
Lundbeckfond Invest A/S(7)	187,500	3,000,000

(1) See Part III, Item 12. "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of this Annual Report on Form 10-K for additional information about shares held by certain of these entities.
(2) David M. Mott, the chairman of our board of directors, was a general partner of New Enterprise Associates, and Sara Nayeem, M.D., who was a member of our board of directors until November 15, 2021, was a partner at New Enterprise Associates until February 2021.
(3) David Bonita, M.D., a member of our board of directors, is a Partner of OrbiMed Advisors.
(4) Mark Chin, a member of our board of directors, is a Managing Director at Arix Bioscience.
(5) RA Capital Healthcare Fund, L.P. was a 5% stockholder at the time of the transaction.
(6) Barbara J. Dalton, Ph.D., a member of our board of directors, is Vice President of Venture Capital of Pfizer, Inc., an affiliate of Pfizer Ventures (US) LLC.
(7) Mette Kirstine Agger, who was a member of our board of directors until June 29, 2021, is a Managing Partner of Lundbeckfonden Ventures.

Follow On Offering

In July 2021, we closed a follow-on public offering, pursuant to which we issued and sold approximately $50.0 million in shares of our common stock. The following table sets forth the aggregate number of shares of our common stock that we

issued and sold to our directors and 5% stockholders and their affiliates and the aggregate purchase price for such shares. Such purchases were made through the underwriters at the public offering price of $6.00 per share.

Purchaser(1)	Shares of Common Stock	Aggregate Purchase Price
OrbiMed Private Investments VII, LP(2)	1,666,666	$ 9,999,996
Arix Bioscience Holdings Limited(3)	1,333,333	7,999,998

(1) See Part III, Item 12. "Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters" of this Annual Report on Form 10-K for additional information about shares held by certain of these entities
(2) David Bonita, M.D., a member of our board of directors, is a General Partner of OrbiMed Advisors.
(3) Mark Chin, a member of our board of directors, is a Managing Director at Arix Bioscience.

Registration Rights

We are a party to an investors' rights agreement with certain holders of our common stock, including our 5% stockholders and their affiliates and entities affiliated with some of our directors. This investors' rights agreement provides these stockholders the right, subject to certain conditions, to demand that we file a registration statement or to request that their shares be covered by a registration statement that we are otherwise filing.

Indemnification Agreements

Our certificate of incorporation provides that we will indemnify our directors and officers to the fullest extent permitted by Delaware law. In addition, we have entered into indemnification agreements with all of our directors and executive officers. These indemnification agreements may require us, among other things, to indemnify each such director or executive officer for some expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by him or her in any action or proceeding arising out of his or her service as one of our directors or executive officers.

Employment Arrangements

We have entered into employment agreements with certain of our executive officers. For more information regarding the agreements with Dr. Ballal, Mr. Gray and Dr. Attie, see Part III, Item 11. "Executive Compensation." of this Annual Report on Form 10-K."

Policies and Procedures for Related Person Transactions

Our board of directors has adopted written policies and procedures for the review of any transaction, arrangement or relationship in which our company is a participant, the amount involved exceeds $120,000 and one of our executive officers, directors, director nominees or 5% stockholders or their immediate family members, each of whom we refer to as a "related person," has a direct or indirect material interest.

If a related person proposes to enter into such a transaction, arrangement or relationship, which we refer to as a "related person transaction," the related person must report the proposed related person transaction to our chief financial officer. The policy calls for the proposed related person transaction to be reviewed and, if deemed appropriate, approved by our audit committee. Whenever practicable, the reporting, review and approval will occur prior to entry into the transaction. If advance review and approval is not practicable, the committee will review, and, in its discretion, may ratify the related person transaction. The policy also permits the chairman of the audit committee to review and, if deemed appropriate, approve proposed related person transactions that arise between committee meetings, subject to ratification by the committee at its next meeting. Any related person transactions that are ongoing in nature will be reviewed annually.

A related person transaction reviewed under the policy will be considered approved or ratified if it is authorized by the audit committee after full disclosure of the related person's interest in the transaction. As appropriate for the circumstances, the audit committee will review and consider:

- the related person's interest in the related person transaction;
- the approximate dollar value of the amount involved in the related person transaction;
- the approximate dollar value of the amount of the related person's interest in the transaction without regard to the amount of any profit or loss;
- whether the transaction was undertaken in the ordinary course of our business;

- whether the terms of the transaction are no less favorable to us than terms that could have been reached with an unrelated third party;
- the purpose of, and the potential benefits to us of, the transaction; and
- any other information regarding the related person transaction or the related person in the context of the proposed transaction that would be material to investors in light of the circumstances of the particular transaction.

Our audit committee may approve or ratify the transaction only if it determines that, under all of the circumstances, the transaction is in, or is not inconsistent with, our best interests. Our audit committee may impose any conditions on the related person transaction that it deems appropriate.

In addition to the transactions that are excluded by the instructions to the SEC's related person transaction disclosure rule, our board of directors has determined that the following transactions do not create a material direct or indirect interest on behalf of related persons and, therefore, are not related person transactions for purposes of this policy:

- interests arising solely from the related person's position as an executive officer of another entity, whether or not the person is also a director of the entity, that is a participant in the transaction where the related person and all other related persons own in the aggregate less than a 10% equity interest in such entity, the related person and his or her immediate family members are not involved in the negotiation of the terms of the transaction and do not receive any special benefits as a result of the transaction and the amount involved in the transaction is less than the greater of $200,000 or 5% of the annual gross revenues of the company receiving payment under the transaction; and
- a transaction that is specifically contemplated by provisions of our certificate of incorporation or bylaws.

The policy provides that transactions involving compensation of executive officers shall be reviewed and approved by our compensation committee in the manner specified in the compensation committee's charter.

Except with respect to our July 2021 follow-on public offering, the transactions described in this section occurred prior to the adoption of the policy. The transactions associated with our July 2021 follow-on public offering were approved in accordance with the policy.

Director Independence

The Nasdaq Stock Market LLC, or Nasdaq, Marketplace Rules, or the Nasdaq Listing Rules, require a majority of a listed company's board of directors to be composed of independent directors within one year of listing. In addition, the Nasdaq Listing Rules require that, subject to specified exceptions, each member of a listed company's audit, compensation and nominating and corporate governance committees be independent under the Securities Exchange Act of 1934, as amended, or the Exchange Act. Audit committee members must also satisfy the independence criteria set forth in Rule 10A-3 under the Exchange Act and compensation committee members must also satisfy the independence criteria set forth in Rule 10C-1 under the Exchange Act. Under the Nasdaq Listing Rules, a director will only qualify as an "independent director" if, in the opinion of the listed company's board of directors, that person does not have a relationship that would interfere with the exercise of independent judgment in carrying out the responsibilities of a director. In order to be considered independent for purposes of Rule 10A-3, a member of an audit committee of a listed company may not, other than in his or her capacity as a member of the audit committee, the board of directors, or any other board committee, accept, directly or indirectly, any consulting, advisory, or other compensatory fee from the listed company or any of its subsidiaries or otherwise be an affiliated person of the listed company or any of its subsidiaries. In order to be considered independent for purposes of Rule 10C-1, the board must consider, for each member of a compensation committee of a listed company, all factors specifically relevant to determining whether a director has a relationship to such company which is material to that director's ability to be independent from management in connection with the duties of a compensation committee member, including, but not limited to: (1) the source of compensation of the director, including any consulting advisory or other compensatory fee paid by such company to the director; and (2) whether the director is affiliated with the company or any of its subsidiaries or affiliates.

In March 2022, our board of directors undertook a review of the composition of our board of directors and its committees and the independence of each director. Based upon information requested from and provided by each director concerning his or her background, employment and affiliations, including family relationships, our board of directors has determined that each of our directors, with the exception of Rahul D. Ballal, are "independent directors" as defined under the Nasdaq Listing Rules. In making such determinations, our board of directors considered the relationships that each such director has with our company and all other facts and circumstances that our board of directors deemed relevant in

determining his or her independence, including the beneficial ownership of our capital stock by each director. Dr. Ballal is not an independent director under these rules because he is our President and Chief Executive Officer.

Item 14. Principal Accountant Fees and Services.

The following table summarizes the fees of Ernst & Young LLP, our independent registered public accounting firm, billed us for each of the last two fiscal years (in thousands):

	Year Ended December 31,	
	2021	2020
Audit Fees (1)	$ 571	$ 556
Audit-Related Fees (2)	10	—
Tax Fees (3)	—	12
All Other Fees	—	4
	$ 581	$ 572

(1) Audit fees consist of fees billed for professional services by Ernst & Young LLP for audits, quarterly reviews of our consolidated financial statements included in our quarterly reports on Form 10-Q, and services in connection with our initial, follow-on, and at-the-market public offerings, including registration statements, comfort letters, and consents. These services included services performed in connection with our Form S-1, S-3 and S-8 filings.

(2) Audit-related fees consisted of fees for accounting consultations reasonably related to the performance of audits or reviews of our financial statements.

(3) Tax fees consist of fees for professional services performed by Ernst & Young LLP with respect to tax compliance, tax advice and tax planning.

Pre-Approval Policies and Procedures

The audit committee of our board of directors has adopted policies and procedures for the pre-approval of audit and non-audit services for the purpose of maintaining the independence of our independent auditor. We may not engage our independent auditor to render any audit or non-audit service unless either the service is approved in advance by the audit committee, or the engagement to render the service is entered into pursuant to the audit committee's pre-approval policies and procedures. Notwithstanding the foregoing, pre-approval is not required with respect to the provision of services, other than audit, review or attest services, by the independent auditor if the aggregate amount of all such services is no more than 5% of the total amount paid by us to the independent auditor during the fiscal year in which the services are provided, such services were not recognized by us at the time of the engagement to be non-audit services and such services are promptly brought to the attention of the audit committee and approved prior to completion of the audit by the audit committee.

From time to time, our audit committee may pre-approve services that are expected to be provided to us by the independent auditor during the following 12 months. At the time such pre-approval is granted, the audit committee must identify the particular pre-approved services in a sufficient level of detail so that our management will not be called upon to make a judgment as to whether a proposed service fits within the pre-approved services and, at each regularly scheduled meeting of the audit committee following such approval, management or the independent auditor shall report to the audit committee regarding each service actually provided to us pursuant to such pre-approval.

The audit committee has delegated to its chairman the authority to grant pre-approvals of audit or non-audit services to be provided by the independent auditor. Any approval of services by the chairman of the audit committee is reported to the committee at its next regularly scheduled meeting.

PART IV

Item 15. Exhibit and Financial Statement Schedules.

(1) The financial statements listed below are filed as part of this Annual Report on Form 10-K.

(2) All financial statement schedules have been omitted because they are not applicable, not required, or the information required is shown in the consolidated financial statements or the notes thereto.

(3) The following is a list of exhibits filed as part of this Annual Report on Form 10-K

Exhibit Index

Exhibit Number	Description
2.1*	Asset Purchase Agreement, dated October 19, 2020, by and between Complexa (assignment for the benefit of creditors), LLC and the Registrant
3.1	Restated Certificate of Incorporation of the Registrant (incorporated by reference to Exhibit 3.1 to the Registrant's Current Report on Form 8-K filed with the SEC on March 16, 2020)
3.2	Amended and Restated Bylaws of the Registrant (incorporated by reference to Exhibit 3.2 of the Registrant's Current Report on Form 8-K filed with the SEC on March 16, 2020)
4.1	Specimen stock certificate evidencing the shares of common stock (incorporated by reference to Exhibit 4.1 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
4.2	Amended and Restated Investors' Rights Agreement, dated as of March 15, 2019, by and among the Registrant and the other parties thereto (incorporated by reference to Exhibit 4.2 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.1	Sales Agreement by and between the Registrant and Cantor Fitzgerald & Co. dated as of April 1, 2021 (incorporated by reference to Exhibit 1.2 to the Registrant's universal shelf registration statement on Form S-3 filed with the SEC on April 1, 2021).
10.2#	2016 Stock Incentive Plan, as amended (incorporated by reference to Exhibit 10.1 of the Registrant's Registration Statement on Form S-1/A, filed with the SEC on March 3, 2020)
10.3#	Form of Incentive Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.2 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.4#	Form of Nonstatutory Stock Option Agreement under the 2016 Stock Incentive Plan (incorporated by reference to Exhibit 10.3 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.5#	2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.4 of the Registrant's Registration Statement on Form S-1/A, filed with the SEC on March 3, 2020)
10.6#	Form of Stock Option Agreement under the 2020 Equity Incentive Plan (incorporated by reference to Exhibit 10.5 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)

10.7#*	Form of Restricted Stock Unit Agreement under the 2020 Equity Incentive Plan
10.8#	2020 Employee Stock Purchase Plan (incorporated by reference to Exhibit 10.6 of the Registrant's Registration Statement on Form S-1/A, filed with the SEC on March 3, 2020)
10.9†	Exclusive License Agreement, dated as of April 11, 2016, by and between H. Lundbeck A/S and the Registrant, as amended (incorporated by reference to Exhibit 10.7 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.10†*	Exclusive License Agreement, dated as of April 23, 2012, by and between the UAB Research Foundation and the Registrant (as successor-in-interest to Complexa, Inc.)
10.11†*	Non-Exclusive License Agreement, dated as of May 27, 2021, by and between the University of Pittsburgh – Of the Commonwealth System of Higher Education and the Registrant
10.12†*	First Amendment to Non-Exclusive License Agreement, dated as of December 8, 2021, by and between the University of Pittsburgh – Of the Commonwealth System of Higher Education and the Registrant
10.13#	Amended and Restated Letter Agreement, dated as of September 23, 2019, by and between the Registrant and Rahul D. Ballal, Ph.D. (incorporated by reference to Exhibit 10.8 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.14#	First Amendment to the Amended and Restated Letter Agreement, dated as of November 5, 2021, by and between the Registrant and Rahul D. Ballal, Ph.D. (incorporated by reference to Exhibit 10.1 of the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 9, 2021)
10.15#	Amended and Restated Letter Agreement, dated as of September 23, 2019, by and between the Registrant and Michael P. Gray (incorporated by reference to Exhibit 10.10 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.16#	First Amendment to the Amended and Restated Letter Agreement, dated as of November 5, 2021, by and between the Registrant and Michael P. Gray (incorporated by reference to Exhibit 10.2 of the Registrant's Quarterly Report on Form 10-Q, filed with the SEC on November 9, 2021)
10.17#*	Letter Agreement, dated as of December 4, 2020, by and between the Registrant and Kenneth M. Attie, M.D.
10.18#*	First Amendment to the Letter Agreement, dated as of November 5, 2021, by and between the Registrant and Kenneth M. Attie, M.D.
10.19#	Form of Indemnification Agreement with directors and executive officers (incorporated by reference to Exhibit 10.12 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.20#	Office Lease Agreement, dated as of May 20, 2019, by and between Columbia REIT – 116 Huntington, LLC and the Registrant (incorporated by reference to Exhibit 10.13 of the Registrant's Registration Statement on Form S-1, filed with the SEC on February 14, 2020)
10.21#	First Amendment to Office Lease Agreement, dated June 8, 2021, by and between the Company and Columbia REIT – 116 Huntington, LLC (incorporated by reference as Exhibit 10.1 to the Company's Current Report on Form 8-K filed with the SEC on June 11, 2021).
21.1*	List of Subsidiaries of the Registrant
23.1*	Consent of Ernst & Young LLP, independent registered public accounting firm
31.1*	Certification of Principal Executive Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
31.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.1*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
32.2*	Certification of Principal Financial Officer Pursuant to 18 U.S.C. Section 1350, as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.

101.INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Presentation Linkbase Document
101.PRE	XBRL Taxonomy Extension Presentation Linkbase Document
104	The cover page from the Company's Annual Report on Form 10-K for the year ended December 31, 2021, has been formatted in Inline XBRL.

* Filed herewith.

\# Indicates a management contract or any compensatory plan, contract or arrangement.

† Certain portions of this exhibit have been omitted because they are not material and would likely cause competitive harm to the Registrant if disclosed.

Item 16. Form 10-K Summary

None.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, as amended, the Registrant has duly caused this Report to be signed on its behalf by the undersigned, thereunto duly authorized**.**

IMARA INC.

Date: March 15, 2022

By: /s/ Rahul D. Ballal

Rahul D. Ballal, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, this Report has been signed below by the following persons on behalf of the Registrant in the capacities and on the dates indicated.

Name	Title	Date
/s/ Rahul D. Ballal **Rahul D. Ballal, Ph.D.**	President and Chief Executive Officer, Director (Principal Executive Officer)	March 15, 2022
/s/ Michael P. Gray **Michael P. Gray**	Chief Financial Officer and Chief Operating Officer (Principal Financial and Accounting Officer)	March 15, 2022
/s/ David M. Mott **David M. Mott**	Chairman of the Board	March 15, 2022
/s/ David Bonita **David Bonita, M.D.**	Director	March 15, 2022
/s/ Mark Chin **Mark Chin**	Director	March 15, 2022
/s/ Edward Conner **Edward Conner, M.D.**	Director	March 15, 2022
/s/ Barbara J. Dalton **Barbara J. Dalton, Ph.D.**	Director	March 15, 2022
/s/ Carl Goldfischer **Carl Goldfischer, M.D.**	Director	March 15, 2022
/s/ Laura Williams **Laura Williams, M.D., MPH**	Director	March 15, 2022

INDEX TO CONSOLIDATED FINANCIAL STATEMENTS

Report of Independent Registered Public Accounting Firm

To the Stockholders and the Board of Directors of IMARA Inc.

Opinion on the Financial Statements

We have audited the accompanying consolidated balance sheets of IMARA Inc. (the Company) as of December 31, 2021 and 2020, the related consolidated statements of operations and comprehensive loss, convertible preferred stock and stockholders' equity (deficit) and cash flows for each of the two years in the period ended December 31, 2021, and the related notes (collectively referred to as the "consolidated financial statements"). In our opinion, the consolidated financial statements present fairly, in all material respects, the financial position of the Company at December 31, 2021 and 2020, and the results of its operations and its cash flows for each of the two years in the period ended December 31, 2021, in conformity with U.S. generally accepted accounting principles.

The Company's Ability to Continue as a Going Concern

The accompanying consolidated financial statements have been prepared assuming that the Company will continue as a going concern. As discussed in Note 1 to the consolidated financial statements, based on the Company's recurring and expected continuing losses from operations and negative cash flows from operations and the need to raise additional capital to finance its future operations, the Company has stated that substantial doubt exists about the Company's ability to continue as a going concern. Management's evaluation of the events and conditions and management's plans regarding these matters are also described in Note 1. The consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty.

Adoption of ASU No. 2016-02

As discussed in Note 2 to the consolidated financial statements, the Company changed its method of accounting for leases in 2021 due to the adoption of Accounting Standards Update (ASU) No. 2016-02 Leases (Topic 842), and the related amendments.

Basis for Opinion

These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on the Company's financial statements based on our audits. We are a public accounting firm registered with the Public Company Accounting Oversight Board (United States) (PCAOB) and are required to be independent with respect to the Company in accordance with the U.S. federal securities laws and the applicable rules and regulations of the Securities and Exchange Commission and the PCAOB.

We conducted our audits in accordance with the standards of the PCAOB. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement, whether due to error or fraud. The Company is not required to have, nor were we engaged to perform, an audit of its internal control over financial reporting. As part of our audits, we are required to obtain an understanding of internal control over financial reporting but not for the purpose of expressing an opinion on the effectiveness of the Company's internal control over financial reporting. Accordingly, we express no such opinion.

Our audits included performing procedures to assess the risks of material misstatement of the financial statements, whether due to error or fraud, and performing procedures that respond to those risks. Such procedures included examining, on a test basis, evidence regarding the amounts and disclosures in the financial statements. Our audits also included evaluating the accounting principles used and significant estimates made by management, as well as evaluating the overall presentation of the financial statements. We believe that our audits provide a reasonable basis for our opinion.

/s/ Ernst & Young LLP

We have served as the Company's auditor since 2018.
Boston, Massachusetts
March 15, 2022

IMARA INC.
Consolidated Balance Sheets
(in thousands, except share and per share data)

	December 31, 2021	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 48,309	$ 47,698
Short-term investments	41,969	40,524
Prepaid expenses and other current assets	2,418	2,183
Total current assets	92,696	90,405
Property and equipment, net	250	349
Right of use assets - operating leases	525	—
Other assets	175	88
Total assets	$ 93,646	$ 90,842
Liabilities and stockholders' equity		
Current liabilities:		
Accounts payable	2,360	1,971
Accrued expenses and other current liabilities	4,604	4,276
Operating lease liability, current	246	—
Total current liabilities	7,210	6,247
Deferred rent	—	160
Operating lease liability, non-current	406	—
Total liabilities	$ 7,616	$ 6,407
Commitments and contingencies (Note 8)		
Stockholders' equity:		
Preferred stock, $0.001 par value per share; 10,000,000 shares authorized; no shares issued or outstanding as of December 31, 2021 and December 31, 2020	—	—
Common stock, par value of $0.001 per share; 200,000,000 shares authorized; 26,287,264 and 17,548,263 shares issued and outstanding as of December 31, 2021 and 2020, respectively	27	18
Additional paid-in capital	233,516	180,526
Accumulated other comprehensive (loss) income	(16)	4
Accumulated deficit	(147,497)	(96,113)
Total stockholders' equity	86,030	84,435
Total liabilities and stockholders’ equity	$ 93,646	$ 90,842

The accompanying notes are an integral part of these consolidated financial statements.

IMARA INC.
Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Years ended December 31,	
	2021	2020
Operating expenses:		
Research and development	$ 38,442	$ 32,154
General and administrative	13,000	9,544
Total operating expenses	$ 51,442	$ 41,698
Loss from operations	(51,442)	(41,698)
Total other income, (net):		
Interest income	233	483
Other expense	(175)	(145)
Total other income, (net)	$ 58	$ 338
Net loss	$ (51,384)	$ (41,360)
Accretion of Series B convertible preferred stock	—	(7,858)
Net loss attributable to common stockholders—basic and diluted	$ (51,384)	$ (49,218)
Net loss per share applicable to common stockholders—basic and diluted	$ (2.37)	$ (3.53)
Weighted-average common shares outstanding—basic and diluted	$ 21,661,450	$ 13,924,730
Comprehensive loss:		
Net loss	(51,384)	(41,360)
Other comprehensive loss:		
Unrealized loss on investments	(20)	(28)
Comprehensive loss	$ (51,404)	$ (41,388)

The accompanying notes are an integral part of these consolidated financial statements.

IMARA INC.
Consolidated Statements of Convertible Preferred Stock and Stockholders' Equity (Deficit)
(in thousands, except share and per share data)

	CONVERTIBLE PREFERRED STOCK											
	SERIES SEED $0.001 PAR VALUE		SERIES A $0.001 PAR VALUE		SERIES B $0.001 PAR VALUE		COMMON STOCK $0.001 PAR VALUE		ADDITIONAL PAID-IN	ACCUMULATED OTHER COMPREHENSIVE	ACCUMULATED	TOTAL STOCKHOLDERS' EQUITY
	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT	SHARES	AMOUNT	CAPITAL	INCOME (LOSS)	DEFICIT	(DEFICIT)
Balance at December 31, 2019	2,712,960	$ 1,460	31,499,040	$ 30,729	26,321,313	$ 45,575	702,510	$ 1	$ 5,872	$ 32	$ (54,753)	$ (48,848)
Issuance of Series B convertible preferred stock, net of issuance costs of $20 and beneficial conversion charge	—	—	—	—	9,845,348	9,271	—	—	7,858	—	—	7,858
Accretion of Series B converted preferred stock	—	—	—	—	—	7,858	—	—	(7,858)	—	—	(7,858)
Conversion of convertible preferred stock into common stock	(2,712,960)	(1,460)	(31,499,040)	(30,729)	(36,166,661)	(62,704)	11,172,955	11	94,882	—	—	94,893
Initial public offering, net of underwriting discounts, commissions and offering costs of $3,902	—	—	—	—	—	—	5,405,000	6	76,520	—	—	76,526
Exercise of stock options and issuance of stock under the Employee Stock Purchase Plan	—	—	—	—	—	—	267,798	—	1,021		—	1,021
Stock-based compensation expense	—	—	—	—	—	—	—	—	2,231	—	—	2,231
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	(28)	—	(28)
Net loss	—	—	—	—	—	—	—	—	—	—	(41,360)	(41,360)
Balance at December 31, 2020	—	$ —	—	$ —	—	$ —	17,548,263	$ 18	$ 180,526	$ 4	$ (96,113)	$ 84,435
Issuance of common stock under ATM and July 2021 offering, net of issuance costs of $579	—	—	—	—	—	—	8,564,624	9	48,231	—	—	48,240
Exercise of stock options and issuance of stock under the Employee Stock Purchase Plan	—	—	—	—	—	—	174,377	—	914	—	—	914
Stock-based compensation expense	—	—	—	—	—	—	—	—	3,845	—	—	3,845
Unrealized loss on investments	—	—	—	—	—	—	—	—	—	(20)	—	(20)
Net loss	—	—	—	—	—	—	—	—	—	—	(51,384)	(51,384)
Balance at December 31, 2021	—	$ —	—	$ —	—	$ —	26,287,264	$ 27	$ 233,516	$ (16)	$ (147,497)	$ 86,030

The accompanying notes are an integral part of these consolidated financial statements.

IMARA Inc.
Consolidated Statements of Cash Flows
(in thousands)

	Year ended December 31,	
	2021	2020
Cash flows from operating activities:		
Net loss	$ (51,384)	$ (41,360)
Adjustments to reconcile net loss to net cash used in operating activities:		
Stock-based compensation expense	3,845	2,231
Depreciation expense	99	97
Amortization and accretion on investments	155	122
Changes in operating assets and liabilities:		
Prepaid expenses and other current assets	(235)	(465)
Other assets	—	(60)
Accounts payable	389	313
Accrued expenses and other current liabilities	393	1,748
Operating lease assets and liabilities, net	(33)	—
Deferred rent	—	(24)
Net cash used in operating activities	(46,771)	(37,398)
Cash flows from investing activities:		
Proceeds from maturities and sales of short-term investments	45,937	47,500
Purchases of short-term investments	(47,557)	(64,203)
Purchases of property and equipment	(12)	(18)
Net cash used in investing activities	(1,632)	(16,721)
Cash flows from financing activities:		
Proceeds from initial public offering, net of underwriting discounts, commissions and offering costs	—	80,427
Proceeds from issuance of Series B convertible preferred stock, net of issuance costs	—	17,150
Proceeds from July 2021 Offering, net of underwriting discounts and commissions	47,000	—
Proceeds from ATM offering, net of underwriting discounts and commissions	1,819	—
Proceeds from exercise of options	860	1,022
Payment of issuance costs	(578)	(1,718)
Net cash provided by financing activities	49,101	96,881
Net increase in cash, cash equivalents and restricted cash	698	42,762
Cash, cash equivalents and restricted cash, beginning of period	47,786	5,024
Cash, cash equivalents and restricted cash, end of period	$ 48,484	$ 47,786
Supplemental disclosure of non-cash investing and financing activities:		
Conversion of convertible preferred stock into common stock	$ —	$ 94,893
Accretion of redeemable convertible preferred stock to redemption value	$ —	$ (7,858)
Reclassification of deferred offering costs from other assets to additional paid-in capital	$ —	$ (2,144)
Offering costs included in accounts payable and accrued expenses	$ 1	$ —
Property and equipment purchases included in accrued expenses	$ —	$ 12
Unrealized loss on investments	$ (20)	$ (28)

The following table provides a reconciliation of the cash, cash equivalents, and restricted cash balances as of each of the dates shown below:

	December 31,	
	2021	2020
Cash and cash equivalents	$ 48,309	$ 47,698
Restricted cash (included in other assets)	175	88
Total cash, cash equivalents and restricted cash	$ 48,484	$ 47,786

The accompanying notes are an integral part of these consolidated financial statements.

1. Nature of the Business

IMARA Inc. ("IMARA" or the "Company") is a clinical-stage biopharmaceutical company dedicated to developing and commercializing novel therapeutics to treat patients suffering from rare inherited genetic disorders of hemoglobin, known as hemoglobinopathies, and other serious diseases. The Company was incorporated in January 2016 under the laws of the State of Delaware, and its principal offices are in Boston, Massachusetts.

The Company is subject to risks and uncertainties common to early-stage companies in the biotechnology industry, including but not limited to, risks associated with completing preclinical studies and clinical trials, receiving regulatory approvals for product candidates, development by competitors of new biopharmaceutical products, dependence on key personnel, protection of proprietary technology, compliance with government regulations and the ability to secure additional capital to fund operations. The Company's lead product candidate currently under development, tovinontrine (IMR-687), as well as any other product candidates the Company may develop, will require significant additional research and development efforts, including preclinical and clinical testing and regulatory approval, prior to commercialization. These efforts require significant amounts of additional capital, adequate personnel and infrastructure and extensive compliance-reporting capabilities. Even if the Company's product development efforts are successful, it is uncertain when, if ever, the Company will realize revenue from product sales.

In February 2020, the Company effected a 1-for-6.299 reverse stock split of the Company's issued and outstanding shares of common stock and a proportional adjustment to the existing conversion ratios for each of the Company's outstanding series of preferred stock. All share and per share amounts in the consolidated financial statements and notes thereto have been retroactively adjusted for all periods presented to give effect to the reverse stock split, including reclassifying an amount equal to the change in par value of common stock to additional paid-in capital.

On February 25, 2020, the Company issued and sold 1,562,994 shares of Series B convertible preferred stock ("Series B Preferred Stock") at a price of $10.9722 per share, upon a waiver of specified milestone conditions from the holders of a majority of the shares then held by holders of Series B Preferred Stock, and raised approximately $17.1 million in net proceeds after deducting less than $0.1 million of issuance costs.

On March 16, 2020, the Company completed an initial public offering ("IPO") of its common stock and issued and sold 4,700,000 shares of common stock at a public offering price of $16.00 per share, resulting in gross proceeds of $75.2 million. On April 13, 2020, the Company issued and sold an additional 705,000 shares of common stock pursuant to the exercise of the underwriters' option to purchase additional shares for aggregate gross proceeds of $11.3 million. Inclusive of the exercise by the underwriters of their option to purchase additional shares, the Company received approximately $76.5 million in net proceeds from the IPO after deducting $10.0 million of underwriting discounts and commissions and offering expenses.

Upon the closing of the IPO, all 70,378,661 shares of outstanding preferred stock automatically converted into 11,172,955 shares of common stock. Upon conversion of the convertible preferred stock, the Company reclassified the carrying value of the convertible preferred stock to common stock and additional paid-in capital.

On April 1, 2021, the Company filed a Registration Statement on Form S-3 (the "Shelf") with the SEC in relation to the registration and potential future issuance of common stock, preferred stock, debt securities, warrants and/or units of any combination thereof in the aggregate amount of up to $200.0 million. The Shelf was declared effective on April 8, 2021. The Company also simultaneously entered into a sales agreement with Cantor Fitzgerald & Co, LLC, as sales agent, providing for the offering, issuance and sale by the Company of up to an aggregate $75.0 million of its common stock from time to time in "at-the-market" offerings under the Shelf. As of December 31, 2021, the Company had issued and sold 231,291 shares of common stock under the sales agreement, resulting in net proceeds of $1.4 million after deducting commissions and offering expenses.

The extent to which the Company utilizes the sales agreement as a source of funding will depend on a number of factors, including the prevailing market price of the Company's common stock, general market conditions, the extent to which the Company is able to secure funds from other sources, and restrictions on the Company's ability to sell common stock pursuant to the sales agreement to the extent the Company is then subject to restrictions on its ability to utilize the Shelf

to sell more than one-third of the market value of the Company's public float, meaning the aggregate market value of voting and non-voting common stock held by non-affiliates, in any trailing 12-month period. The Company's public float did not exceed $75 million at any point during the 60 days prior to filing of this Annual Report on Form 10-K. As a result, until such time as its public float exceeds $75 million, the Company will be subject to the restrictions on its ability to utilize the Shelf as described in the prior sentence.

On July 16, 2021, the Company completed a public offering of shares of its common stock. In connection with the offering, the Company issued and sold 8,333,333 shares of common stock at a public offering price of $6.00 per share, resulting in net proceeds of $46.8 million after deducting underwriting discounts and commissions and offering expenses.

Liquidity

In accordance with the Financial Accounting Standards Board ("FASB") Accounting Standards Update ("ASU") 2014-15, Disclosure of Uncertainties about an Entity's Ability to Continue as a Going Concern (Subtopic 205-40), the Company has evaluated whether there are conditions and events, considered in the aggregate, that raise substantial doubt about the Company's ability to continue as a going concern within one year after the date that the consolidated financial statements are issued.

The Company has incurred recurring negative cash flows since inception and has funded its operations primarily from the sale of convertible preferred stock and proceeds from the IPO and subsequent common stock offerings. As of December 31, 2021, the Company had cash, cash equivalents, and investments of $90.3 million and an accumulated deficit of $147.5 million. The Company expects its operating losses and negative operating cash flows to continue into the foreseeable future as it continues to expand its research and development efforts.

As of the issuance date of these consolidated financial statements, the Company expects its cash, cash equivalents, and investments of $90.3 million as of December 31, 2021 will not be sufficient to fund the operating expenses and capital expenditure requirements necessary to advance its research efforts and clinical trials for the next twelve months, and the Company will need to obtain additional funding. The Company expects to finance its operations through potential public or private equity financings, debt financings, collaboration agreements or other capital sources. There can be no assurances, however, that the current operating plan will be achieved or that additional funding will be available on terms acceptable to the Company, or at all. If the Company is unable to obtain sufficient funding, it could be required to delay its development efforts, limit activities and reduce research and development costs, which could adversely affect its business prospects.

Based on the Company's recurring losses and negative cash flows from operations since inception, expectation of continuing operating losses and negative cash flows from operations for the foreseeable future, and the need to raise additional capital to finance its future operations, the Company's management concluded that there is substantial doubt about the Company's ability to continue as a going concern for at least twelve months from the date of filing this Annual Report on Form 10-K.

The accompanying consolidated financial statements do not include any adjustments that might result from the outcome of this uncertainty. Accordingly, the consolidated financial statements have been prepared on a basis that assumes the Company will continue as a going concern and which contemplates the realization of assets and satisfaction of liabilities and commitments in the ordinary course of business.

2. Summary of Significant Accounting Policies

Basis of presentation

The accompanying consolidated financial statements have been prepared in conformity with accounting principles generally accepted in the United States of America ("GAAP"). Any reference in these notes to applicable guidance is meant to refer to the authoritative GAAP as found in the Accounting Standards Codification ("ASC") and as amended by Accounting Standards Updates of the FASB.

Principles of Consolidation

The accompanying consolidated financial statements of the Company include the accounts of its then-existing wholly owned subsidiaries, IMARA Security Corporation and IMARA E.U. Limited. All intercompany transactions and balances have been eliminated in consolidation. IMARA E.U. Limited was dissolved in July 2021 and the dissolution of the subsidiary

did not have any material accounting implications on the Company's consolidated financial statements as of and for the year ended December 31, 2021.

Use of Estimates

The preparation of consolidated financial statements in conformity with GAAP requires management to make estimates and assumptions that affect the reported amounts of assets and liabilities, the disclosure of contingent assets and liabilities at the date of the consolidated financial statements and the reported amounts of expenses during the reporting periods. Significant estimates and assumptions reflected in these consolidated financial statements include, but are not limited to, accrued research and development expenses, stock-based compensation expense, the fair value of the common stock and the intrinsic value of the beneficial conversation feature present in the second tranche of the Series B Preferred Stock issued in February of 2020 and income taxes. Actual results could differ materially from those estimates.

Segments

Operating segments are defined as components of an enterprise for which separate and discrete information is available for evaluation by the chief operating decision-maker in deciding how to allocate resources and assess performance. The Company has one operating segment. The Company's chief operating decision maker, its Chief Executive Officer, manages the Company's operations on a consolidated basis for the purpose of allocating resources. All of the Company's long-lived assets are held in the United States.

Cash and Cash Equivalents

The Company considers all highly liquid investments that are readily convertible into cash with original maturities of three months or less from the date of purchase to be cash equivalents. Cash and cash equivalents include cash held in banks and amounts held in money market funds. Cash equivalents are stated at cost, which approximates market value.

Restricted Cash

Restricted cash of $0.2 million and $0.1 million as of December 31, 2021 and December 31, 2020, respectively, represents a letter of credit held as collateral in support of the Company's operating lease at 116 Huntington Avenue in Boston, Massachusetts. Restricted cash is included as a component of other assets on the Company's consolidated balance sheets.

Investments

The Company's investments are maintained by investment managers and consist of corporate debt securities and commercial paper with original maturities of over 90 days, all of which are considered available-for-sale securities. The Company classifies its available-for-sale securities as short-term investments on the consolidated balance sheets, even though the stated maturity date may be one year or more beyond the current balance sheet date, as the Company views those securities as available for use in current operations, if needed.

Available-for-sale securities are carried at fair value with their unrealized gains and losses included in accumulated other comprehensive income within stockholders' equity (deficit), until such gains and losses are realized in other income (expense) within the consolidated statements of operations and comprehensive loss or until an unrealized loss is considered other-than-temporary.

The Company evaluates its investments with unrealized losses for other-than-temporary impairment. When assessing investments for other-than-temporary declines in value, the Company considers such factors as, among other things, how significant the decline in value is as a percentage of the original cost, how long the market value of the investment has been less than its original cost, the Company's ability and intent to retain the investment for a period of time sufficient to allow for any anticipated recovery in fair value and market conditions. If the Company determines from this analysis that it does not expect to receive cash flows sufficient to recover the entire amortized cost of the security, a credit loss exists, the impairment is considered other-than-temporary and is recognized in the consolidated statements of operations and comprehensive loss.

Offering Costs

The Company capitalizes certain legal, professional, accounting and other third-party fees that are directly associated with in-process equity issuances as deferred offering costs until such equity issuances are consummated. After consummation of the equity issuance, these costs are recorded as a reduction in the capitalized amount associated with the equity issuance. Should the equity issuance be abandoned, the deferred offering costs will be expensed immediately as a charge to operating expenses in the consolidated statement of operations and comprehensive loss. There were no deferred offering costs as of December 31, 2021 or December 31, 2020.

Concentrations of Credit Risk and Off-Balance Sheet Risk

Financial instruments that potentially expose the Company to concentrations of credit risk consist primarily of cash, cash equivalents and investments. Periodically, the Company maintains deposits in accredited financial institutions in excess of federally insured limits. The Company deposits its cash in financial institutions that it believes have high credit quality and have not experienced any losses on such accounts and does not believe it is exposed to any unusual credit risk beyond the normal credit risk associated with commercial banking relationships. Such deposits have and will continue to exceed federally insured limits. The Company has not experienced any losses on its cash deposits. The Company's available-for-sale investments primarily consist of high-grade corporate debt and commercial paper, and potentially subject the Company to concentrations of credit risk. The Company has adopted an investment policy that limits the amounts the Company may invest in any one type of investment and requires all investments held by the Company to be highly rated, thereby reducing credit risk exposure.

As of December 31, 2021 and 2020, the Company had no off-balance sheet risk such as foreign exchange contracts, option contracts, or other hedging arrangements.

Comprehensive Loss

Comprehensive loss includes net loss and certain changes in stockholders' equity (deficit) that are excluded from net loss. For the years ended December 31, 2021 and 2020, as a result of the Company's investments in available-for-sale securities, the Company's comprehensive loss includes unrealized losses on those available-for-sale securities.

Fair Value Measurements

Certain assets and liabilities of the Company are carried at fair value under GAAP. Fair value is defined as the exchange price that would be received for an asset or paid to transfer a liability (an exit price) in the principal or most advantageous market for the asset or liability in an orderly transaction between market participants on the measurement date. Valuation techniques used to measure fair value must maximize the use of observable inputs and minimize the use of unobservable inputs. Financial assets and liabilities carried at fair value are to be classified and disclosed in one of the following three levels of the fair value hierarchy, of which the first two are considered observable and the last is considered unobservable:

- Level 1—Quoted prices in active markets for identical assets or liabilities.
- Level 2—Observable inputs (other than Level 1 quoted prices), such as quoted prices in active markets for similar assets or liabilities, quoted prices in markets that are not active for identical or similar assets or liabilities, or other inputs that are observable or can be corroborated by observable market data.
- Level 3—Unobservable inputs that are supported by little or no market activity that are significant to determining the fair value of the assets or liabilities, including pricing models, discounted cash flow methodologies and similar techniques.

To the extent that the valuation is based on models or inputs that are less observable or unobservable in the market, the determination of fair value requires more judgment. Accordingly, the degree of judgment exercised by the Company in determining fair value is greatest for instruments categorized in Level 3. A financial instrument's level within the fair value hierarchy is based on the lowest level of any input that is significant to the fair value measurement.

An entity may choose to measure many financial instruments and certain other items at fair value at specified election dates. Subsequent unrealized gains and losses on items for which the fair value option has been elected will be reported in earnings.

The carrying amounts reflected in the consolidated balance sheets for prepaid expenses and other current assets, accounts payable and accrued expenses approximate their fair values due to their short-term nature of these assets and liabilities.

Property and Equipment, Net

Property and equipment is stated at cost, net of accumulated depreciation. Depreciation is calculated using the straight-line method over the estimated useful lives of the assets, which are as follows:

	Estimated Useful Life
Computer equipment and software	3 years
Furniture and fixtures	5 years
Laboratory equipment	5 years
Leasehold improvements	Shorter of useful life or remaining lease term

Purchased assets that are not yet in service are recorded to construction-in-process and no depreciation expense is recorded. Once they are placed in service they are reclassified to the appropriate asset class. Upon the retirement or sale of an asset, the related cost and accumulated depreciation is removed from the accounts and any resulting gain or loss is recorded to other income (expense), net. Expenditures for maintenance and repairs are expensed as incurred.

Leases

In February 2016, the FASB issued ASU No. 2016-02, Leases (Topic 842) ("ASU 2016-02"). This standard established a right-of-use model that requires all lessees to recognize on their balance sheets right-of-use assets and lease liabilities that arise from leases as well as provide disclosures with respect to certain qualitative and quantitative information related to a company's leasing arrangements to meet the objective of allowing users of financial statements to assess the amount, timing and uncertainty of cash flows arising from leases. The FASB subsequently issued the following amendments to ASU 2016-02 that have the same effective date and transition date: ASU No. 2018-01, Leases (Topic 842): Land Easement Practical Expedient for Transition to Topic 842, ASU No. 2018-10, Codification Improvements to Topic 842, Leases, ASU No. 2018-11, Leases (Topic 842): Targeted Improvements, ASU No. 2018-20, Narrow-Scope Improvement for Lessors, and ASU No. 2019-01, Leases (Topic 842): Codification Improvements. The Company early adopted these amendments with ASU 2016-02 (collectively, the "new leasing standards"), effective January 1, 2021.

The Company adopted the new leasing standards using the modified retrospective transition approach, with no restatement of prior periods and there was no cumulative adjustment to retained earnings. Upon adoption, the Company elected the package of transition practical expedients, which allowed the Company to not reassess the following: (i) whether any expired or existing contracts are or contain leases, (ii) the lease classification for any expired or existing leases and (iii) the treatment of initial direct costs for existing leases. The Company made an accounting policy election to not recognize short-term leases with an initial term of twelve months or less within its consolidated balance sheets and to recognize those lease payments on a straight-line basis in its consolidated statements of operations over the lease term. Upon adopting the new leasing standards, the Company recognized an operating lease right-of-use asset of $0.7 million and a corresponding current and non-current operating lease liability of $0.3 million and $0.6 million, respectively, which are included in its consolidated balance sheets. The adoption of the new leasing standards did not have a material impact on the Company's consolidated statements of operations.

The Company determines if an arrangement is a lease at contract inception. Operating lease right-of-use assets represent the Company's right to use an underlying asset for the lease term and operating lease liabilities represent its obligation to make lease payments arising from the lease. Operating right-of-use assets and liabilities are recognized at the commencement date of the lease based upon the present value of lease payments over the lease term. When determining the lease term, the Company includes options to extend or terminate the lease when it is reasonably certain that the option will be exercised.

The Company uses the implicit rate when readily determinable and uses its incremental borrowing rate when the implicit rate is not readily determinable, based upon the information available at the commencement date in determining the present value of the lease payments. The incremental borrowing rate is determined using a secured borrowing rate for the same currency and term as the associated lease.

The lease payments used to determine operating lease right-of-use assets may include lease incentives and stated rent increases. The Company's lease agreements may include both lease and non-lease components, which the Company accounts for as a single lease component when the payments are fixed, for all classes of underlying assets. Variable payments included in the lease agreement are expensed as incurred.

The Company's operating leases are reflected in operating lease right-of-use assets and in current operating lease liabilities and long-term operating lease liabilities in its consolidated balance sheets. The Company's operating lease right-of-use asset as of December 31, 2021 did not include any material lease incentives. Lease expense for future lease payments is recognized on a straight-line basis over the lease term.

Prior to the adoption of the new leasing standards, the Company recognized lease costs on a straight-line basis once it gained control of the space, without regard to deferred payment terms, such as rent holidays, that would defer the commencement date of required payments or escalating payment amounts. Any lease incentives received were treated as a reduction of costs over the term of the lease agreement, as they were considered an inseparable part of the lease agreement. The difference between required lease payments and rent expense was recorded as deferred rent, which was reflected as deferred rent in the December 31, 2020 consolidated balance sheet.

Research and Development Expenses

Research and development costs are expensed as incurred. Research and development expenses consist of costs incurred in performing research and development activities, including salaries, stock-based compensation and benefits, facilities costs, depreciation, third-party license fees, and external costs of outside vendors engaged to conduct preclinical development activities and clinical trials as well as to manufacture research and development materials. Non-refundable prepayments for goods or services that will be used or rendered for future research and development activities are deferred and capitalized. Such amounts are expensed as the goods are delivered or the related services are performed or until it is no longer expected that the goods will be delivered, or the services rendered.

Costs incurred in obtaining technology licenses are recognized as research and development expense as incurred if the technology licensed has not reached technological feasibility and has no alternative future uses.

Accrued Research and Development Expenses

The Company has entered into various research and development related contracts with parties both inside and outside of the United States, including contracts with third-party contract research organizations and contract manufacturing organizations. These agreements are cancelable, and related payments are recognized as research and development expenses as incurred. The Company records accrued liabilities for estimated ongoing research costs. When evaluating the adequacy of the accrued liabilities, the Company analyzes the progress of the studies or clinical trials, including the phase or completion of events, invoices received and contracted costs. Significant judgments and estimates are made in determining the accrued balances at the end of any reporting period. Actual results could differ from the Company's estimates. To date, the Company's historical accrual estimates have not been materially different from the actual costs.

Patent Costs

All patent-related costs incurred in connection with filing and prosecuting patent applications are expensed as incurred due to the uncertainty about the recovery of the expenditure and are classified as general and administrative expenses.

Stock-Based Compensation

The Company accounts for all stock-based awards granted to employees and non-employees as stock-based compensation expense at fair value. For stock-based awards issued to employees and members of the Company's board of directors (the "Board") for their services as a member of the Board, the Company measures the estimated fair value of the stock-based award on the date of grant.

Since the Company's initial public offering in March 2020, the fair value of the common stock has been determined based on the closing price of the Company's stock on the Nasdaq Global Select Market on the date of grant. Prior to the Company's initial public offering, the Company determined the fair value of the underlying common stock based on input from management and approved by the Board, which utilized the valuation of the Company's enterprise value determined utilizing various methods including the back-solve method, the option-pricing method ("OPM") or a hybrid of the probability-weighted expected return method ("PWERM") and the OPM. The total enterprise value was then allocated to the various outstanding equity instruments, including the underlying common stock, utilizing the OPM.

For employee and non-employee awards, the Company recognizes compensation expense over the requisite service period, which is generally the vesting period of the respective award based on the grant date fair value of the award. For

awards that include performance-based vesting conditions expense is recognized using the accelerated attribution method when the performance condition is deemed to be probable. The Company accounts for forfeitures as they occur. The Company determines the fair value of restricted stock awards in reference to the fair value of its common stock less any applicable purchase price.

The fair value of each stock option grant is estimated on the date of grant using the Black-Scholes option-pricing model, which requires inputs based on certain subjective assumptions, including the expected stock price volatility, the expected term of the option, the risk-free interest rate for a period that approximates the expected term of the option and the Company's expected dividend yield. The fair value of each restricted stock award is determined on the date of grant based on the fair value of the Company's common stock on that same date. Given the Company's limited trading history as a public company, the Company determines the volatility for awards granted based on an analysis of reported data for a group of guideline companies that issued options with substantially similar terms. The expected volatility has been determined using a weighted-average of the historical volatility measures of this group of guideline companies. The Company expects to continue to do so until such time as it has adequate historical data regarding the volatility of its own traded stock price. The expected term of the Company's stock options granted to employees has been determined utilizing the "simplified" method for awards that qualify as "plain-vanilla" options. Under the simplified method, the expected term is presumed to be the midpoint between the vesting date and the end of the contractual term. The Company utilizes this method due to lack of historical exercise data and the plain nature of its stock-based awards. Prior to the Company's IPO, the expected term of stock options granted to non-employees also used the "simplified" method. Following the Company's IPO, the expected term of options granted to non-employees is determined by contractual term. The risk-free interest rate is determined by reference to the U.S. Treasury yield curve in effect at the time of grant of the award for time periods approximately equal to the expected term of the award. The Company has not paid, and does not anticipate paying, cash dividends on its common stock; therefore, the expected dividend yield is assumed to be zero.

The Company classifies stock-based compensation expense in its consolidated statements of operations and comprehensive loss in the same manner in which the award recipient's cash compensation costs are classified.

Income Taxes

The Company accounts for income taxes using the asset and liability method, which requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of events that have been recognized in the financial statements or the Company's tax returns. Under this method, deferred tax assets and liabilities are determined based on the differences between the consolidated financial statements and tax basis of assets and liabilities using enacted tax rates in effect for the year in which the differences are expected to reverse. Changes in deferred tax assets and liabilities are recorded in the provision for income taxes. The Company assesses the likelihood that its deferred tax assets will be recovered from future taxable income and, to the extent it believes, based upon the weight of available evidence, that it is more likely than not that all or a portion of the deferred tax assets will not be realized, a valuation allowance is established.

The Company accounts for uncertain tax positions recognized in the consolidated financial statements by prescribing a more-likely-than-not threshold for financial statement recognition and measurement of a tax position taken or expected to be taken in a tax return. The provision for income taxes includes the effects of any resulting tax reserves, or unrecognized tax benefits, that are considered appropriate as well as the related net interest and penalties.

Net Loss per Share

Basic net loss per share is computed by dividing net loss by the weighted-average number of common shares outstanding during the period. Diluted net loss per share is computed using the weighted-average number of common shares outstanding during the period and, if dilutive, the weighted-average number of potential shares of common stock. Net loss per share attributable to common stockholders is calculated using the two-class method, which is an earnings allocation formula that determines net loss per share for the holders of the Company's common shares and participating securities. The Company's Preferred Stock contained participation rights in any dividend paid by the Company and is deemed to be a participating security. Net loss attributable to common stockholders and participating preferred shares are allocated to each share on an as-converted basis as if all of the earnings for the period had been distributed. The participating securities do not include a contractual obligation to share in losses of the Company and are not included in the calculation of net loss per share in the periods in which a net loss is recorded.

Diluted net loss per share is computed using the more dilutive of (a) the two-class method or (b) the if-converted method. The Company allocates earnings first to preferred stockholders based on dividend rights and then to

common and preferred stockholders based on ownership interests. The weighted-average number of common shares included in the computation of diluted net loss effect to all potentially dilutive common equivalent shares, including outstanding stock options and Preferred Stock. Common stock equivalent shares are excluded from the computation of diluted net loss per share if their effect is antidilutive. In periods in which the Company reports a net loss attributable to common stockholders, diluted net loss per share attributable to common stockholders is generally the same as basic net loss per share attributable to common stockholders since dilutive common shares are not assumed to have been issued if their effect is anti-dilutive.

Recently Issued Accounting Pronouncements

In February 2016, the FASB issued ASU 2016-02, Leases (Topic 842), which sets out the principles for the recognition, measurement, presentation and disclosure of leases for both parties to a contract (i.e., lessees and lessors). The new standard requires lessees to apply a dual approach, classifying leases as either finance or operating leases based on the principle of whether or not the lease is effectively a financed purchase by the lessee. This classification will determine whether lease expense is recognized based on an effective interest method or on a straight-line basis over the term of the lease, respectively. A lessee is also required to record a right-of-use asset and a lease liability for all leases with a term of greater than 12 months regardless of their classification. Leases with a term of 12 months or less will be accounted for similar to existing guidance for operating leases today. ASU 2016-02 supersedes the previous leases standard, ASC 840, Leases. For additional information on the adoption of the new leasing standards, please read the Company's policy above entitled Leases, and Note 8, Commitments and Contingencies, to these consolidated financial statements.

In March 2020, the FASB issued "ASU 2020-03", Codification Improvements to Financial Instruments, ("ASU 2020-03") which addressed, among other topics, Amendments related to ASU 2016-13 Financial Instruments—Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments ("ASU 2016-13"). The amendments align the contractual term under Topic 326 and Topic 842 (Leases) to be consistent, and also clarifies when an entity should record an allowance for credit losses in accordance with Topic 326. For public business entities that meet the definition of a SEC filer, excluding entities eligible to be smaller reporting companies as defined by the SEC, the standard is effective for fiscal years beginning after December 15, 2019, including interim periods within those fiscal years. For all other entities, the standard is effective for fiscal years beginning after December 15, 2022, including interim periods within those fiscal years. Early adoption is permitted. The Company is currently evaluating the impact of this new guidance on the Company's consolidated financial statements and related disclosures but does not expect the adoption of ASU 2020-03 or ASU 2016-13 to be material.

3. Fair Value of Financial Assets and Liabilities

The following table presents information about the Company's financial assets and liabilities measured at fair value on a recurring basis and indicates the level of the fair value hierarchy utilized to determine such fair values (in thousands):

	December 31, 2021			
Description	Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets:				
Money market funds, included in cash and cash equivalents	$ 24,798	$ 24,798	$ —	$ —
Marketable securities:				
Commercial paper	$ 26,131	—	26,131	—
Corporate debt securities	15,838	—	15,838	—
Total financial assets	$ 66,767	$ 24,798	$ 41,969	$ —

Description	December 31, 2020 Total	Quoted Prices in Active Markets for Identical Assets (Level 1)	Significant Other Observable Inputs (Level 2)	Significant Other Observable Inputs (Level 3)
Assets:				
Money market funds, included in cash and cash equivalents	$ 41,208	$ 41,208	$ —	$ —
Marketable securities:				
Corporate debt securities	14,807	—	14,807	—
Commercial paper	25,717	—	25,717	—
Total financial assets	$ 81,732	$ 41,208	$ 40,524	$ —

As of December 31, 2021 and 2020, the Company's cash equivalents consisted of money market funds, classified as Level 1 financial assets, as these assets are valued using quoted market prices in active markets without any valuation adjustment. The financial assets valued based on Level 2 inputs consist of corporate debt securities and commercial paper, which consist of investments in highly-rated investment-grade securities. The Company estimates the fair values of these marketable securities by taking into consideration valuations obtained from third-party pricing sources. These pricing sources utilize industry standard valuation models, including both income and market-based approaches, for which all significant inputs are observable, either directly or indirectly, to estimate fair value. These inputs include market pricing based on real-time trade data for the same or similar securities, issuer credit spreads, benchmark yields, and other observable inputs. The Company validates the prices provided by its third-party pricing sources by understanding the models used, obtaining market values from other pricing sources and analyzing pricing data in certain instances.

During the years ended December 31, 2021 and 2020, there were no transfers between fair value measurement levels.

4. Investments

As of December 31, 2021, the Company had short-term investments consisting of corporate debt securities and commercial paper, which are considered to be available-for-sale investments. These are included in short-term investments on the consolidated balance sheets, even though the stated maturity date may be one year or more beyond the current balance sheet date, as the Company views those securities as available for use in current operations, if needed. The following table summarizes the Company's investments as of December 31, 2021 and 2020 (in thousands):

	December 31, 2021 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Current:				
Commercial paper	$ 26,131	$ —	$ —	$ 26,131
Corporate debt securities	15,854	—	(16)	15,838
Total	$ 41,985	$ —	$ (16)	$ 41,969

	December 31, 2020 Amortized Cost	Gross Unrealized Gains	Gross Unrealized Loss	Fair Value
Current:				
Commercial paper	$ 25,716	$ 1	$ —	$ 25,717
Corporate debt securities	14,804	3	—	14,807
Total	$ 40,520	$ 4	$ —	$ 40,524

As of December 31, 2021, the Company held seven available-for-sale securities with an aggregate value of approximately $15.8 million in an unrealized loss position for less than twelve months. As of December 31, 2020, the Company had no available-for-sale securities in unrealized loss positions. The Company has the intent and ability to hold such securities until recovery. The Company determined that there was no material change in the credit risk of its investments. As a result, the Company determined it did not hold any investments with an other-than-temporary impairment as of December 31, 2021 and 2020.

5. Property and Equipment, net

Property and equipment, net consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Property and equipment:		
Leasehold improvements	$ 336	$ 336
Furniture and fixtures	143	143
Property and equipment	$ 479	$ 479
Less: accumulated depreciation	(229)	(130)
Property and equipment, net	$ 250	$ 349

Depreciation expense was $0.1 million and $0.1 million for the years ended December 31, 2021 and 2020, respectively.

6. Accrued Expenses

Accrued expenses consisted of the following (in thousands):

	December 31, 2021	December 31, 2020
Accrued research and development expenses	$ 2,288	$ 2,732
Accrued compensation and benefits	2,024	1,090
Accrued professional services	249	355
Accrued other	43	99
Total accrued expenses	$ 4,604	$ 4,276

7. License and Purchase Agreements

Tovinontrine (IMR-687) – Exclusive License Agreement with Lundbeck

In April 2016, the Company entered into a license agreement with Lundbeck (the "Lundbeck Agreement") pursuant to which Lundbeck granted the Company the following licenses within the field of prevention, treatment or diagnosis of hemoglobinopathy disorders and/or other diseases or disorders, including those directly or indirectly related to hemoglobinopathies: (1) an exclusive, royalty-bearing license to certain patent rights and certain know-how owned or otherwise controlled by Lundbeck ("Licensed Technology") to research, develop, make, use, sell, and commercialize products ("Licensed Products") from PDE9 inhibitors, which included tovinontrine ("Licensed Compounds"); (2) a non-exclusive license to the Licensed Technology to make, research, develop, and use such Licensed Technology to enable research and development, with certain restrictions; and (3) a sublicensing right that allows the Company to grant sublicenses to third parties to use the Licensed Technology subject to the certain terms detailed in the Lundbeck Agreement. Under the Lundbeck Agreement, the Company is subject to certain achievement dates for development milestones as defined in the agreement. The regulatory milestones due under the Lundbeck Agreement depend on the products being developed. Development milestones due under the Lundbeck Agreement with respect to the Licensed Compounds total up to $23.5 million, and, for any products that contain PDE9 inhibitors other than Licensed Compounds, total up to $11.8 million. The Company also agreed to pay tiered royalties based on net sales of all products licensed under the agreement in the low single-digit percentages.

To date, pursuant to the license agreement, the Company has made cash payments to Lundbeck of $1.8 million consisting of an upfront payment and ongoing milestone payments, which are recorded as research and development expense. No payments were made during the years ended December 31, 2021 or December 31, 2020. As partial consideration for the license, the Company issued 167,523 shares of common stock to Lundbeck in 2016, which represented 8.0% of the Company's then outstanding equity pursuant to a restricted stock agreement. The shares were fully vested on the date of issuance.

The Lundbeck Agreement can be terminated by the Company at any time with 180 days' written notice. The Company or Lundbeck may terminate the agreement by written notice within a specified period of time in the event of a material breach.

IMR-261 – Asset Purchase Agreement with Complexa (assignment for the benefit of creditors), LLC and related license agreements

In October 2020, the Company entered into an asset purchase agreement ("Complexa APA") with Complexa (assignment for the benefit of creditors), LLC ("Complexa ABC"), pursuant to which the Company acquired all of Complexa ABC's right, title and interest in and to the assets comprising the Nrf2 program, including CXA-10 (subsequently renamed IMR-261). As consideration for the assets acquired under the Complexa APA, the Company made a one-time payment of approximately $0.1 million which was expensed to research and development expense and agreed to pay up to an additional approximately $3.8 million in milestone payments based on the achievement of specified clinical and commercial sale milestones as set for the in the Complexa APA. As of December 31, 2021, no Milestone payments have been triggered under this agreement.

8. Commitments and Contingencies

Lease Agreements

In May 2019, the Company entered into a new operating lease agreement for office space totaling 4,210 square feet, located in Boston, Massachusetts with a 62-month term (the "May 2019 Lease Agreement). The lease includes a rent escalation clause which results in cash rental payments of approximately $0.3 million annually. Rent expense is being recognized on a straight-line basis over the lease term. In addition to the base rent, the Company is also responsible for its share of operating expenses, electricity and real estate taxes, in accordance with the terms of the Lease Agreement. The Company provided a security deposit of approximately $0.1 million during the year ended December 31, 2019, which is included as a component of other assets on the Company's consolidated balance sheets. The Company occupied the space in August 2019 and commenced recognition of rent expense. The Company recorded rent expense of $0.3 million and $0.2 million during the years ended December 31, 2021 and 2020, respectively

In June 2021, the Company entered into an amendment to the May 2019 Lease Agreement (the "June 2021 Amended Lease Agreement"). Under the terms of the June 2021 Amended Lease Agreement, the Company will expand its current premises in Boston, Massachusetts by an additional 5,026 square feet, bringing the total office space to 9,236 square feet. The term of the June 2021 Amended Lease Agreement will commence upon completion of the buildout of the additional space, which is expected to occur by the end of March 2022, and expires on March 31, 2027. As of the date of this Annual Report on Form 10-K, the Company has not taken possession of the expanded space and as such has not recognized a lease liability or a right of use asset related to this space. The Company has the option to extend the term for one additional five-year period upon the Company's written notice to the landlord at least 12 months and no more than 15 months in advance of the extension period. Upon commencement of the term of the June 2021 Amended Lease Agreement, the annual base rent obligation is approximately $0.6 million, with a total cash obligation for base rent over the initial five-year term of the lease of approximately $3.2 million. In addition to the base rent, the Company is also responsible for its share of operating expenses, electricity and real estate taxes. Upon execution of the June 2021 Amended Lease Agreement, the Company provided an additional security deposit in the amount of $0.1 million, with security deposits under the May 2019 Lease Agreement and June 2021 Amended Lease Agreement totaling $0.2 million.

The following table summarizes the future lease payments due under the May 2019 Lease Agreement only, as the term of the June 2021 Amended Lease Agreement has not yet commenced (in thousands):

	December 31, 2021
2022	$ 278
2023	284
2024	229
Total Lease Payments	$ 791
Less Imputed Interest	(139)
Present Value of operating lease liabilities	$ 652
Operating cash flows used for operating leases	$ 249
Weighted-average remaining lease term (years)	2.83
Weighted-average discount rate	8%

Under the prior lease accounting guidance, minimum rental commitments under non-cancelable leases as of December 31, 2020 were as follows (in thousands):

	Minimum Lease Payments
2021	$ 273
2022	278
2023	284
2024	229
	$ 1,064

Legal Proceedings

The Company may from time to time be party to litigation arising in the ordinary course of business. The Company was not subject to any material legal proceedings during the years ended December 31, 2021 and 2020, and no material legal proceedings are currently pending or, to the best of its knowledge, threatened.

Indemnification Agreements

The Company enters into standard indemnification agreements in the ordinary course of business. Pursuant to the indemnification agreements, the Company agrees to indemnify, hold harmless, and to reimburse the indemnified party for losses suffered or incurred by the indemnified party, generally the Company's business partners, in connection with any U.S. patent or any copyright or other intellectual property infringement claim by any third-party with respect to the Company's products. The term of these indemnification agreements is generally perpetual any time after execution of the agreement. The maximum potential amount of future payments the Company could be required to make under these indemnification agreements is unlimited. The Company has never incurred costs to defend lawsuits or settle claims related to these indemnification agreements.

9. Convertible Preferred Stock

Prior to the sale of common stock in connection with its IPO, the Company had funded its operations primarily with proceeds from the sale of preferred stock.

On February 25, 2020, the Company raised $17.1 million in net proceeds from the sale of 1,562,994 shares of Series B Preferred Stock, at a price of $10.9722 per share, upon a waiver of specified milestone conditions from the holders of a majority of the shares then held by the holders of Series B Preferred Stock. Upon issuance, each share of Series B Preferred Stock included an embedded beneficial conversion feature as the estimated fair value of the Company's common stock on the date of issuance of the Series B Preferred Stock was higher than the effective conversion price of the Series B Preferred Stock of $10.9722 per share. Given the proximity of the issuance to the Company's public offering, the Company utilized the $16.00 public offing price of its common stock to determine the intrinsic value of the beneficial conversion feature. As a result, the Company recorded the intrinsic value of the beneficial conversion feature of $7.9 million as a discount on the

Series B Preferred Stock at issuance. Because the Series B Preferred Stock was immediately convertible upon issuance and did not include mandatory redemption provisions, the discount on the Series B Preferred Stock was immediately accreted.

Upon the completion of the IPO on March 16, 2020, all 70,378,661 shares of outstanding preferred stock of the Company automatically converted into 11,172,955 shares of common stock. No dividends have been declared by the Company's board of directors since inception.

10. Stockholders' Equity (Deficit)

On August 13, 2019, the Company's board of directors, and on February 26, 2020, the Company's stockholders, approved the Company's restated certificate of incorporation, which became effective upon closing of the IPO on March 16, 2020, to authorize 10,000,000 shares of undesignated preferred stock, $0.001 per share par value, and to increase the number of authorized shares of common stock from 100,000,000 to 200,000,000 shares, $0.001 per share par value.

Common stockholders are entitled to receive dividends, as may be declared by the Board, if any, subject to the preferential dividend rights of any preferred stock then outstanding. Through December 31, 2021, no cash dividends have been declared or paid.

As of December 31, 2021, 10,000,000 shares of preferred stock were authorized and no shares of preferred stock were issued or outstanding.

As of December 31, 2021 and December 31, 2020, the Company has reserved for future issuance the following shares of common stock:

	December 31, 2021	December 31, 2020
Shares reserved for future issuance under the 2020 Equity Incentive Plan	1,216,532	1,110,675
Shares reserved for future issuance under the 2020 Employee Stock Purchase Plan	175,667	191,363
	1,392,199	1,302,038

11. Stock-Based Compensation

2016 Stock Incentive Plan

The Company's 2016 Stock Incentive Plan, (the "2016 Plan") provided for the grant of restricted stock, restricted stock units, stock appreciation rights, incentive stock options, non-statutory stock options and other stock-based awards to employees, officers, members of the Board, consultants and advisors of the Company.

As of the effective date of the 2020 Equity Incentive Plan, no shares remained available for future issuance under the 2016 Plan. Any options or awards outstanding under the 2016 Plan remained outstanding and effective.

2020 Equity Incentive Plan

On October 1, 2019, the Company's board of directors adopted, and on February 26, 2020 the Company's stockholders approved, the 2020 Equity Incentive Plan (the "2020 Plan"), which became effective on March 11, 2020. The 2020 Plan provides for the grant of incentive stock options, non-qualified stock options, stock appreciation rights, restricted stock awards, restricted stock units and other stock-based awards. The number of shares reserved for issuance under the 2020 Plan is the sum of: (1) 1,220,283 shares of the Company's common stock; plus (2) the number of shares (up to a maximum of 2,091,969 shares) equal to the sum of (x) 228,852 shares, which represents the Company's common stock reserved for issuance under the 2016 Plan that remained available for grant under the 2016 Plan as of March 11, 2020 and (y) the number of shares of the Company's common stock subject to outstanding awards granted under the 2016 Plan that expire, terminate or are otherwise surrendered, cancelled, forfeited or repurchased by the Company at their original issuance price pursuant to a contractual repurchase right. The number of shares reserved shall be annually increased on the first day of each fiscal year, beginning with the fiscal year ending December 31, 2021 and continuing until, and including, the fiscal year ending December 31, 2030, equal to the lesser of (i) 4% of the number of shares of the Company's common stock outstanding on the first day of such fiscal year and (ii) an amount determined by the Company's board of directors. On January 1, 2021, 701,930 additional shares were reserved for issuance under the 2020 Plan pursuant to this provision. On January 1, 2022, a further

1,051,490 shares were reserved for future under the 2020 Plan pursuant to this provision. No more than 8,541,982 shares of common stock may be issued as incentive stock options under the 2020 Plan. The shares of common stock underlying any awards that expire, terminate, or are otherwise surrendered, cancelled, forfeited or repurchased by the Company under the 2016 Plan or the 2020 Plan will be added back to the shares of common stock available for issuance under the 2020 Plan.

As of December 31, 2021, there were 1,216,532 shares available for future issuance under the 2020 Plan.

For financial reporting purposes, prior to the IPO the Company performed common stock valuations with the assistance of a third-party specialist to determine stock-based compensation expense for stock options. Upon completion of the IPO, the fair value of the common stock on the grant date was based on the closing price of the stock on the Nasdaq Global Select Market on the date of grant.

The following table summarizes the Company's stock option activity:

	Number of Shares	Weighted-Average Exercise Price	Weighted-Average Remaining Contractual Term (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	1,935,632	$ 9.85	8.14	
Granted	952,953	10.19		
Exercised	(158,681)	4.34		
Forfeited	(356,880)	14.69		
Outstanding as of December 31, 2021	2,373,024	$ 9.63	8.19	$ —
Options vested and exercisable as of December 31, 2021	880,958	$ 7.07	7.33	$ —

The aggregate intrinsic value of options is calculated as the difference between the exercise price of the stock options and the fair value of the Company's common stock for those stock options that had exercise prices lower than the fair value of the common stock as of the end of the period.

The weighted-average grant date fair value of the Company's stock options granted during the years ended December 31, 2021 and 2020 was $7.00 and $12.95, respectively.

The assumptions that the Company used to determine the grant date fair value of stock options granted to employees, non-employees and members of the Board during the years ended December 31, 2021 and 2020 were as follows, presented on a weighted-average basis:

	Year Ended December 31,	
	2021	2020
Expected term (in years)	6.20	6.17
Expected volatility	81.0%	74.7%
Expected dividend yield	0.00%	0.00%
Risk-free interest rate	0.81%	0.52%

Performance-based awards

The Company granted stock options to purchase an aggregate of 220,928 shares of common stock to certain employees, officers and consultants and advisors of the Company on May 16, 2019, June 5, 2019 and June 21, 2019, which contain performance-based vesting criteria. Vesting of these options was contingent on the closing of the second tranche of Series B Preferred Stock financing. Stock-based compensation expense associated with performance-based stock options is recognized if the performance conditions are considered probable of being achieved, using management's best estimates. As a result of the performance condition being met on February 25, 2020, these options vested as to 25% of the shares underlying each option on February 25, 2021 and vest as to the remainder of the shares in equal quarterly installments for three years thereafter. The Company recognized stock-based compensation expense of $0.2 million and $0.3 million for these options during the years ended December 31, 2021 and December 31, 2020, respectively.

Stock-Based Compensation

Stock-based compensation expense included in the Company's consolidated statements of operations and comprehensive loss is as follows (in thousands):

	Year Ended December 31,	
	2021	2020
General and administrative	$ 2,441	$ 1,490
Research and development	1,404	741
Total stock-based compensation expense	$ 3,845	$ 2,231

As of December 31, 2021, total unrecognized compensation cost related to the unvested stock-based awards was $9.4 million, to be recognized over a weighted-average period of 2.65 years.

2020 Employee Stock Purchase Plan

On October 1, 2019, the Company's board of directors adopted, and on February 26, 2020, the Company's stockholders approved the 2020 Employee Stock Purchase Plan (the "2020 ESPP"), which became effective on March 11, 2020. The 2020 ESPP permits eligible employees who elect to participate, in six-month offering periods, to purchase shares of common stock through payroll deductions at a price equal to 85% of the fair market value of the common stock on the first or last business day of each applicable six-month offering period, whichever is lower. Purchase dates under the ESPP occur on or about June 14 and December 14 each year.

The 2020 ESPP initially provides participating employees with the opportunity to purchase up to an aggregate of 193,216 shares of the Company's common stock. The number of shares of the Company's common stock reserved for issuance under the 2020 ESPP will automatically increase on the first day of each fiscal year, beginning with the fiscal year commencing on January 1, 2021 and continuing until, and including, the fiscal year commencing on January 1, 2031, in an amount equal to the lowest of (i) 386,432 shares of the Company's common stock, (ii) 1% of the number of shares of the Company's common stock outstanding on the first day of such fiscal year and (iii) an amount determined by the Company's board of directors. The Company's board of directors decided not to increase the number of shares of the Company's common stock reserved for issuance under the 2020 ESPP for the 2021 fiscal year. On January 1, 2022, 262,872 additional shares were reserved for issuance under the 2020 ESPP pursuant to this provision.

During the year ended December 31, 2021, less than $0.1 million was withheld from employees, on an after-tax basis, in order to purchase 15,696 shares of the Company's common stock. The Company recorded stock-based compensation expense related to the 2020 ESPP of less than $0.1 million. As of December 31, 2021, 175,667 shares of the Company's common stock remained available for issuance under the 2020 ESPP.

As of December 31, 2021, there was less than $0.1 million of total unrecognized stock-based compensation expense related to the ESPP. The expense is expected to be recognized over a period of 5.5 months.

12. Income Taxes

For the years ended December 31, 2021 and 2020, the Company did not record a current or deferred income tax expense or benefit due to current and historical losses incurred by the Company. The Company's losses before income taxes consist solely of losses from domestic operations.

On March 27, 2020, the United States enacted the Coronavirus Aid, Relief, and Economic Security Act ("CARES Act"). The Cares Act includes provisions relating to refundable payroll tax credits, deferment of the employer portion of certain payroll taxes, net operating loss carryback periods, alternative minimum tax credit refunds, modifications to the net interest deduction limitations and technical corrections to tax depreciation methods for qualified improvement property. The CARES Act also established a Paycheck Protection Program whereby certain small businesses are eligible for a loan to fund payroll expenses, rent, and related costs.

The CARES Act provided for an Employee Retention Credit ("ERC"), which is a refundable payroll tax credit that encouraged businesses to keep employees on the payroll during the COVID-19 pandemic. Eligible employers are entitled to a refundable tax credit equal to 50% of qualified wages paid to employees between March 13, 2020, and December 31, 2020,

up to a maximum of $5,000 credit per employee. In late December 2020 Congress expanded and amended the CARES Act by enacting Public Law 116-260. Per the amendment to the CARES Act, eligible employers are entitled to a refundable tax credit equal to 70% of the qualified wages paid to employees between January 1, 2021, and June 30, 2021, up to a maximum of$10,000 of wages per employee per quarter, with a maximum of $7,000 per employee per calendar quarter. Congress further extended the credit with the American Rescue Plan signed into law on March 11, 2021; the American Rescue Plan extended the credit for the period July 1, 2021 to December 31, 2021 with the same limitations as the prior amendment (i.e., tax credit equal to 70% of qualified wages up to a maximum of $10,000 of wages per employee per quarter). However, on November 15, 2021, President Biden signed into law the Infrastructure Investment and Jobs Act which redacted the credit for calendar quarter 4 of 2021. Qualified Wages must be paid on or after March 13, 2020 and before October 1, 2021, and may include wages paid to employees, as well as so much of the employer's qualified health plan expenses as are properly allocable to such wages, not to exceed $10,000 per employee for calendar year 2020 or $10,000 per employee per calendar quarter in quarter 1, 2, or 3 of 2021 ("2021 Eligible Quarter"). The Retention Credit may be claimed for up to $5,000 per employee for calendar year 2020 (i.e., 50% of the $10,000 maximum in Qualified Wages for calendar year 2020) or $7,000 per employee per 2021 Eligible Quarter (i.e., 70% of the $10,000 maximum in Qualified Wages per 2021 Eligible Quarter). Therefore, the maximum Retention Credit per employee in 2020 is $5,000 and in 2021 is $21,000.

Based on the Company's evaluation of this provision and pandemic-related impact on its operations in 2020 and 2021, it was determined that the Company qualified to claim ERC in the second, third and fourth calendar quarters of 2020, as well as in both the first, second, and third calendar quarters of 2021. The Company recognized an ERC of approximately $1.0 million as an offset to payroll tax expenses for the year ended December 31, 2021, respectively, in its consolidated statements of operations.

A reconciliation of income tax expense (benefit) computed at the statutory federal income tax rate to income taxes as reflected in the consolidated financial statements is as follows:

	2021	2020
Income taxes at U.S. statutory rate	21%	21%
State income taxes	6	6
Tax Credit	5	7
Other	0	2
Change in valuation allowance	(32)	(36)
Total provision for income taxes	0%	0%

Deferred taxes are recognized for temporary differences between the basis of assets and liabilities for financial statement and income tax purposes. The significant components of the Company's deferred tax assets and liabilities as of December 31, 2021 and 2020 are comprised of the following (in thousands):

	Year Ended December 31,	
	2021	2020
Deferred tax assets		
Net operating loss carryforwards	$ 37,411	$ 24,657
Tax credits carryforwards	6,968	3,948
Stock-based compensation	1,268	686
Amortization	493	545
Accruals	545	272
Lease incentive liability	—	17
Lease liability	175	—
Unrealized gains/losses on investments	4	—
Other	31	42
Total deferred tax assets	46,895	30,167
Valuation allowance	(46,742)	(30,149)
Net deferred tax assets	153	18
Deferred tax liabilities		
Tenant improvement allowance	(12)	(17)
Unrealized gains/losses on investments	—	(1)
Right of Use Asset	(141)	—
Total deferred tax liabilities	(153)	(18)
Net deferred taxes	$ —	$ —

The Company has evaluated the positive and negative evidence bearing upon its ability to realize its deferred tax assets, which are comprised primarily of net operating loss carryforwards and tax credits. Management has considered the Company's history of cumulative net losses in the United States, estimated future taxable income and prudent and feasible tax planning strategies and has concluded that it is more likely than not that the Company will not realize the benefits of its U.S. federal and state deferred tax assets. Accordingly, a full valuation allowance has been established against these net deferred tax assets as of December 31, 2021 and 2020, respectively. The Company reevaluates the positive and negative evidence at each reporting period. The Company's valuation allowance increased during 2021 by approximately $16.6 million primarily due to the generation of net operating loss and tax credit carryforwards.

As of December 31, 2021 and 2020, the Company had U.S. federal net operating loss carryforwards of $139.2 million and $91.7 million, respectively, which may be available to offset future income tax liabilities. The 2017 Tax Cuts and Jobs Act ("TCJA") will generally allow losses incurred after 2017 to be carried over indefinitely but will generally limit the net operating loss deduction to the lesser of the net operating loss carryover or 80% of a corporation's taxable income (subject to Section 382 of the Internal Revenue Code of 1986, as amended). Also, there will be no carryback for losses incurred after 2017. Losses incurred prior to 2018 will generally be deductible to the extent of the lesser of a corporation's net operating loss carryover or 100% of a corporation's taxable income and be available for twenty years from the period the loss was generated. The Company has federal net operating losses generated following 2017 of $74.5 million, which do not expire. The federal net operating losses generated prior to 2018 of $17.2 million will expire at various dates through 2037. The CARES Act temporarily allows the Company to carryback net operating losses arising in 2018, 2019 and 2020 to the five prior tax years. In addition, net operating losses generated in these years could fully offset prior year taxable income without the 80% taxable income limitation under the TCJA. The Company has been generating losses since its inception. As such, the net operating loss carryback provision under the CARES Act is not applicable to the Company.

As of December 31, 2021 and 2020, the Company also had U.S. state net operating loss carryforwards of $129.4 million and $85.5 million, respectively, which may be available to offset future income tax liabilities and expire at various dates through 2040.

As of December 31, 2021 and 2020, the Company had federal tax credit carryforwards of approximately $6.5 million and $3.6 million, respectively, available to reduce future tax liabilities which expire at various dates through 2040. As of December 31, 2021 and 2020, the Company had state research and development tax credit carryforwards of approximately $0.6 million and $0.4 million, respectively, available to reduce future tax liabilities which expire at various dates through 2035.

Utilization of the U.S. federal and state net operating loss and research and development and orphan drug credit carryforwards may be subject to a substantial annual limitation under Sections 382 and 383 of the Internal Revenue Code of 1986, as amended, and corresponding provisions of state law, due to ownership changes that have occurred previously or that could occur in the future. These ownership changes may limit the amount of net operating loss and research and development credit carryforwards that can be utilized annually to offset future taxable income and tax liabilities, respectively. The Company has not completed a study to assess whether a change of ownership has occurred, or whether there have been multiple ownership changes since its formation, due to the significant cost and complexity associated with such a study. Any limitation may result in expiration of a portion of the net operating loss carryforwards or research and development and orphan drug credit carryforwards before utilization. Further, until a study is completed by the Company and any limitation is known, no amounts are being presented as an uncertain tax position.

The Company has not, as of yet, conducted a study of research and development and orphan drug credit carryforwards. Such a study, once undertaken by the Company, may result in an adjustment to the Company's research and development and orphan drug credit carryforwards; however, until a study is completed and any adjustment is known, no amounts are being presented as an uncertain tax position. A full valuation allowance has been provided against the Company's research and development and orphan drug credits and, if an adjustment is required, this adjustment would be offset by an adjustment to the valuation allowance. Thus, there would be no impact to the balance sheet or statement of operations if an adjustment is required.

The Company files tax returns in the United States and Massachusetts. The Company is subject to U.S. federal and state tax examinations by tax authorities for years 2017 through present. As of December 31, 2021 and 2020, the Company has recorded no liability for unrecognized tax benefits, interest, or penalties related to federal and state income tax matters and there currently no pending tax examinations. The Company will recognize interest and penalties related to uncertain tax positions in income tax expense.

13. Net Loss Per Share

The following table sets forth the computation of the Company's basic and diluted net loss per share for the years ended December 31, 2021 and 2020 (in thousands, except share and per share amounts):

	Year Ended December 31,	
	2021	2020
Numerator:		
Net loss attributable to common stockholders—basic and diluted	$ (51,384)	$ (49,218)
Denominator:		
Weighted-average number of common shares used in net loss per share—basic and diluted	21,661,450	13,924,730
Net loss per share—basic and diluted	$ (2.37)	$ (3.53)

In 2020, the net loss applicable to common stockholders did not equal net loss due to the accretion of the beneficial conversion feature of Series B Preferred Stock in the amount of $7.9 million. The beneficial conversion feature was initially recorded as a discount on the Series B Preferred Stock with a corresponding amount recorded to Additional Paid-in Capital. The discount on the Series B Preferred Stock was then immediately written off as a deemed dividend as the Series B Preferred Stock does not have a stated redemption date and is immediately convertible at the option of the holder. The Company has computed diluted net loss per common share after giving consideration to all potentially dilutive common shares, including convertible preferred stock and options to purchase common stock during the period determined using the if-converted method, except where the effect of including such securities would be antidilutive. Because the Company has reported net losses since inception, these potential common shares have been anti-dilutive and basic and diluted loss per share have been the same.

The Company excluded the following potential common shares from the computation of diluted net loss per share attributable to common stockholders for the years ended December 31, 2021 and 2020 because including them would have had an anti-dilutive effect:

	Year Ended December 31,	
	2021	2020
Options to purchase common stock	2,373,024	1,935,632
Shares reserved for future issuance under the ESPP	175,667	191,363

14. Related Party Transactions

Lundbeck

Lundbeckfond Invest A/S is one of the Company's stockholders and participated in all tranches of the Series A convertible preferred stock ("Series A Preferred Stock") financing and both tranches of the Series B Preferred Stock financing. Prior to the conversion of the Company's preferred stock, Lundbeckfond Invest A/S owned 5,470,492 shares of Series A Preferred Stock as of December 31, 2019, and 478,749 shares of Series Seed convertible preferred stock as of December 31, 2019. Lundbeckfond Invest A/S owned 1,326,111 shares of Series B Preferred Stock as of December 31, 2019. All shares of preferred stock converted into shares of common stock upon closing of the IPO. Lundbeckfond Invest A/S also purchased 187,500 shares of common stock in the IPO. This reflects a 5.0% and a 7.4% ownership interest on a fully diluted basis as of December 31, 2021 and 2020, respectively. Mette Kirstine Agger, who was a member of the Company's board of directors until June 29, 2021, is a Managing Partner at Lundbeckfonden Ventures, which is an affiliate of Lundbeckfond Invest A/S.

Lundbeck, an affiliate of Lundbeckfond Invest A/S, is also one of the Company's stockholders and participated in the fourth tranche of the Company's Series A Preferred Stock financing. Prior to the conversion of the Company's preferred stock, Lundbeck owned 499,069 shares of Series A Preferred Stock as of December 31, 2019, as well as 443,271 shares of common stock issued in conjunction with the Lundbeck Agreement (See Note 7). All shares of preferred stock converted into shares of common stock upon closing of the IPO. This reflects a 1.8% and a 2.7% ownership interest on a fully diluted basis as of December 31, 2021 and 2020, respectively. Lundbeck did not participate in the Series B Preferred Stock financing.

To date, pursuant to the Lundbeck Agreement, the Company has made cash payments to Lundbeck of $1.8 million consisting of an upfront payment and ongoing milestone payments which are recorded as research and development expense.

15. Benefit Plans

The Company established a defined contribution savings plan under Section 401(k) of the Internal Revenue Code effective as of January 2019. This plan covers substantially all employees who meet minimum age and service requirements and allows participants to defer a portion of their annual compensation on a pre-tax basis. Matching contributions to the plan may be made at the discretion of the Board. The Company contributed a match of $0.2 million and $0.1 million to the plan during the years ended December 31, 2021 and 2020, respectively.

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

ASSET PURCHASE AGREEMENT

This Asset Purchase Agreement (the "***Agreement***") is hereby entered into on October 19, 2020 (the "***Effective Date***"), by and between Complexa (assignment for the benefit of creditors), LLC, a Delaware limited liability company (in its sole and limited capacity as assignee for the benefit of creditors of Complexa, Inc., the "***Seller***"), with its principal office located at 3945 Freedom Circle, Suite 560, Santa Clara, California 95054, United States, and Imara Inc. (the "***Buyer***"), with its principal office located at 116 Huntington Ave, Sixth Floor, Boston, MA 02116, United States.

RECITALS

A. By resolution of the board of directors (the "***Board***") of Complexa, Inc., a Delaware corporation (the "***Assignor***"), as memorialized in Assignor's duly executed board resolution, Assignor has transferred ownership of all of its right, title and interest in and to all of its tangible and intangible assets (the "***Assets***") to Seller, and, in so doing, has also designated Seller to act, pursuant to Delaware law, as the assignee for the benefit of creditors of Assignor. The General Assignment agreement (the "***General Assignment***") between Assignor and Seller, as assignee, is attached hereto as Exhibit 1.

B. Seller and Buyer have identified a subset of the Assets that Buyer desires to purchase from Seller (the ***"Purchased Assets"***). The Purchased Assets are defined in Section 1.2 below. After consummation of the Closing contemplated under this Agreement, Seller intends to sell or otherwise liquidate any and all remaining non-cash Assets that are not Purchased Assets and will undertake the winding down of Assignor's assignment estate, which shall ultimately include, but shall not be limited to, the distribution to Assignor's creditors of the assignment estate's net funds remaining after payment of all fees and costs associated with the liquidation of the assignment estate.

C. Seller desires to sell to Buyer, and Buyer desires to purchase from Seller, the Purchased Assets, on the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the above recitals and the mutual covenants hereinafter set forth, Buyer and Seller hereby agree as follows:

1. PURCHASE AND SALE OF THE PURCHASED ASSETS.

1.1 Agreement to Sell and Purchase the Purchased Assets. Subject to the terms and conditions of this Agreement, and in reliance on the representations, warranties and covenants set forth in this Agreement, Seller hereby agrees to sell, assign, transfer and convey to Buyer at the Closing (as defined in Section 2.2 below), and Buyer hereby agrees to purchase and acquire from Seller at the Closing, all of Seller's right, title and interest in and to all of the Purchased Assets. The Purchased Assets will be sold, assigned, transferred and conveyed to Buyer (subject to Section 1.3) on the Closing Date on a "AS IS" and "WHERE IS" basis, with no representations or

warranties other than those specifically set forth below, and subject to any and all existing pledges, liens, licenses, rights of possession, security interests, restrictions, encumbrances, charges, title retention, conditional sale or other security arrangements of any nature whatsoever (collectively, ***"Encumbrances"***).

1.2 Purchased Assets Defined. As used in this Agreement, the term "***Purchased Assets***" means, collectively, Seller's right, title and interest in and to the assets listed in Exhibit 1.2(a) attached hereto, provided, however, that the Purchased Assets specifically do not, under any circumstances, include any of Seller's or Assignor's (i) cash, (ii) accounts receivable, (iii) claims for preference or fraudulent conveyance recoveries under applicable law or any other litigation recoveries, (iv) state or federal tax refunds, (v) insurance refunds or recoveries, (vi) utility or leasehold security deposits, (vii) all corporate governance and human resource documents and business books and records (which for clarity, shall not include regulatory or scientific documents related to the Purchased Assets), or (viii) any of the ***"Excluded Assets"*** (defined below). Buyer shall promptly execute and deliver to Seller any and all such further assignments, endorsements and other documents as Seller may reasonably request for the purpose of effectuating the terms and conditions of this Section.

For the avoidance of doubt, it is the intent of the parties hereto that none of the Excluded Assets shall be transferred to Buyer. For purposes of this Agreement, the term "***Excluded Assets***" means (i) the assets identified on Exhibit 1.2(b) and (ii) all properties, rights, contracts, claims or other assets other than those specifically listed or described in Exhibit 1.2(a) hereto.

1.3 Asset Transfer; Passage of Title; Delivery.

(a) Title Passage. Except as otherwise provided in this Agreement, upon the Closing, (i) title to all of the Purchased Assets shall pass to Buyer; (ii) Seller shall make available to Buyer possession of all of the Purchased Assets as provided in subsection 1.3(b); and (iii) upon Buyer's request, Seller shall execute assignments, conveyances and/or bills of sale reasonably requested to convey to Buyer title to all of the Purchased Assets, subject to the Encumbrances, in accordance with Section 1.1 of this Agreement, as well as such other instruments of conveyance as Buyer may reasonably deem necessary to effect or evidence the transfers contemplated hereby.

(b) Delivery of Purchased Assets. On the Closing Date (as defined in Section 2.2), Seller shall make available to Buyer possession of the Purchased Assets, provided, however, that the expenses of retrieving, removing and transferring the Purchased Assets shall be borne exclusively by Buyer, and provided further that in the event that any of the Purchased Assets are located outside of the physical control of Seller, such as in warehouses or foreign locations controlled by third parties, Seller is not making any representation or warranty to Buyer as to the quantities of Purchased Assets under the control of such third parties or the accessibility of such Purchased Assets.

(c) Retention of Documents. As assignee, Seller is responsible for maintaining business records during the assignment process and, among other things, will prepare and file final tax returns. To the extent Buyer requires business records of Assignor that Seller has retained to

administer the assignment estate, Buyer shall, at its own expense, arrange to obtain copies of such records from Seller.

2. PURCHASE PRICE; PAYMENTS.

2.1 Purchase Price.

(a) Upfront Consideration. In partial consideration of the sale, transfer, conveyance and assignment of all of the Purchased Assets to Buyer at the Closing, Buyer shall, as of the Closing, assume only those liabilities, if any, expressly set forth as Assumed Liabilities in Section 3.1 of this Agreement and shall pay by wire transfer to an account designated by Seller at the Closing the sum of seventy-five thousand U.S. dollars ($75,000) (the "***Upfront Payment***").

(b) Contingent Consideration. As additional consideration for the Purchased Assets, Buyer shall pay to Seller by wire transfer to an account designated by Seller the contingent payments (each a "***Contingent Payment***") set forth in Exhibit 2.1 based on the achievement by or on behalf of Buyer of the corresponding milestone event set forth in Exhibit 2.1. For the avoidance of doubt, a Contingent Payment shall be due and payable only once (and only one Contingent Payment shall be payable with respect to each milestone event) and shall be paid by Buyer to Seller promptly, but in no event later than [**] following the occurrence of the applicable milestone event by wire transfer to Seller. The Upfront Payment and the Contingent Payments are collectively referred to herein as the "***Purchase Price***." Notwithstanding the foregoing, from and after the Closing, Buyer shall, in its sole and absolute discretion, make all decisions with respect to the research, development and commercialization of the Purchased Assets and shall have no obligation to undertake any efforts to achieve the milestone events.

2.2 Closing. The consummation of the purchase and sale of the Purchased Assets contemplated hereby will take place at a closing to be held at the offices of Seller (the ***"Closing"***), as soon as possible but in no event later than the third (3rd) business day following the satisfaction or waiver of the last of the conditions set forth in Section 8 (the ***"Closing Date"***), or at such other time or date, and at such place, or by such other means of exchanging documents, as may be agreed to by Buyer and Seller. If the Closing does not occur on or prior to November 30, 2020, or such later date upon which Buyer and Seller agree in writing, this Agreement shall terminate upon written notice of termination given by either party hereto that is not in default of its obligations hereunder, and thereupon this Agreement shall become null and void and no party hereto will have any further rights or obligations hereunder, except that Section 6.1 shall survive such termination.

3. OBLIGATIONS ASSUMED.

3.1 Liabilities. Buyer agrees, upon consummation of, and effective as of, the Closing, to assume those (and only those) liabilities of Seller and of Assignor directly relating to all obligations arising after the Closing under contracts of Assignor listed in Exhibit 3.1 that are effectively assigned to, and assumed by, Buyer (collectively, the "***Assumed Liabilities***").

3.2 Liabilities and Obligations Not Assumed. Except as expressly set forth in Section 3.1 above, Buyer shall not assume or become obligated in any way to pay or perform any liabilities,

debts or obligations of Seller or of Assignor whatsoever, including, but not limited to, any liabilities or obligations now or hereafter arising from Assignor's business activities that took place prior to the Closing or any liabilities arising out of or connected to the liquidation and winding down of Assignor's business. All liabilities, debts and obligations of Seller and of Assignor not expressly assumed by Buyer hereunder are hereinafter referred to as the "***Excluded Liabilities***."

3.3 **No Obligations to Third Parties.** The execution and delivery of this Agreement shall not be deemed to confer any rights upon any person or entity other than the parties hereto, or make any person or entity a third party beneficiary of this Agreement, or to obligate either party to any person or entity other than the parties to this Agreement. The assumption by Buyer of any liabilities or obligations of Seller under Section 3.1 shall in no way expand the rights or remedies of third parties against Buyer as compared to the rights and remedies such parties would have against Seller if the Closing was not consummated.

4. REPRESENTATIONS AND WARRANTIES OF BUYER.

Buyer hereby represents and warrants to Seller that all the following statements are true, accurate and correct:

4.1 **Due Organization.** Buyer is a corporation duly organized, validly existing, and in good standing under the laws of Delaware. Buyer has all necessary power and authority to enter into this Agreement and to execute and deliver all other documents that Buyer is required to execute and deliver hereunder, and Buyer holds or will timely hold all permits, licenses, orders and approvals of all federal, state and local governmental or regulatory bodies necessary and required therefore.

4.2 **Power and Authority; No Default.** Buyer has all requisite power and authority to enter into and deliver this Agreement and to perform its obligations hereunder. The execution, delivery and performance by Buyer of this Agreement, and the consummation of all the transactions contemplated hereby, have been duly and validly authorized by Buyer. This Agreement, when signed and delivered by Buyer, will be duly and validly executed and delivered and will be the valid and binding obligation of Buyer, enforceable against Buyer in accordance with its terms, subject to the laws relating to bankruptcy, insolvency and relief of debtors, and rules and laws governing specific performance, injunctions, relief and other equitable remedies.

4.3 **Authorization for this Agreement.** No authorization, approval, consent of, or filing with any governmental body, department, bureau, agency, public board, authority or other third party is required for the consummation by Buyer of the transactions contemplated by this Agreement.

4.4 **Litigation.** To the best of Buyer's knowledge, there is no litigation, suit, action, arbitration, inquiry, investigation or proceeding pending or, to the knowledge of Buyer, threatened, before any court, agency or other governmental body against Buyer (or any corporation or entity affiliated with Buyer) which seeks to enjoin or prohibit or otherwise prevent the transactions contemplated hereby.

4.5 **Funding.** Buyer currently has available to it, and will have available to it at the Closing, sufficient funds to pay the Purchase Price to Seller at the Closing. Buyer's ability to perform its financial obligations under this Agreement is therefore not subject to any financing contingency.

5. REPRESENTATIONS AND WARRANTIES OF SELLER.

Seller represents and warrants to Buyer that all of the following statements are true, accurate and correct:

5.1 **Corporate Organization.** Seller is a limited liability company duly organized, validly existing, and in good standing under the laws of the State of California.

5.2 **Power and Authority; No Default Upon Transfer.** As assignee, Seller has all requisite power and authority to enter into and deliver this Agreement and to perform its obligations hereunder and under the General Assignment. The signing, delivery and performance by Seller of this Agreement, and the consummation of all of the transactions contemplated hereby, have been duly and validly authorized by Seller. To the best of Seller's knowledge, the General Assignment was duly authorized by Assignor's Board and is a valid agreement binding on the Assignor and Seller. This Agreement, when signed and delivered by Seller, will be duly and validly executed and delivered and will be the valid and binding obligation of Seller, enforceable against Seller, as assignee, in accordance with its terms as governed by applicable law, regulations and rules. Neither the signing and delivery of this Agreement by Seller, nor the performance by Seller of its obligations under this Agreement, will (i) violate Seller's Articles of Organization or Operating Agreement, or (ii) violate any law, statute, rule or regulation or order, judgment, injunction or decree of any court, administrative agency or government body applicable to Seller.

5.3 **Title.** To the best of Seller's knowledge after reasonable inquiry, Seller, as assignee, has good and marketable title to all of the Purchased Assets. Seller sells, assigns, transfers and conveys the Purchased Assets to Buyer on an "AS IS" and "WHERE IS" basis, with no representations or warranties as to merchantability, fitness or use, and the Purchased Assets shall be subject to the Encumbrances.

(a) **AS-IS SALE; DISCLAIMERS; RELEASE. IT IS UNDERSTOOD AND AGREED THAT, UNLESS EXPRESSLY STATED HEREIN, SELLER IS NOT MAKING AND HAS NOT AT ANY TIME MADE ANY WARRANTIES OR REPRESENTATIONS OF ANY KIND OR CHARACTER, EXPRESS OR IMPLIED, WITH RESPECT TO THE PURCHASED ASSETS, INCLUDING, BUT NOT LIMITED TO, ANY WARRANTIES OR REPRESENTATIONS AS TO MERCHANTABILITY OR FITNESS FOR A PARTICULAR PURPOSE.**

(b) **BUYER ACKNOWLEDGES AND AGREES THAT UPON THE CLOSING SELLER SHALL SELL AND CONVEY TO BUYER AND BUYER SHALL ACCEPT THE PURCHASED ASSETS "AS IS, WHERE IS, WITH ALL FAULTS." BUYER HAS NOT RELIED UPON AND WILL NOT RELY ON, AND SELLER IS NOT LIABLE FOR OR BOUND BY, ANY EXPRESS OR IMPLIED WARRANTIES,**

GUARANTEES, STATEMENTS, REPRESENTATIONS OR INFORMATION PERTAINING TO THE PURCHASED ASSETS OR RELATING THERETO MADE OR FURNISHED BY SELLER OR ITS REPRESENTATIVES TO WHOMEVER MADE OR GIVEN, DIRECTLY OR INDIRECTLY, ORALLY OR IN WRITING, EXCEPT AS EXPRESSLY STATED HEREIN. BUYER ALSO ACKNOWLEDGES THAT THE PURCHASE PRICE REFLECTS AND TAKES INTO ACCOUNT THAT THE PURCHASED ASSETS ARE BEING SOLD "AS IS, WHERE IS, WITH ALL FAULTS."

(c) **BUYER ACKNOWLEDGES TO SELLER THAT BUYER WILL HAVE THE OPPORTUNITY TO CONDUCT PRIOR TO CLOSING SUCH INSPECTIONS AND INVESTIGATIONS OF THE PURCHASED ASSETS AS BUYER DEEMS NECESSARY OR DESIRABLE TO SATISFY ITSELF AS TO THE PURCHASED ASSETS AND ITS ACQUISITION THEREOF. BUYER FURTHER WARRANTS AND REPRESENTS TO SELLER THAT BUYER WILL RELY SOLELY ON ITS OWN REVIEW AND OTHER INSPECTIONS AND INVESTIGATIONS IN THIS TRANSACTION AND NOT UPON THE INFORMATION PROVIDED BY OR ON BEHALF OF SELLER, OR ITS AGENTS, EMPLOYEES OR REPRESENTATIVES WITH RESPECT THERETO. BUYER HEREBY ASSUMES THE RISK THAT ADVERSE MATTERS, INCLUDING, BUT NOT LIMITED TO, LATENT OR PATENT DEFECTS, ADVERSE PHYSICAL OR OTHER ADVERSE MATTERS, MAY NOT HAVE BEEN REVEALED BY BUYER'S REVIEW AND INSPECTIONS AND INVESTIGATIONS.**

(d) **BUYER ACKNOWLEDGES THAT SOME OF THE PURCHASED ASSETS DESCRIBED IN EXHIBIT 1.2(a) MAY CONTAIN THIRD-PARTY INTELLECTUAL PROPERTY THAT MAY HAVE BEEN LICENSED BY ASSIGNOR OR OTHERWISE ACQUIRED BY ASSIGNOR. BUYER UNDERSTANDS THAT SELLER MAY BE UNABLE TO TRANSFER INTELLECTUAL PROPERTY BELONGING TO A THIRD-PARTY WITHOUT THE EXPRESS WRITTEN CONSENT OF THAT THIRD-PARTY, WHICH, EXCEPT AS SET FORTH IN EXHIBIT 8.1(E), WILL NOT BE OBTAINED OR SOUGHT BY SELLER AS A PART OF, OR CONDITION TO, THIS AGREEMENT. BUYER SHALL ACCEPT FULL RESPONSIBILITY FOR COMMUNICATING WITH ANY SUCH THIRD-PARTIES WHOSE INTELLECTUAL PROPERTY MAY BE INCLUDED IN THE PURCHASED ASSETS TRANSFERRED HEREBY AND SHALL PAY ANY AND ALL LICENSING OR OTHER FEES, COSTS, EXPENSES OR CHARGES THAT MAY BE ASSOCIATED WITH USING ANY SUCH PURCHASED ASSETS FOLLOWING THE CLOSING. ASSIGNOR SHALL REMAIN RESPONSIBLE FOR ANY AND ALL LICENSING OR OTHER FEES, COSTS, EXPENSES OR CHARGES THAT MAY BE ASSOCIATED WITH USING ANY SUCH PURCHASED ASSETS PRIOR TO THE CLOSING.**

5.4 Litigation. To the best of Seller's knowledge, there is no claim, action, arbitration, inquiry, investigation, suit or proceeding pending or, to Seller's knowledge, threatened, against Seller or Assignor that might affect in any way any of the Purchased Assets or the transactions contemplated by this Agreement, nor is Seller aware or have grounds to know of any reasonable basis therefor. To the best of Seller's knowledge, there are no judgments, decrees, injunctions or

orders of any court, governmental body, department, commission, agency, instrumentality or arbitrator against Seller or Assignor affecting the Purchased Assets.

5.5 Authorization for this Agreement. Except to the extent consent may be required to assign the Pittsburgh and UAB Agreements (as defined in Exhibit 1.2(a)), no authorization, approval, consent of, or filing with any governmental body, department, bureau, agency, public board, authority or other third party is required for the consummation by Seller of the transactions contemplated by this Agreement.

5.6 Assignee. All rights of Seller with regard to the ownership and possession of the Purchased Assets are rights held as assignee pursuant to the General Assignment made by Assignor. Pursuant to the General Assignment, Assignor has informed Seller that it transferred to Seller all of Assignor's right, title and interest in and to the Purchased Assets. Pursuant to this Agreement, Seller, solely in its capacity as assignee, will at Closing sell, assign, and transfer all of its right, title and interest in and to the Purchased Assets to Buyer.

6. COVENANTS OF BUYER.

6.1 Confidential Information. All copies, if any, of financial information, pricing, marketing plans, business plans, and other confidential and/or proprietary information of Assignor and/or Seller disclosed to Buyer in the course of negotiating the transactions contemplated by this Agreement, including the terms of this Agreement ("***Seller Confidential Information***"), will be held in confidence and not be used or disclosed by Buyer or any of its employees, affiliates or stockholders, except to any public or private lender, for a period of [**] from the Effective Date and will be promptly destroyed by Buyer or returned to Seller, upon Seller's written request to Buyer; *provided*, *however*, that from and after the Closing, the foregoing covenant shall not be applicable to any Seller Confidential Information included in the Purchased Assets. It is agreed that Seller Confidential Information will not include information that: (a) is proven to have been known to Buyer prior to receipt of such information from Seller; (b) is disclosed by a third party having the legal right to disclose such information and who owes no obligation of confidence to Seller; (c) is now, or later becomes, part of the general public knowledge or literature, other than as a result of a breach of this Agreement by Buyer; or (d) is independently developed by Buyer without the use of any Seller Confidential Information. The restrictions set forth in this Section 6.1 shall not apply any Seller Confidential Information that Buyer is required to disclose by law, applicable government regulation or by order of a court of competent jurisdiction.

6.2 Press Releases and Public Announcements. Buyer shall not issue any press release or make any public disclosure or announcement relating to the financial terms of this Agreement or identifying Seller without the prior written approval of Seller, which shall not be unreasonably withheld. Notwithstanding the foregoing, Buyer may disclose certain information relating to this Agreement if required to do so by law, applicable governmental regulation or by order of a court of competent jurisdiction.

6.3 Taxes and any Other Charges Related to the Sale. Buyer agrees to promptly pay all sales, transfer, use or other taxes, duties, claims or charges imposed on and/or related to the sale of the Purchased Assets under this Agreement by any tax authority or other governmental

agency and to defend, indemnify and hold Seller harmless from and against any such taxes, duties, claims, or charges for payment thereof by any tax authority or other governmental agency. Buyer agrees that it will pay to the appropriate governmental agency any sales tax resulting from the sale of the Purchased Assets under this Agreement within [**] following the Effective Date, and will provide to Seller written proof of Buyer having made such sales tax payment within [**] of the date that Buyer made such sales tax payment. Exhibit 6.3 hereto contains an allocation of the Purchase Price among the Purchased Assets.

6.4 **Discontinued Studies**. Following the Closing, and upon the transfer of the INDs (as defined in Exhibit 8.1(a)) to the Buyer, the Buyer shall, at its own cost and expense, close any and all Food and Drug Administration studies that the Buyer chooses not to continue in its discretion.

6.5 **Survival of Covenants.** The covenants set forth in this Section shall survive the Closing. The covenants set forth in Section 6.1 above shall, in addition, survive the termination of this Agreement for any reason.

7. COVENANTS OF SELLER.

Seller covenants and agrees with Buyer as follows:

7.1 **Further Assurances.** From and after the Closing Date, Seller shall cooperate with Buyer and promptly sign and deliver to Buyer any and such additional documents, instruments, endorsements and related information and take actions as Buyer may reasonably request for the purpose of effecting the transfer of Seller's and/or Assignor's title to the Purchased Assets to Buyer, and/or carrying out the provisions of this Agreement, provided, however, that Seller shall be reimbursed for its reasonable costs and expenses incurred in providing such documents, instruments, endorsements or related information, which additional documents, instruments, endorsements or related information shall be prepared solely by Buyer.

7.2 **Press Releases and Public Announcements.** Seller shall not issue any press release or make any public disclosure or announcement relating to this Agreement or identify Buyer without Buyer's prior written approval, which shall not be unreasonably withheld. Notwithstanding the foregoing, Seller may disclose certain information relating to this Agreement if required to do so by law, applicable governmental regulation, or by order of a court of competent jurisdiction, and Seller shall be permitted, at its discretion, to prepare and distribute a tombstone regarding the General Assignment and this Agreement without mentioning the identity of Buyer or the terms of this Agreement.

7.3 **Survival of Covenants.** Each of the covenants set forth in this Section 7 shall survive the Closing.

8. CONDITIONS TO CLOSING.

8.1 Conditions to Buyer's Obligations. Buyer's obligations hereunder shall be subject to the satisfaction and fulfillment of each of the following conditions, except as Buyer may expressly waive the same in writing:

(a) Accuracy of Representations and Warranties on the Closing Date. The representations and warranties made herein by Seller shall be true and correct in all material respects, and not misleading in any material respect, on and as of the date given, and on and as of the Closing Date, with the same force and effect as though such representations and warranties were made on and as of the Closing Date.

(b) Compliance. As of the Closing Date, Seller shall have complied in all material respects with, and shall have fully performed, in all material respects, all conditions, covenants and obligations of this Agreement imposed on Seller and required to be performed or complied with by Seller at, or prior to, the Closing Date.

(c) Delivery of Purchased Assets. Seller shall have made the Purchased Assets available to Buyer as set forth in Section 1.3 above.

(d) Delivery of Closing Documents. Seller shall have delivered, and Buyer shall have received, the documents described in Section 9.2 hereof.

(e) Proper Assignment. Seller shall have satisfied, in Buyer's reasonable discretion, each of the requirements set forth on Exhibit 8.1(e).

(f) No Bankruptcy. As of the Closing Date, neither Assignor nor Seller shall have become subject to any bankruptcy or receivership proceeding.

(g) Lien Search. The results of a confirmatory lien search identify no additional liens on the Purchased Assets as of the Closing Date as compared to those in existence on the Effective Date.

8.2 Conditions to Seller's Obligations. The obligations of Seller hereunder shall be subject to the satisfaction and fulfillment of each of the following conditions, except as Seller may expressly waive the same in writing:

(a) Accuracy of Representations and Warranties on Closing Date. The representations and warranties made herein by Buyer shall be true and correct in all material respects, and not misleading in any material respect, on and as of the date given, and on and as of the Closing Date with the same force and effect as though such representations and warranties were made on and as of the Closing Date.

(b) Compliance. Buyer shall have complied in all material respects with, and shall have fully performed, the terms, conditions, covenants and obligations of this Agreement imposed thereon to be performed or complied with by Buyer at, or prior to, the Closing Date.

(c) Payment. Buyer shall have transmitted by wire transfer and Seller shall have received payment of the Upfront Payment.

9. CLOSING OBLIGATIONS.

9.1 Buyer's Closing Obligations. At the Closing, Buyer shall deliver to Seller each of the following:

(a) Payment of the Upfront Payment by wire transfer.

(b) The Assignment and Bill of Sale Agreement, in the form attached hereto as Exhibit 9.1 (b), signed by an authorized officer of Buyer on behalf of Buyer.

(c) The Patent Assignment Agreement, in the form attached hereto as Exhibit 9.1 (c), signed by an authorized officer of Buyer on behalf of Buyer.

9.2 Seller's Closing Obligations. At the Closing, Seller shall deliver to Buyer each of the following:

(a) The Purchased Assets in accordance with Section 1.3.

(b) The Assignment and Bill of Sale Agreement, in the form attached hereto as Exhibit 9.1 (b), signed by an authorized representative of Seller on behalf of Seller.

(c) The Patent Assignment Agreement, in the form attached hereto as Exhibit 9.1 (c), signed by an authorized representative of Seller on behalf of Seller.

10. SURVIVAL OF WARRANTIES AND INDEMNIFICATION.

10.1 Survival of Warranties. All representations and warranties made by Buyer herein, or in any certificate, schedule or exhibit delivered pursuant hereto, shall survive the Closing for a period of one (1) year after the Closing. All representations and warranties made by Seller herein shall terminate effective as of the Closing; provided that such representations and warranties made by Seller herein shall survive the Closing solely for the purpose of providing recourse to Buyer to offset any future Contingent Payments.

10.2 Indemnified Losses. For the purpose of this Section 10.2 and when used elsewhere in this agreement, "***Loss***" shall mean and include any and all liability, loss, damage, claim, expense, cost, fine, fee, penalty, obligation or injury including, without limitation, those resulting from any and all actions, suits, proceedings, demands, assessments, judgments, award or arbitration, together with reasonable costs and expenses including the reasonable attorneys' fees and other legal costs and expenses relating thereto.

10.3 No Indemnification by Seller. Seller is selling to Buyer the Purchased Assets defined in this Agreement on an "AS IS" and "WHERE IS" basis, with no representations or

warranties as to merchantability, fitness or usability or in any other regard (except for the limited representations and warranties specifically set forth above), and Seller does not agree to defend, indemnify or hold harmless Buyer, any parent, subsidiary or affiliate of Buyer or any director, officer, employee, stockholder, agent or attorney of Buyer or of any parent, subsidiary or affiliate of Buyer from and against and in respect of any Loss which arises out of or results from the transactions described herein.

10.4 Indemnification By Buyer. Subject to the provisions and limitations set forth in this Section 10, Buyer agrees to defend, indemnify and hold harmless Seller, any parent, subsidiary or affiliate of Seller, and any officers, directors, members, agents, managers, representatives, employees or attorneys of Seller or of any parent, subsidiary or affiliate of Seller (collectively, the ***"Seller Indemnitees"***) from and against and in respect of any Loss which arises out of or results from:

(a) any breach by Buyer of any covenant made herein, or the inaccuracy or untruth of any representation or warranty of Buyer made herein; or

(b) the use of the Purchased Assets after the Closing;

provided, *however*, that nothing in this Section 10.4 shall impose on Buyer any duty to indemnify Seller for any Excluded Liabilities or Excluded Assets.

10.5 Period for Making Claims. A claim for indemnification by Seller under this Section 10 may be brought, if at all, at any time after the Closing Date, with respect to any claim or claims for indemnification under this Section 10, provided, however, that any claim under Section 10.4(a) with respect to the inaccuracy or untruth of any representation or warranty must be brought, if at all, prior to the time such representation or warranty expires pursuant to Section 10.1.

11. MISCELLANEOUS.

11.1 Expenses. Each of the parties hereto shall bear its own expenses (including without limitation attorneys' fees) in connection with the negotiation and consummation of the transactions contemplated hereby.

11.2 Notices. Any notice required or permitted to be given under this Agreement shall be in writing and shall be personally delivered or sent by certified or registered United States mail, postage prepaid, or sent by a nationally recognized overnight express courier and addressed as follows:

(a) If to Seller:

Complexa (assignment for the benefit of creditors), LLC
3945 Freedom Circle, Suite 560
Santa Clara, California 95054
United States

Telephone: (650) 329-9996
Facsimile: (650) 329-0980
Email: mam@shrwood.com
Attention: Michael A. Maidy

With copy to:

Saul Ewing Arnstein & Lehr LLP
1201 N. Market Street, Suite 2300
Wilmington, DE 19801
Telephone: (302) 421-6806
Facsimile: (302) 421-6813
Email: monique.disabatino@saul.com
Attention: Monique B. DiSabatino, Esq.

(b) If to Buyer:

Imara Inc.
116 Huntington Ave, Sixth Floor
Boston, MA 02116
Telephone: 617-206-2020
Email: rballal@imaratx.com
Attention: Rahul Ballal, Chief Executive Officer

With copy to:

Legal Department
Email: smigausky@imaratx.com
Attention: Steve Migausky, General Counsel

11.3 Entire Agreement. This Asset Purchase Agreement, the Exhibits hereto (which are incorporated herein by reference) and any agreements to be executed and delivered in connection herewith, together constitute the entire agreement and understanding between the parties and there are no agreements or commitments with respect to the transactions contemplated herein except as set forth in this Agreement. This Agreement supersedes any prior offer, agreement or understanding between the parties with respect to the transactions contemplated hereby.

11.4 Amendment; Waiver. Any term or provision of this Agreement may be amended only by a writing signed by both Seller and Buyer. The observance of any term or provision of this Agreement may be waived (either generally or in a particular instance and either retroactively or prospectively) only by a writing signed by the party to be bound by such waiver. No waiver by a party of any breach of this Agreement will be deemed to constitute a waiver of any other breach or any succeeding breach.

11.5 **No Third Party Beneficiaries.** Nothing expressed or implied in this Agreement is intended, or shall be construed, to confer upon or to give any person, firm or corporation, other than the parties hereto, any rights or remedies under or by reason of this Agreement.

11.6 **Execution in Counterparts.** For the convenience of the parties, this Agreement may be executed in one or more counterparts, each of which shall be deemed an original and all of which together shall constitute one and the same instrument. Facsimile or electronically transmitted signatures to this Agreement shall be as valid and binding as a signed original.

11.7 **Benefit and Burden.** This Agreement shall be binding upon, shall inure to the benefit of, and shall be enforceable by and against, the parties hereto and their respective successors and permitted assigns.

11.8 **Governing Law.** This Agreement shall be governed by and construed in accordance with the internal laws of the State of Delaware (excluding application of any choice of law doctrines that would make applicable the law of any other state or jurisdiction) and, where appropriate, applicable federal law. All claims and disputes arising under or in connection with this Agreement, whether for or in respect of, breach of contract, tort, equity, or otherwise, shall be adjudicated exclusively in federal or state courts located in Delaware, and each party waives its right to a trial by jury of any such claims or disputes.

11.9 **Severability.** If any provision of this Agreement is for any reason and to any extent deemed to be invalid or unenforceable, then such provision shall not be voided but rather shall be enforced to the maximum extent then permissible under then applicable law and so as to reasonably effect the intent of the parties hereto, and the remainder of this Agreement will remain in full force and effect.

11.10 **Attorneys' Fees.** Should a suit or arbitration be brought to enforce or interpret any provision of this Agreement, the prevailing party shall be entitled to recover from the other party the prevailing party's reasonable attorneys' fees to be fixed in amount by the Court or the Arbitrator(s) (including without limitation costs, expenses and fees on any appeal). The prevailing party will be entitled to recover its costs of suit or arbitration, as applicable, regardless of whether such suit or arbitration proceeds to a final judgment or award.

11.11 **Limitation of Liability. BUYER HEREBY RECOGNIZES, ACKNOWLEDGES AND AGREES THAT UNDER NO CIRCUMSTANCE MAY BUYER OR ANY OF ITS AFFILIATES ASSERT ANY CLAIM AGAINST OR SEEK ANY RECOVERY FROM ANY OFFICERS, DIRECTORS, MEMBERS, AGENTS, MANAGERS, REPRESENTATIVES OR EMPLOYEES OF SELLER OR ANY OF THE OFFICERS, DIRECTORS, MEMBERS, AGENTS, MANAGERS, REPRESENTATIVES OR EMPLOYEES OF ANY MEMBER OR AFFILIATE OF SELLER ON ACCOUNT OF ANY ACTION OR INACTION OR FOR ANY REASON WHATSOEVER RELATING TO THIS AGREEMENT OR THE TRANSACTIONS CONTEMPLATED BY THIS AGREEMENT, INCLUDING, BUT NOT LIMITED TO, AS A RESULT OF, ARISING OUT OF, OR IN ANY WAY RELATING TO ANY BREACH OF ANY**

REPRESENTATION, WARRANTY AGREEMENT OR COVENANT MADE BY OR TO BE PERFORMED BY SELLER UNDER THIS AGREEMENT.

11.12 Limitation of Remedy in Favor of Buyer. BUYER HEREBY AGREES THAT ITS SOLE REMEDY RESULTING FROM ANY BREACH OF ANY REPRESENTATION(S) OR WARRANTY(IES) PROVIDED BY SELLER HEREIN IS TO ASSERT A GENERAL UNSECURED CLAIM AGAINST SELLER'S ASSIGNMENT ESTATE FOR DAMAGES INCURRED BY BUYER AS A RESULT OF SUCH BREACH, WITH ANY SUCH CLAIM, TO THE EXTENT AGREED TO BY SELLER OR ALLOWED BY A COURT OF LAW, TO BE TREATED IN THE SAME MANNER AS ALL OTHER GENERAL UNSECURED CLAIMS ASSERTED AGAINST SELLER'S ASSIGNMENT ESTATE. BUYER HEREBY FURTHER AGREES THAT UNDER NO CIRCUMSTANCE MAY ANY SUCH CLAIM(S) ASSERTED BY BUYER EXCEED, IN THE AGGREGATE, THE PURCHASE PRICE OR BE ASSERTED AFTER THE ASSIGNMENT ESTATE'S CLAIMS BAR DATE, WHICH IS FEBRUARY 11, 2021.

IN WITNESS WHEREOF, Buyer and Seller have executed and delivered this Asset Purchase Agreement by their duly authorized representatives as of the Effective Date.

SELLER:	**BUYER:**
Complexa (assignment for the benefit of creditors), LLC, solely as assignee for the benefit of creditors of Complexa, Inc.	Imara Inc.
By: Michael A. Maidy	By: /s/ Rahul Ballal, P.h.D.
Its: Manager	Its: Chief Executive Officer

EXHIBIT 1.2(a)

Purchased Assets

Seller is not making any representation, expressed or implied, with regard to the availability of the Purchased Assets due to the additional expenses that may be incurred to retrieve them, expressed or implied liens that may be asserted by vendors, former employees or consultants holding inventory, raw materials or other Purchased Assets. Buyer, at its own expense, may elect to pursue such Purchased Assets or use whatever means necessary to obtain them. Some Purchased Assets described in this Exhibit may contain third-party intellectual property that may have been licensed by, or otherwise acquired, by Assignor. Buyer acknowledges that Seller may be unable to transfer certain intellectual property belonging to a third party without the express written consent of that third party which, except as set forth in Exhibit 8.1(e), shall not be obtained or sought by Seller as part of this Agreement. Buyer accepts full responsibility for communicating with any such third parties whose intellectual property may be included in the Purchased Assets and Buyer shall be responsible for paying all licensing fees, costs, expenses, or other charges associated with using such Purchased Assets following the closing. Assignor shall remain responsible for any and all licensing or other fees, costs, expenses or charges that may be associated with using any such Purchased Assets prior to the Closing.

The Purchased Assets shall include all assets comprising the nuclear factor erythroid 2–related factor 2 small molecule program (the "***NRF2 Program***"), including CXA-10 and analogs, held by Assignor immediately prior to being assigned to Seller. Without limiting the foregoing, the Purchased Assets shall include all of Seller's rights, title and interest in the following:

(i) all rights to research, develop, manufacture and commercialize compounds comprising the NRF2 Program (including CXA-10), including all rights and claims to all clinical study data, manufacturing data, reports and analyses to the extent related to the NRF2 Program;

(ii) all intellectual property related to the NRF2 Program that exists now or as of the Closing anywhere in the world, including:

a. the patents identified in Exhibit 9.1(c);

b. the Exclusive License Agreement, dated August 18, 2014, between the University of Pittsburgh – Of the Commonwealth System of Higher Education and Seller (as assignee of the Assignor) (as amended, the "***Pittsburgh Agreement***");

c. the Exclusive License Agreement, dated April 23, 2012, between the UAB Research Foundation and Seller (as assignee of the Assignor) (the "***UAB Agreement***").

(iii) all regulatory documentation related to the NRF2 Program, including (as applicable) all regulatory applications and renewals thereof (including investigational new drug applications, orphan designations, new drug applications, abbreviated new drug applications and marketing authorization applications), and the safety reports, information on adverse events, and copies of all correspondence, reports, or minutes with any governmental entity, and all data submitted to governmental entities in connection with such regulatory applications;

(iv) all inventory of compounds comprising the NRF2 Program and reference standards, retains and intermediates related thereto, ingredients and any other raw materials, work-in-progress materials, package inserts, packaging and labeling materials, supplies and other inventories used in the manufacturing or production of any compound comprising the NRF2 Program;

(v) the following records related to the NRF2 Program: (a) written records lab notebooks, accounts, notes, reports, batch records and data, (b) research and development data (of any kind) from discovery through to submission (raw data, stability, validation, quality by design work), all analytical methods development and validation and (iv) manufacturing data (of any kind), batch records, quality control lab commissioning, validation protocols, testing protocols and reports.

EXHIBIT 1.2(b)

Excluded Assets

All contracts of the Assignor and the Seller other than the following:

1. The Pittsburgh Agreement;

2. The UAB Agreement; and

[**]

For clarity, while any applicable contacts of Assignor or Seller with [**] shall be deemed Excluded Assets, all existing inventory as of the Closing that was manufactured under any such contract shall be deemed a Purchased Asset.

Should the Buyer determine after the Closing Date that it needs one or more additional contracts that are Excluded Assets hereunder, Seller shall reasonably cooperate with Buyer to assign such contracts in accordance with Section 7.1 of this Agreement.

Certain portions of this exhibit have been omitted because they are not material and is the type of information that the registrant treats as private or confidential.

EXHIBIT 2.1

Contingent Consideration

[**]

Certain portions of this exhibit have been omitted because they are not material and is the type of information that the registrant treats as private or confidential.

EXHIBIT 3.1

Assumed Liabilities

1. The Pittsburgh Agreement

2. The UAB Agreement

[*]

Exhibit 10.7

RSU Agreement
IMARA Inc.

RESTRICTED STOCK UNIT AGREEMENT

IMARA Inc. (the "Company") hereby grants the following restricted stock units pursuant to its 2020 Equity Incentive Plan. The terms and conditions attached hereto are also a part hereof.

Notice of Grant

Name of recipient (the "Participant"):	
Grant Date:	
Number of restricted stock units ("RSUs") granted:	
Number, if any, of RSUs that vest immediately on the grant date:	
RSUs that are subject to vesting schedule:	
Vesting Start Date:	

Vesting Schedule:

Vesting Date:	Number of RSUs that Vest:
All vesting is dependent on the Participant remaining an Eligible Participant, as provided herein.	

This grant of RSUs satisfies in full all commitments that the Company has to the Participant with respect to the issuance of stock, stock options or other equity securities.

IMARA Inc.

Signature of Participant

By: _____

Street Address

Name of Officer
Title:

City/State/Zip Code

IMARA Inc.

Restricted Stock Unit Agreement
Incorporated Terms and Conditions

1. Award of Restricted Stock Units. In consideration of services rendered and to be rendered to the Company, by the Participant, the Company has granted to the Participant, subject to the terms and conditions set forth in this Restricted Stock Unit Agreement (this "Agreement") and in the Company's 2020 Equity Incentive Plan (the "Plan"), an award with respect to the number of restricted stock units (the "RSUs") set forth in the Notice of Grant that forms part of this Agreement (the "Notice of Grant"). Each RSU represents the right to receive one share of common stock, $0.001 par value per share, of the Company (the "Common Stock") upon vesting of the RSU, subject to the terms and conditions set forth herein.

2. Vesting. The RSUs shall vest in accordance with the Vesting Schedule set forth in the Notice of Grant (the "Vesting Schedule"). Any fractional shares resulting from the application of any percentages used in the Vesting Schedule shall be rounded down to the nearest whole number of RSUs. As soon as practicable after the vesting of the RSU, the Company will deliver to the Participant, for each RSU that becomes vested, one share of Common Stock, subject to the payment of any taxes pursuant to Section 7. The Common Stock will be delivered to the Participant as soon as practicable following each vesting date, but in any event within 30 days of such date.

3. Forfeiture of Unvested RSUs Upon Cessation of Service. In the event that the Participant ceases to be an Eligible Participant (as defined below) for any reason or no reason, with or without cause, all of the RSUs that are unvested as of the time of such cessation shall be forfeited immediately and automatically to the Company, without the payment of any consideration to the Participant, effective as of such cessation. The Participant shall have no further rights with respect to the unvested RSUs or any Common Stock that may have been issuable with respect thereto. The Participant shall be an "Eligible Participant" if the individual is an employee, director or officer of, or consultant or advisor to, the Company or any other entity the employees, officers, directors, consultants or advisors of which are eligible to receive awards of RSUs under the Plan.

4. Restrictions on Transfer. The Participant shall not sell, assign, transfer, pledge, hypothecate, encumber or otherwise dispose of, by operation of law or otherwise (collectively "transfer") any RSUs, or any interest therein. The Company shall not be required to treat as the owner of any RSUs or issue any Common Stock to any transferee to whom such RSUs have been transferred in violation of any of the provisions of this Agreement.

5. Rights as a Stockholder. The Participant shall have no rights as a stockholder of the Company with respect to any shares of Common Stock that may be issuable with respect to the RSUs until the issuance of the shares of Common Stock to the Participant following the vesting of the RSUs.

6. Provisions of the Plan. This Agreement is subject to the provisions of the Plan, a copy of which is furnished to the Participant with this Agreement.

7. Tax Matters.

(a) Acknowledgments; No Section 83(b) Election. The Participant acknowledges that he or she is responsible for obtaining the advice of the Participant's own tax advisors with respect to the award of RSUs and the Participant is relying solely on such advisors and not on any statements or representations of the Company or any of its agents with respect to the tax consequences relating to the RSUs. The Participant understands that the Participant (and not the Company) shall be responsible for the Participant's tax liability that may arise in connection with the acquisition, vesting and/or disposition of the RSUs. The Participant acknowledges that no election under Section 83(b) of the Internal Revenue Code of 1986, as amended, (the "Code") is available with respect to RSUs.

(b) Withholding. The Participant acknowledges and agrees that the Company has the right to deduct from payments of any kind otherwise due to the Participant any federal, state, local or other taxes of any kind required by law to be withheld with respect to the vesting of the RSUs. At such time as the Participant is not aware of any material nonpublic information about the Company or the Common Stock and the Participant is not subject to any restriction on trading activities with respect to the Common Stock pursuant to any Company insider trading or other policy, the Participant shall execute the instructions set forth in Schedule A attached hereto (the "Durable Automatic Sale Instructions") as the means of satisfying such tax obligation, unless the Participant has already executed such Durable Automatic Sale Instructions and the Company has such instructions on file. If the Participant has not executed the Durable Automatic Sale Instructions prior to an applicable vesting date, then the Participant agrees that if under applicable law the Participant will owe taxes at such vesting date on the portion of the award then vested the Company shall be entitled to immediate payment from the Participant of the amount of any tax required to be withheld by the Company. The Company shall not deliver any shares of Common Stock to the Participant until it is satisfied that all required withholdings have been made.

8. Miscellaneous.

(a) Section 409A. The RSUs awarded pursuant to this Agreement are intended to be exempt from or comply with the requirements of Section 409A of the Code and the Treasury Regulations issued thereunder ("Section 409A"). The delivery of shares of Common Stock on the vesting of the RSUs may not be accelerated or deferred unless permitted or required by Section 409A.

(b) Participant's Acknowledgements. The Participant acknowledges that he or she: (i) has read this Agreement; (ii) has been represented in the preparation, negotiation and execution of this Agreement by legal counsel of the Participant's own choice or has voluntarily declined to seek such counsel; (iii) understands the terms and consequences of this Agreement; (iv) is fully aware of the legal and binding effect of this Agreement; and (v) agrees that in accepting this award, the Participant will be bound by any clawback policy that the Company may adopt in the future.

Schedule A

DURABLE AUTOMATIC SALE INSTRUCTION

This Durable Automatic Sale Instruction is being delivered to IMARA Inc. (the "Company") by the undersigned on the date set forth below.

I hereby acknowledge that the Company has granted, or may in the future from time to time grant, to me restricted stock units ("RSUs") under the Company's equity incentive plans as in effect from time to time.

I acknowledge that upon the vesting dates applicable to any such RSUs, I will have compensation income equal to the fair market value of the shares of the Company's common stock subject to the RSU that vest on such date and that the Company is required to withhold income and employment taxes in respect of that compensation income on the applicable vesting date.

I desire to establish a process to satisfy such withholding obligation in respect of all RSUs that have been, or may in the future be, granted by the Company to me through an automatic sale of a portion of the shares of the Company's common stock that would otherwise be issued to me on each applicable vesting date, such portion to be in an amount sufficient to satisfy such withholding obligation, with the proceeds of such sale delivered to the Company in satisfaction of such withholding obligation.

I understand that the Company has arranged for the administration and execution of its equity incentive plans and the sale of securities by plan participants thereunder pursuant to an Internet-based platform administered by a third party (the "Administrator") and the Administrator's designated brokerage partner.

Upon any vesting of my RSUs from and after the date of this Durable Automatic Sale Instruction, I hereby appoint the Administrator (or any successor administrator) to automatically sell such number of shares of the Company's common stock issuable with respect to my RSUs that vest as is sufficient to generate net proceeds sufficient to satisfy the Company's minimum statutory withholding obligations with respect to the income recognized by me upon the vesting of the RSUs (based on minimum statutory withholding rates for all tax purposes, including payroll and social security taxes, that are applicable to such income), and the Company shall receive such net proceeds in satisfaction of such tax withholding obligation.

I hereby appoint the Chief Executive Officer, the Chief Financial Officer and General Counsel, and any of them acting alone and with full power of substitution, to serve as my attorneys in fact to arrange for the sale of shares of common stock in accordance with these durable automatic sale instructions. I agree to execute and deliver such documents, instruments and certificates as may reasonably be required in connection with the sale of the shares of common stock pursuant to these durable automatic sale instructions.

By signing below, I hereby represent to the Company that, as of the date hereof, I am not aware of any material nonpublic information about the Company or its common stock and that I am not prohibited from entering into these durable automatic sale instructions by the

Company's insider trading policy or otherwise. I have structured these automatic sale instructions to constitute a "binding contract" relating to the sale of common stock, consistent with the affirmative defense to liability under Section 10(b) of the Securities Exchange Act of 1934 under Rule 10b5-1(c) promulgated under such Act.

Print Name: _____

Date: _____

Exhibit 10.10

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

EXCLUSIVE LICENSE AGREEMENT

This license agreement (this "Agreement") is made and is effective as of April 25, 2012 (the "Effective Date") between The UAB Research Foundation ("UABRF") and Complexa, Inc. (the "Licensee").

RECITALS

WHEREAS, UABRF, by and through its authority as the lead institution under an Inter Institutional Agreement (the "IIA") with the University of Oregon, Morehouse School of Medicine, and Cardiff University and their Affiliates ("Other Owners") holds all right to transfer all rights, title and interest in the intellectual property described in UABRF intellectual property disclosure numbered U2003-0061, entitled "Cell Signaling by Nitrated Hydrocarbons" which was developed by inventor employees from UABRF and Other Owners, which are Bruce Freeman et al., UABRF; Valerie O'Donell, Cardiff University; Eugene Chen, Morehouse School of Medicine; and Bruce Branchaud, University of Oregon ("Inventors").

WHEREAS UABRF and Other Owners own all right, title, and interest to inventions made by University personnel during the course of their employment. UABRF and Other Owners entered into and duly authorized the IIA dated February 28, 2012 which gives UABRF full authority to negotiate and grant exclusive licenses for the commercial development and exploitation of their jointly owned patent and intellectual property rights in the abovementioned intellectual property disclosures.

WHEREAS, the Licensee, a company engaged in the area of drug design and discovery, desires to obtain a license to the Licensed Patents upon the terms and conditions set forth in this Agreement.

NOW, THEREFORE, in consideration of the premises described above and the mutual promises and agreements set forth in this Agreement, the Parties agree as set forth below.

ARTICLE 1
DEFINITIONS

The Definitions used in this Agreement are set forth below.

1.1 "Affiliate" means any Person that directly or indirectly controls, is controlled by, or is under common control with a Party. "Control" means (i) the beneficial ownership of at least fifty percent (50%) of the voting securities of a Person with voting equity, or (ii) thepower to direct or cause the direction of the management or policies of a Person.

1.2 "Agreement" means this agreement, as amended from time to time in accordance with the terms and conditions set forth in this agreement.

1.3 "Applicable Law" means all laws, statutes and regulations promulgated by all Regulatory Authorities and all Governmental Authorities.

1.4 "Development and Commercialization Plan" means development, manufacturing, marketing and commercialization activities proposed to be undertaken by the Licensee with respect to

the Licensed Patents as set forth on attached Exhibit B.

1.5 "Disclaimed Licensed Patent(s)" means any Licensed Patent in respect of which the Licensee decides not to pursue protective rights, undertake, or be responsible for, the payment of Procurement Expenses, as described in Section 4.1(d) of this Agreement.

1.6 "First Commercial Sale" means the first Sale of a Licensed Product to a Third Party.

1.7 "For Value" means any consideration, remuneration or benefit of any kind, whether received directly or indirectly, including, but not limited to, cash, equity, debt, preferential treatment, including waiver, rebate, discount, etc.

1.8 "Governmental Authorities" means, with respect to each country or jurisdiction, all legislative and governmental authorities, bodies, commissions, agencies or other instrumentalities of such country or jurisdiction.

1.9 "Infringement Notice" is defined in Section 7.1 of this Agreement.

1.10 "Inventors" are defined in the first two recitals of this Agreement.

1.11 "Licensed Field of Use" means human therapeutics and diagnostics, including any and all uses incidental to human prophylactic and therapeutic applications, applications in veterinary medicine and commercial laboratory research applications for human prophylactic or therapeutic use.

1.12 "Licensed Patents" means (a) the patents and/or patent applications set forth on attached Exhibit A, (b) any foreign patent applications based thereon, (c) all patents proceeding from such domestic and foreign patent applications, (d) all claims of continuations-in-part that are entitled to the benefit of the priority date of the parent Licensed Patent and are enabled by subject matter that is disclosed in the parent Licensed Patent, and (e) all divisionals, continuations, reissues, reexaminations and extensions of any patent or patent application described in (a) - (d) above. Licensed Patents does not include any patent and/or patent application that relates to a Disclaimed Licensed Patent.

1.13 "Licensed Product" means any product or part thereof, process or service, the development, manufacture, use, import, export, offer for sale or sale of which, but for this Agreement, would infringe a Valid Patent Claim set forth in any Licensed Patent.

1.14 "Licensed Territory" means worldwide.

1.15 "Management Activities" means any and all Procurement Activities and any other steps deemed necessary and reasonable to commercialize the Disclaimed Licensed Patents.

1.16 "Net Sales" means the gross amount set forth on the invoice relating to any Sale of a Licensed Product, less [**]. Where a Licensed Product is not used, transferred or exchanged For Value, the Net Sales will be [**]. Where there is no comparable sale or transfer For Value, the Net Sale will be [**].

1.17 "Non-Commercial Research Purposes" means any use and practice solely for academic research and/or educational purposes and not for any commercial or for-profit purposes, whether directly or indirectly.

1.18 "Non-Royalty Income" means anything received by Licensee For Value in lieu of a royalty payment associated with product sales and made directly in connection with a grant of rights to a Third Party to sell or offer for sale Licensed Products, including, but not limited to, fees and advances. For clarity purposes, Non-Royalty Income shall not include any consideration received by Licensee For Value from a Third Party in connection with a merger, sale of assets or otherwise, of all or substantially all of the business of the Licensee to which the subject matter of this Agreement relates; and Non-Royalty Income shall not include any consideration received by Licensee For Value made directly in connection with a grant of rights to a Third Party to sell or offer for sale Licensed Products when such consideration is in addition to a running royalty payment by the Third Party on the sale of Licensed Products.

1.19 "Parties" means UABRF and the Licensee and each of them individually is a "Party."

1.20 "Person" means an individual, corporation, partnership, trust, business trust, association or any other entity with a separate legal identity, including the Parties.

1.21 "Proprietary Information" is defined in Section 8.4.

1.22 "Procurement Activities" means all actions deemed necessary and desirable to procure the Licensed Patents, including, but not limited to, obtaining, filing for, securing, pursuing, prosecuting, continuing or maintaining, and defending the patents and patent applications within the Licensed Patents.

1.23 "Procurement Expenses" means all legal fees, costs and expenses reasonably incurred by UABRF in the performance of the Procurement Activities, such fees, costs and expenses to be documented by written invoice.

1.24 "Regulatory Authority" means, with respect to any particular country or jurisdiction, the Governmental Authority with the primary responsibility for the evaluation or approval of diagnostic or therapeutic drug products before such products can be tested, marketed, promoted, distributed or sold in such country, including Governmental Authorities that have jurisdiction over the pricing of such products. The term Regulatory Authority includes the Food and Drug Administration of the United States.

1.25 "Representative(s)" means, with respect to each Party, all trustees, directors, officers, employees, agents and advisors.

1.26 "Sale or Sales" means any use, transfer or exchange, For Value or otherwise, of a Licensed Product. Sales include all Sales by the Licensee, and its Sublicensees and include any transfer by the Licensee or a Sublicensee to an Affiliate or sublicensee where there is no

subsequent Sale (i.e., the Licensed Product is not further resold or transferred). For the avoidance of doubt, Sales shall not be deemed to include (a) any transfer by the Licensee or a Sublicensee to an Affiliate or Sublicensee where there is a subsequent Sale of the Licensed Product; only the subsequent Sale is used to calculate any amount due, (b) the use, performance or provision of a Licensed Product for research and development purposes, or (c) reasonable distributions as samples or given as donations for indigent use.

1.27 "Sublicensee" means a Person to whom the Licensee has granted a sublicense pursuant to Section 2.5 of this Agreement.

1.28 "Term" is defined in Section 10.1.

1.29 "Third Party" means any Person other than the Parties and their Affiliates.

1.30 "United States" means the United States of America.

1.31 "United States Government" means the Federal Government of the United States.

1.32 "Valid Patent Claim" means an issued and unexpired patent claim included within the Licensed Patents which has not been held permanently revoked, unenforceable or invalid by a decision of a court or other governmental agency of competent jurisdiction, to which an appeal has not or cannot be taken within the time allowed for appeal, and which has not been disclaimed, denied or admitted to be invalid or unenforceable through reissue, disclaimer or otherwise.

ARTICLE 2
GRANT OF LICENSE

2.1 Grant of License. Subject to the terms and upon the conditions set forth in this Agreement, UABRF hereby grants to the Licensee an exclusive right and license, subject to UABRF's rights in Section 2.3, to (a) practice and fully exploit, including the right to enforce as set forth in Article 7, the Licensed Patents and (b) make, have made, develop, use, lease, offer to sell, sell, import and export Licensed Products, within the Licensed Field of Use in the Licensed Territory during the Term. The Licensee may transfer its rights under this Agreement to an Affiliate, provided such Affiliate assumes all of the obligations of the Licensee under this Agreement, or as otherwise provided in this Agreement under Section 12.5.

2.2 Rights of the United States Government. It is understood that a United States Governmental Authority (National Heart, Lung, and Blood Institute - Grant Number HL0581 l 5) has funded research, during the course of or under which the Licensed Patents were conceived or made, the United States Government is entitled, as a right, under the provisions of 35 U.S.C. §§ 200-212 and applicable regulations of Chapter 37 of the Code of Federal Regulations, to a non exclusive, non-transferable, paid-up license to practice or have practiced and use the Licensed Patents for governmental purposes. The Licensee acknowledges that the rights and license granted to it pursuant to this Agreement are subject to any and all rights of the United States Government.

2.3 Reservation of Rights by UABRF, its Affiliates, and the Other Owners. UABRF reservesthe right, for itself, for its Affiliates, and for the Other Owners, to:

(a) practice and use, and to permit its Representatives to practice and use, the Licensed Patents for Non-Commercial Research Purposes;
(b) grant to non-profit academic, educational or research institutions and governmental agencies, non-exclusive, royalty-free licenses to make and use the Licensed Patents for Non-Commercial Research Purposes;
(c) permit their respective Representatives to disseminate and publish scientific findings from research related to the Licensed Patents, subject to Section 8.2; and
(d) license the Licensed Patents to Third Parties for applications and uses outside of the Field of Use.

2.4 Title Remains with UABRF and Other Owners. All title in and to the Licensed Patents remains with UABRF and Other Owners. Except as provided in this Agreement, no express or implied licenses with respect to the Licensed Patents or any other rights are transferred or granted to the Licensee by implication, estoppel or otherwise.

2.5 Right to Grant Sublicenses. The Licensee has the right to grant sublicenses to any Person under this Agreement on the following terms and conditions:
(a) the execution of a sublicense shall not in any way diminish, reduce or eliminate any of the Licensee's obligations under this Agreement, and the Licensee shall remain primarily liable for such obligations and any breach of any provision of this Agreement by a Sublicensee;
(b) sublicenses may not be granted to Persons who are Affiliates of the Licensee, or who are otherwise immediate family members of, or controlled by the immediate family members of, Persons who control the Licensee;
(c) the Licensee shall obtain UABRF's prior written consent of all sublicense agreements, which consent shall not be unreasonably withheld, conditioned or delayed;
(d) any sublicense so granted is limited to the Licensed Field of Use;
(e) any sublicense so granted shall be subject and subordinate to, and consistent with,the terms of this Agreement;
(f) the Licensee may not sublicense the right to prosecute the Licensed Patents to a Sublicensee;
(g) any sublicense shall also provide that, in the event this Agreement is terminated orupon the expiration of the Term, such sublicenses shall automatically become a direct license with UABRF on the terms stated therein;
(h) all sublicenses are to be For Value and the Licensee shall not receive from a Sublicensee anything of value in lieu of cash payments in consideration for any sublicense under this Agreement without the prior written consent of UABRF;
(i) the Licensee shall provide UABRF with a copy of any such sublicense granted byit under this Agreement within [**] of the execution of the sublicense;
(j) all such copies of sublicense agreements may be redacted to exclude confidential scientific information and other information required by the Sublicensee to be kept confidential, provided that all relevant financial terms and information shall be retained and shall not be redacted; the disclosure of sublicense agreements to UABRF shall be subject to the confidentiality obligations set forth in this Agreement;
(k) UABRF is a third party beneficiary to each sublicense and each agreement evidencing a sublicensing arrangement shall include a statement and an acknowledgement by the Sublicensee to this effect; and

(l) Sublicensees are prohibited from further sublicensing the Sublicensee's rights to any other Person without the prior written consent of UABRF, which shall not be unreasonably withheld, conditioned or delayed.

ARTICLE 3
DEVELOPMENT AND COMMERCIALIZATION

3.1 Development and Commercialization Plan. During the Term, the Licensee shall use commercially reasonable efforts to develop, manufacture, commercialize and market a Licensed Product in accordance with the procedures and practices that are usual and customary for similar technologies and industries. The Parties acknowledge that the Licensee has provided to UABRF the Development and Commercialization Plan set forth on attached Exhibit B which sets forth its current development and commercialization objectives. The Parties further acknowledge and agree that the Development and Commercialization Plan is, and the development and commercialization milestones set forth therein are reasonable.

3.2 Amendment of Development and Commercialization Plan. All variations and deviations from and changes to the Development and Commercialization Plan must be expressly approved in writing by UABRF, such approval not to be unreasonably withheld, conditioned or delayed.

3.3 Development and Commercialization Report. The Licensee shall provide UABRF, [**], with written progress reports detailing the activities of the Licensee relating to the Development and Commercialization Plan. As a general guide, each such report shall provide information regarding the accomplishments and progress made by the Licensee during the prior reporting period and the objectives and goals to be reached during the forthcoming reporting period. The Licensee will thereafter provide such reports to UABRF on an annual basis on the anniversary of the Effective Date.

3.4 Regulatory Approvals. With respect to each Licensed Product, and to the extent regulatory approval is required, the Licensee shall use commercially reasonable efforts to obtain the approval of each applicable Regulatory Authority prior to the First Commercial Sale in each country/jurisdiction in which the Licensee intends to sell Licensed Products.

3.5 Patent Markings. The Licensee shall ensure that each Licensed Product manufactured and/or sold in the United States shall bear patent markings that meet all applicable requirements of 35 U.S.C. §287, as amended from time to time. All Licensed Products manufactured and/or sold outside of the United States shall be marked in such a manner as to conform to the Applicable Law of such country/jurisdiction.

3.6 Manufacturing in the United States. The Licensee shall use [**] to substantially manufacture in the United States any Licensed Products sold in the United States.

ARTICLE 4
PROCUREMENT OF THE LICENSED PATENTS; PA TENT PROSECUTION

4.1 Future Procurement Activities.

(a) *UABRF Retains Primary Responsibility.* Subject to the terms and conditions set forth in this Agreement, UABRF shall, from the Effective Date, continue to be primarily responsible for undertaking all Procurement Activities relating to the Licensed Patents. UABRF shall, subject to consultation with the Licensee, select such legal counsel as it in its sole discretion deems appropriate to assist it in this process.

(b) *Co-operation of the Licensee.* The Licensee shall use commercially reasonable efforts to co-operate with UABRF and its designated legal counsel in connection with the Procurement Activities.

(c) *Consultation with the Licensee.* UABRF shall, and shall cause its designated legal counsel to, consult with the Licensee in connection with such Procurement Activities and the Licensee shall be given reasonable opportunity to discuss, advise and review issues with UABRF and its designated legal counsel in connection therewith. UABRF shall, and shall cause its designated legal counsel to, consider the Licensee's comments and suggestions prior to taking any material actions with respect to the Procurement Activities and will take all Procurement Actions reasonably suggested by the Licensee. UABRF will authorize the Licensee to communicate directly with UABRF's designated legal counsel.

(d) *Disclaimed Licensed Patents.* The Licensee may, at any time during the Term, provide at least [**] written notice to UABRF that it no longer wishes to be responsible for the Procurement Expenses in connection with one or more Licensed Patents. In such cases, (i) the Licensee shall continue to be responsible for all Procurement Expenses incurred in connection therewith until the expirationof such [**] notice period and thereafter shall not be responsible for such expenses and (ii) the Licensed Patent(s) so affected shall no longer be deemed to be licensed to the Licensee and shall be deemed to have been disclaimed by the Licensee (each, a "Disclaimed Licensed Patent"), (iii) the Licensee shall forfeit and shall no longer have any rights or obligations with respect thereto and (iv) Exhibit A shall be amended accordingly to delete the affected Licensed Patent(s).

4.2 Information to the Licensee. UABRF shall provide copies of all patent applications and all filings, correspondence and other related documentation pertaining to prosecutorial matters arising from the Protection Activities, including, but not limited to, all office actions, requests forexaminations and restriction requirements.

ARTICLE 5
FINANCIAL TERMS

5.1 Accrued Procurement Expenses. Within one (1) year of the Effective Date, the Licensee shall reimburse UABRF for all Procurement Expenses incurred prior to the Effective Date.

5.2 Future Procurement Expenses. During the Term and with respect to each Licensed Patent,other than Disclaimed Licensed Patents, the Licensee will be financially responsible for the

payment of all Procurement Expenses incurred after the Effective Date. The Licensee shall pay such amounts to UABRF within [**] of receipt of an invoice for the same from UABRF. UABRF shall be responsible for all Procurement Expenses incurred in connection with each Disclaimed Licensed Patent in countries/jurisdictions not designated by the Licensee pursuant to Section 4.1(d) above

5.3 License Fee. On or before the Effective Date, the Licensee shall pay to UABRF a non refundable, non-creditable license fee of TWENTY-FIVE THOUSAND DOLLARS ($25,000.00).

5.4 Milestone Payments. Within [**] of the receipt, by Licensee, of the approval of an NDA from the United States Food and Drug Administration (the "FDA"), or an equivalent approval from any other Regulatory Authority authorized to issue such approvals in markets other than the United States, for the first Licensed Product, Licensee shall make a one-time payment of [**] to UABRF.

5.5 Patent Issue Fee: Upon the first issuance of any Licensed Patent, a divisional, continuation,continuation-in part, reissues, or foreign counterparts, any claim of which covers a Licensed Product, Licensee shall pay a one-time, non-creditable, non-refundable License Issue Fee of FIFTEEN THOUSAND DOLLARS ($15,000.00), which shall be paid to UABRF no later than December 1, 2013. This provision will apply only once and only to the first issued Licensed Patent.

5.6 Running Royalty Payments. During the Term and with respect to each country or jurisdiction within the Licensed Territory, the Licensee shall pay to UABRF a continuing royaltyof [**] on all Net Sales arising in such country/jurisdiction until the expiration of the last Valid Patent Claim in that country/jurisdiction. All amounts owing to UABRF under thisSection 5.6 shall be paid on a quarterly basis, on or before the [**] following the end of the calendar quarter in which such amounts were earned. If Licensee is compelled to takea license from a Third Party in order to bring Licensed Product to market, the royalty due to UABRF shall be reduced by no more than [**] to offset royalties due to such Third Party or Third Parties. For clarification, regardless of the number of Third Party licenses, Licensee is compelled to enter into to bring Licensed Product to market, the royalty payments due to UABRF under this Section 5.6 will never be reduced to lower than [**] of Net Sales made by Licensee, Sublicensees, or Affiliates.

Licensee will notify UABRF immediately after Licensee's obligation to pay royalties to a Third Party under a valid license agreement in place between the Licensee and the Third Party is triggered and will provide UABRF with a copy of such license which may be redacted for other proprietary matters, but which contains the full royalty agreement between Licensee and the Third Party.

5.7 Minimum Royalty Payments. Beginning on [**] ofthis Agreement, the Licensee shall be obligated to pay minimum annual royalty payments to UABRF. In the event that the aggregate running royalty payments paid by the Licensee to UABRF pursuant to Section 5.6 above do not reach the minimum payment obligations set forth below by the date set forth below, then the Licensee shall, within [**] following eachof the dates specified, pay UABRF the difference between such aggregate royalty payment actually paid to UABRF and the

minimum payment set forth below. All such minimum annual royalty payments shall be nonrefundable.

Calendar Year Ending	Minimum Payment
December 1, 2014	[**]
December 1, 2015	[**]
December 1, 2016	[**]
Each calendar year thereafter during the Term	[**]

All running royalty payments paid by the Licensee to UABRF during any one calendar year shall be credited against the minimum annual payment due to be paid by December 1 of that calendar year. Running royalties paid in any one calendar year may not be carried forward to be credited against the minimum annual royalty payment due in any subsequent calendar year. All such minimum annual royalty payments shall be nonrefundable. Upon the expiration of the Term or earlier termination of this Agreement, any minimum royalties shall be pro-rated as of the date of termination or expiration by the number of days elapsed in the applicable twelve- (12-)month period.

5.8 Royalty Reports. Commencing with the first day of the calendar quarter following the calendar quarter in which the obligation of the Licensee to pay running royalty payments pursuant to Section 5.7 of this Agreement is triggered, the Licensee shall provide to UABRF a written report setting forth all applicable information specified in Exhibit E, which such report shall accompany the payment of all running royalties due to be paid to UABRF by the Licensee with respect to the preceding calendar quarter. Reports furnished must include the calculation of running royalties by Licensed Product and by country/jurisdiction and must include the rate of currency conversion and the date such conversion was calculated as described in Section 5.13 of this Agreement, all in substantially the format set forth in Exhibit E. If the Licensee is required to pay an annual minimum royalty payment, at the time such payment is made, the Licensee shall also furnish a written report providing, to the extent not already provided to UABRF, all of the information required to be set forth in the quarterly reports discussed above and the additional amount being paid by the Licensee which accompanies the report, being the difference between aggregate running royalty payment actually paid to UABRF in that calendar year and the minimum payment required to be paid.

5.9 Non-Royalty Income. The Licensee shall not receive any Non-Royalty Income without the prior written consent of UABRF, which such consent shall not be unreasonably withheld, conditioned or delayed. All Non-Royalty Income received by Licensee during the Term [**]. All such payments shall be accompanied by a written notification of the nature and origin of the payment, the identity of the original maker of the payment and, if the original payment was made in a foreign currency, must include the rate of currency conversion and the date such conversion was calculated as described in Section 5.14 of this Agreement. In the event that the Licensee receives Non-Royalty Income that is not cash or a cash equivalent, the percentage of non-cash payments shall be calculated as percentage of the then current fair market value of such non-cash

consideration.

5.10 Royalty Payments from Sublicensees. The Licensee shall pay to UABRF an amount equal to that which the Licensee would have been required to pay to UABRF had the Licensee effected the Sales actually effected by the Sublicensee.

5.11 Address for Payments. Except as otherwise directed by UABRF, all amounts due to be paid by the Licensee to UABRF pursuant to this Agreement shall be paid to UABRF at the address set forth below its signature on the signature page of this Agreement.

5.12 Late Payment Penalty. The balance of any amount which remains unpaid more than [**] after it is due to UABRF shall accrue interest until paid at the rate equal to the lesser of [**] per calendar month or the maximum amount allowed under Applicable Law. However, in no event shall this interest provision be construed as a grant of permission for payment delays.

5.13 Currency Conversion. All amounts due to be paid to UABRF pursuant to this Agreement shall be made in United States dollars. Any and all amounts received by the Licensee or generated in foreign currency shall be converted into United States dollars at the official rate of exchange from such currency to United States dollars at the rate quoted in the Wall Street Journal (United States edition) for the last business day of the calendar quarter in which running royalties are due and payable to UABRF or on a business day no earlier than [**] before payment is made to UABRF.

5.14 Foreign Taxes. UABRF is exempt from paying income taxes under United States law; therefore, all payments under this Agreement shall be made without deduction for taxes, assessments or other charges of any kind which may be imposed on UABRF by any government outside of the United States or any political subdivision of such government with respect to any amounts payable to UABRF pursuant to this Agreement. All such taxes, assessments or other charges shall be assumed by the Licensee.

ARTICLE 6
RECORDKEEPING AND AUDIT RIGHTS

6.1 Books and Records. The Licensee shall keep complete and accurate books, accounts andother records and documentation necessary to ascertain all transactions and events pursuant to which payments due to UABRF pursuant to this Agreement arise and are accrued and to verify the accuracy and completeness of such amounts. All such books, accounts and other records anddocumentation shall be kept at the Licensee's principal place of business for a period of not less than [**] following the end of the calendar year to which they pertain.

6.2 Right to Audit. UABRF shall have the right to have the Licensee's books and records audited, at UABRF's expense, by a qualified, independent accounting firm of its choosing, underappropriate confidentiality provisions such as those set forth in Section 8.4 of this Agreement, to ascertain the accuracy of the reports and payments due to UABRF under this Agreement and compliance by the Licensee, its Affiliates and its Sublicensees with their obligations pursuant to this Agreement and any sublicense. Such audit shall be conducted on [**] advance notice during normal business hours and in a manner that does not interfere unreasonably with the Licensee's business but not more than [**]. If any such examination reveals that the Licensee has underpaid

or underreported any amount due under this Agreement to UABRF for any calendar quarter examined, the Licensee shall immediately pay to UABRF the amount so underpaid or underreported.

6.3 Reimbursement of Cost of Audit. If any such examination reveals that the Licensee has underpaid or underreported any amount due under this Agreement to UABRF by more than [**] for any calendar quarter examined, the Licensee shall immediately reimburse UABRF the full costs and expenses incurred by it with respect to the audit.

ARTICLE 7
INFRINGEMENT; ENFORCEMENT

7.1 Notification of Infringement. During the Term, each Party shall provide prompt written notice to the other Party of any actual infringement or suspected/potential infringement of the Licensed Patents of which such Party is or becomes aware and shall provide, to the extent reasonable and practicable, any available evidence of such infringement by a Third Party (an "Infringement Notice").

7.2 Licensee Right to Pursue/Prosecute. During the Term, the Licensee shall have the first right, but not the obligation, to resolve, in the Licensed Field of Use and in the Licensed Territory, any suspected/potential infringement and prosecute any infringement of any Licensed Patents, in its own name and at its own expense, provided:

(a) the affected Licensed Patents remains exclusively licensed to the Licensee and isnot a Disclaimed Licensed Patent;
(b) the claim relates to a Valid Patent Claim; and
(c) the Licensee remains in compliance, in all material respects, with its obligationsunder this Agreement.

Before the Licensee commences an action with respect to any infringement or potential infringement, it shall give careful consideration to the views of UABRF and the potential effects on the public interest in making its decision whether or not to sue. UABRF and the Other Owners shall use their best efforts to co-operate with the Licensee in connection with any remedial action undertaken by the Licensee and shall be responsible for the costs and expenses incurred by it and for those costs and expenses incurred by it at the reasonable request of the Licensee with respect to such co-operation.

7.3 Control of Suit; Joinder; Expenses.

(a) *Initiated by the Licensee.* If the Licensee wishes to commence a lawsuit, it mustdo so within [**] following the date of the relevant Infringement Notice and it shall bear all costs and expenses incurred by it in connection with such lawsuit. UABRF and the Other Owners shall use its best efforts to co operate with the Licensee in connection with such lawsuit and shall be responsiblefor the costs and expenses incurred by it and for those costs and expenses incurred by it at the reasonable request of the Licensee with respect to such co-operation.

(b) *Initiated by UABRF*. If the Licensee elects not to exercise its right to commence,or fails to commence, an action within [**] of the date of the relevant Infringement Notice, UABRF may do so at its own expense, and shall retain sole control over the direction of such lawsuit. The Licensee shall co-operate fully with UABRF in connection with such lawsuit and shall be responsible for the costs and expenses incurred by it with respect to such co-operation. If UABRF files an infringement lawsuit, the Licensee may not thereafter commence a lawsuit against the same infringing party with respect to the same acts of infringement which are the subject of UABRF's lawsuit or with respect to which settlement is reached by the infringing party and UABRF; however, Licensee may elect to joinin as a party to any infringement lawsuit initiated by UABRF, in which case, bothParties shall jointly control the lawsuit and shall equally share the responsibilityof all legal fees, costs and expenses, unless otherwise agreed to by the Parties.

(c) *Joinder by UABRF*. UABRF, to the extent permitted by Applicable Law, may elect to join in as a party to any infringement lawsuit initiated by the Licensee, in which case, both Parties shall jointly control the lawsuit and shall equally sharethe responsibility of all legal fees, costs and expenses, unless otherwise agreed to by the Parties. The Licensee may not join UABRF in as a party to any lawsuit initiated by it without the prior written consent of UABRF which such consent shall not be unreasonably withheld, conditioned or delayed and without prior written agreement between the Parties as to the responsibility between the Parties for all costs and expenses incurred by the Parties. If UABRF is involuntarily joined as a party to a lawsuit initiated by the Licensee, the Licensee shall pay all legal fees, costs and expenses incurred by UABRF arising out of such joinder and participation, including, but not limited to legal fees, costs and expenses reasonably incurred by legal counsel selected and retained by UABRF to represent it in such lawsuit. While UABRF remains a party to any infringement lawsuit initiated by the Licensee, UABRF may not thereafter commence a lawsuit against the same infringing party with respect to the same acts of infringement which are the subject of the Licensee's lawsuit or with respect to which settlementis reached by the infringing party, the Licensee and UABRF.

7.4 Settlement. The Licensee may not settle, enter into a consent judgment or other voluntary final disposition of any lawsuit initiated by it or to which it is a party without the prior written consent of UABRF, which consent shall not be unreasonably withheld, conditioned or delayed. Neither Party may settle or otherwise dispose of any lawsuit to which it is a party, which admits liability on the part of the other Party or which requires the other Party to pay money damages nor issue a formal statement without such other Party's prior written consent.

7.5 Recoveries.

(a) *Lawsuit initiated by the Licensee and in which only the Licensee is a party.* With respect to any lawsuit commenced by the Licensee pursuant to Section 7.3(a) above and in which UABRF is not a party, any recovery of damages shall first be applied in satisfaction of the costs and expenses incurred by the Licensee in bringing such lawsuit, including attorneys' fees, provided they are reasonably incurred, and any

balance shall be treated as Net Sales in accordance with Section 5.6 of this Agreement.

(b) *Lawsuit initiated by the Licensee and in which UABRF ioins.*

(i) With respect to any lawsuit commenced by the Licensee pursuant to Section 7.3(a) above and in which UABRF is involuntarily joined as a party, any recovery of damages shall first be applied in satisfaction of the costs and expenses incurred by the Licensee and UABRF in bringing such lawsuit, including attorneys' fees, provided they are reasonably incurred (which such costs and expenses shall include all costs and expenses incurred by UABRF arising out of such joinder and participation, including, but not limited to legal fees and expenses reasonably incurred by legal counsel selected and retained by UABRF to represent it in such lawsuit), and any balance shall be treated as Net Sales in accordance with Section 5.6 of this Agreement.

(ii) With respect to any lawsuit commenced by the Licensee pursuant to Section 7.3(a) above and in which UABRF voluntarily joins as a party, any recovery of damages (whether compensatory or punitive in nature) shall first be applied, pro rata, in satisfaction of the costs and expenses incurred by the Parties in bringing such lawsuit, including attorneys' fees, provided they are reasonably incurred, and any balance shall be treated as Net Sales in accordance with Section 5.6 of this Agreement.

(c) *Lawsuit initiated by UABRF and in which only UABRF is a party.* With respect to any lawsuit commenced by UABRF pursuant to Section 7.3(b) above and in which Licensee is not a party, all recoveries of damages shall belong to UABRF. Furthermore, the Licensee shall pay over to UABRF any payments (whether or not designated as "royalties") made by the alleged infringer to the Licensee under any existing or future sublicense authorizing Licensed Products, up to the amount of UABRF's unreimbursed litigation expenses (including, but not limited to, reasonable attorneys' fees).

(d) *Lawsuit initiated by UABRF and in which Licensee ioins.* With respect to any lawsuit commenced by UABRF pursuant to Section 7.3(b) above and in which Licensee joins as a party, any recovery of damages (whether compensatory or punitive in nature) shall first be applied, pro rata, in satisfaction of the costs and expenses incurred by the Parties in bringing such lawsuit, including attorneys' fees, provided they are reasonably incurred, and any balance shall be shared [**] UABRF and [**] Licensee.

7.6 Inapplicability of Licensee's Rights. Notwithstanding Sections 7.1 -7.5 above, the rights and obligations of the Licensee under this article shall not apply to any Disclaimed Licensed Patent.

ARTICLE 8
OTHER COVENANTS AND AGREEMENTS

8.1 Use of Names. No Party may, without the prior written consent of the other Party:

(i) use (a) the name of the other Party or its Affiliates, if applicable, (b) the name or image of any Representative of the other Party, or (c) any trade-name, trademark, trade device, service mark, symbol, image, icon, abbreviation, contraction or simulation thereof owned by the other Party in any publication, advertising or sales promotional material, press release or in any marketing or advertising documentation or material; or

(ii) represent, either directly or indirectly, that any product or service of the other Party is a product or service of the representing Party or that it is made m accordance with or utilizes the information or documents of the other Party.

Notwithstanding the above, the Licensee may disclose that it has received a license from UABRF in connection with any Licensed Product, and either Party may use the name of the other Party to the extent such use is reasonably necessary for complying with Applicable Law.

8.2 Publications. In furtherance of the rights reserved in Section 2.3(c) of this Agreement, UABRF or its Affiliates shall submit the proposed publication or disclosure to the Licensee at least [**] prior to submission for publication or disclosure to allow the Licensee to review the matter for disclosure of Proprietary Information of the Licensee. The Licensee shall have [**] from its receipt of such proposed publication or disclosure to review and to provide written notice to UABRF or its Affiliate who provided the submission requiring removal of the Licensee's Proprietary Information and UABRF or its Affiliate shall remove the Licensee's Proprietary Information prior to publication or disclosure. If the Licensee does not provide written notice of such request to UABRF or its Affiliate who provided the submission within [**] afterreceipt of the proposed publication or disclosure from UABRF or its Affiliate, UABRF or its Affiliate shall be free to publish or disclose to third parties the proposed publication or disclosurewithout further obligation to the Licensee.

8.3 Insurance Coverage. Prior to commencing any Clinical Trial and thereafter during the Term, the Licensee shall cause to be in effect through purchase from a reputable insurance company or, upon the consent of UABRF, through a self-insurance program, at its sole expense, shall maintain "occurrence based type" liability insurance coverage or, if the Licensee is unable to obtain "occurrence based type" liability insurance, a "claims made type" liability insurance coverage (with at least [**] tail coverage). Such insurance coverage shall include a contractual endorsement providing coverage for all liability which may be incurred in connection with this Agreement, including, but not limited to general liability and products liability, and such other type of insurance coverage required by Applicable Law or which it deems necessary to enable the Licensee to perform its obligations under this Agreement. All such insurance coverage shall list UABRF and Other Owners as additional insureds. The Licensee shall provide evidence of such insurance coverage to UABRF upon the reasonable request of UABRF. All such insurance coverage shall require the insurance provider, or in the case of a self insurance program, the Licensee, to provide UABRF with at least [**] prior written notice of any change in the terms or cancellation of coverage.

8.4 Confidentiality.

(a) *Exchange of Proprietary Information.* The Parties acknowledge that during the Term they are likely to share information with each other that they each consider to be

confidential and proprietary ("Proprietary Information"). For the purposes of this Agreement, the Party that discloses Proprietary Information shall be referred to as the "Disclosing Party" and the Party receiving the Proprietary Information, the Receiving Party.

(b) *Nature of Proprietary Information.* The Parties agree that all information that is provided to the other Party shall be deemed to be Proprietary Information. Notwithstanding the above, the Parties specifically agree that any reports provided by the Licensee pursuant to this Agreement shall be considered Proprietary Information.

(c) *Restrictions.* With respect to all Proprietary Information disclosed to it, the Receiving Party (i) shall keep it confidential (other than as permitted by this Agreement), (ii) shall store and maintain it with the same diligence and care as its own proprietary information, but no less than reasonable diligence and care, (iii) may only use it for the purpose for which it was disclosed by the Disclosing Party, (iv) may not disclose it (other than as permitted by this Agreement), (v) may not deconstruct, modify or copy it (other than as permitted by this Agreement), and (vi) may not transfer or assign it to any Third Party.

(d) *Access to the Proprietary Information.* The Proprietary Information may be used by, and disclosed to, on an "as-needed" basis, the Receiving Party's Representatives. The Licensee may disclose UABRF's Proprietary Information relating to the Licensed Patents to investors, prospective investors, consultants, collaborators, sublicensees,potential assignees and other Third Parties in the chain of manufacturing and distribution, if and only if, the Licensee obtains from such recipient a written confidentiality agreement, the provisions of which are at least asprotective of UABRF's Proprietary Information as these set forth in this Section 8.4. Each Party will promptly notify the other Party of any unauthorized use of or access to the other Party's Proprietary Information of which it becomes aware.

(e) *Exceptions to Confidentiality Obligation*. The restrictions of confidentiality described above shall not apply to Proprietary Information (i) which as of the Effective Date or subsequent thereto is or becomes available to the public without breach of this Agreement, (ii) if it is lawfully obtained from a Third Party not bound by similar confidentiality and use restrictions and obligations, (iii) if it is known by the Receiving Party prior to disclosure as evidenced by contemporaneous records, or (iv) if it is at any time developed by the Receiving Party independently of any disclosure made pursuant to this Agreement as evidenced by contemporaneous records. In addition, the confidentiality obligations shall not apply to the Receiving Party if the Receiving Party is legally required by applicable law, court order or Governmental Authority to disclose the Information, provided the Receiving Party discloses only the minimum to complyand, if possible and in light of the circumstances, provides reasonable prior notice to the Disclosing Party to enable it to contest the requirement or to seek a protective order.

(f) *Termination or Expiration of this Agreement.* Upon the expiration of the Term, orthe earlier termination of this Agreement, each Receiving Party shall, at the Disclosing Party's option and upon written notice thereof to the Receiving Party, return all Proprietary Information, copies and other tangible expressions thereof, to the Disclosing Party or provide the Disclosing Party with written notice that theProprietary Information in its possession, or in the possession of its Representatives,

has been destroyed within [**] after receipt of the Disclosing Party's written notice to the Receiving Party requiring the Receiving Party to destroy the Proprietary Information in its possession. The Receiving Party may retain one archival copy of the Information for purposes of complianceof its obligations under this Agreement.

(g) *Continuing Obligations after Termination/Expiration*. The restrictions and obligations set forth in Section 8.4(c) above shall continue for [**] from the termination or expiration of this Agreement.

ARTICLE 9
TERM AND TERMINATION

9.1 Term. This Agreement shall commence on the Effective Date and shall continue on a country-by-country basis until the date of expiration of the last to expire of any Valid Patent Claim (inclusive of any extensions, supplementary protection certificates or their equivalents) within the Licensed Patents, unless terminated sooner in accordance with the terms of this Agreement (the "Term").

9.2 Termination by the Licensee. The Licensee may terminate this Agreement at any time, in its sole discretion, by giving not less than ninety (90) days prior written notice to UABRF. Upon the reasonable request of UABRF, the Licensee shall provide assistance, at UABRF's expense, to UABRF to enable UABRF to facilitate and effect the transfer of applicable information and documents in Licensee's actual possession regarding the Licensed Patents to a new licensee.

9.3 Termination by UABRF. UABRF shall have the right to immediately terminate this Agreement upon the occurrence of any one or more of the following events:

(a) if the Licensee is in material default of any provision of this Agreement or its obligations under this Agreement and such default has not been remedied within [**] after receipt of a notice to cure from UABRF;
(b) upon the occurrence of the third separate default by the Licensee within any consecutive [**] period for failure to make payments when due under this Agreement;
(c) if the Licensee fails to meet any of the development and commercialization milestones set forth in the Development and Commercialization Plan;
(d) if by the end of the third (3rd) calendar year after the First Commercial Sale occurred, [**] of the minimum royalty payment described in Section 5.8 of this Agreement due in that calendar year is not originating from Net Sales;
(e) if an examination by UABRF pursuant to Section 6.2 shows an underreporting or underpayment by the Licensee in excess of [**] of any amounts dueto UABRF under this Agreement in any twelve (12) month period;
(f) if the Licensee is convicted of a felony (or similar crime in a jurisdiction outside of the United States) relating to the manufacture, use or sale of a Licensed Product; or
(g) if the Licensee shall become insolvent, shall make an assignment for the benefit of its creditors, or shall have a petition in bankruptcy filed for or against it, which has not been discharged, stayed or dismissed within [**] thereafter; or
(h) if the Licensee disclaims payment of all Procurement Expenses.

9.4 Effect of Termination or Expiration. Upon the termination of this Agreement or the expiration of the Term, all payments then or thereafter due to the Licensee pursuant to any sublicense shall, immediately and automatically, become owed directly to UABRF.

ARTICLE 10
COVENANTS; REPRESENTATIONS AND WARRANTIES; LIMITATIONS ON UABRF's OBLIGATIONS

10.1 The Licensee.The Licensee makes the following representations and warranties toUABRF.

(a) The Licensee is a corporation, duly incorporated, validly existing and in good standing under the laws of the State of Pennsylvania.
(b) The Licensee has all necessary corporate power and authority to enter into this Agreement and to consummate the transactions contemplated hereby.
(c) The execution, delivery and performance of this Agreement by the Licensee will not conflict with or result in a breach of, or entitle any party thereto to terminate, an agreement or instrument to which the Licensee is a party, or by which any of the Licensee's assets or properties are bound.
(d) This Agreement has been duly authorized, executed and delivered by the Licenseeand constitutes a legal, valid and binding agreement of the Licensee, enforceable against the Licensee in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, moratorium, reorganization or other similar laws affecting creditors' rights generally.
(e) The Licensee possesses the necessary expertise and skill in the technical areas pertaining to the Licensed Patents, to make Licensed Products, and to make and has made, its own evaluation of the capabilities, safety, utility and commercial application of the Licensed Patents.
(f) Any activity undertaken with the Licensed Patents and the Licensed Products will be conducted in compliance with all Applicable Laws.

10.2 UABRF. UABRF makes the following representations and warranties to the Licensee.

(a) UABRF is a non-profit corporation, duly incorporated, validly existing and in good standing under the laws of the State of Alabama.
(b) UABRF has all necessary corporate power and authority to enter into this Agreement and to consummate the transactions contemplated hereby.
(c) The execution, delivery and performance of this Agreement by UABRF does not conflict with or contravene its governing documentation, nor will the execution, delivery and performance of this Agreement by UABRF conflict with or result ina breach of, or entitle any party thereto to terminate, an agreement or instrument to which UABRF is a party, or by which any of UABRF's assets or properties are bound.
(d) This Agreement has been duly authorized, executed and delivered by UABRF andconstitutes a legal, valid and binding agreement of UABRF, enforceable against UABRF in accordance with its terms, except as such enforceability may be limited by bankruptcy, insolvency, moratorium, reorganization or other similar laws affecting creditors' rights generally.
(e) UABRF has the right to grant the exclusive rights in the Licensed Patents pursuant to the license under this Agreement.

(f) To UABRF's and the Other Owners best knowledge, UABRF and the Others Owners own all right, title and interest in the Licensed Patents and there have been no claims made against UABRF or Other Owners asserting the invalidity or non-enforceability of, or with respect to, the Licensed Patents, and UABRF and the Other Owners are not aware that any such claims exist.

(g) The performance of Management Activities with respect to a Disclaimed Licensed Patent will not conflict with or result in a breach of any of the terms, conditions, or provisions of, or constitute a default under, this Agreement, and will not give rise to a cause of action by a Third Party against the Licensee, with respect to the remaining Licensed Patents licensed to the Licensee pursuant to thisAgreement.

10.3 Limitations on UABRF's Representations and Warranties. Except as set forth in this Agreement, UABRF makes no other representations or warranties of any kind. In particular, UABRF makes no express or implied warranties regarding merchantability, fitness for a particular purpose, non infringement of the intellectual property rights of third parties, validity and scope of any Licensed Patents, the capability, safety, efficacy, utility or commercial application or usefulness for any purpose of any Licensed Patents, or that it will not grant licenses to one or more Third Parties to make, use or sell products or perform processes that maybe similar to and/or compete with any Licensed Product, provided, however, that such license grant to one or more Third Parties is not otherwise inconsistent with the terms of this Agreement.

10.4 No Obligation of UABRF. UABRF has no obligation to:

(a) supervise, monitor, review or otherwise assume responsibility for the production,manufacture, testing, marketing, sale or disposition of any Licensed Product;

(b) furnish any knowhow or other information relating to the Licensed Patents, otherthan as specifically provided in this Agreement; or

(c) bring or prosecute legal action against any Person for infringement of theLicensed Patents, except as otherwise set forth in Article 7.

ARTICLE 11
LIABILITY AND INDEMNIFICATION

11.1 No Liability of UABRF or the Other Owners. Neither UABRF, the Other Owners,, nor any of their Representatives have any liability whatsoever to the Licensee, or any Sublicensee or any Person for or on account of any injury, loss or damage of any kind or nature, sustained by, assessed or asserted against, or any other liability incurred by or imposed upon the Licensee, or any Sublicensee or any Person, arising out of or in connection with or resulting from:

(a) the use of the Licensed Patents during the Term;

(b) the production, use, practice, lease, or sale of any Licensed Product;

(c) any advertising or other promotional activities with respect to (a) and/or (b) above;or

(d) the Licensee's compliance with, and performance of the Licensee's representations and warranties given under, and the Licensee's obligations pursuant to, this Agreement;

provided, however, that such liability is not based upon, arising out of or otherwise relating to UABRF, the Other Owners, and/or their Representative(s)'s gross negligence or willful misconduct.

11.2 Indemnification by the Licensee. The Licensee agrees to indemnify and hold UABRF,the Other Owners, and their Representatives harmless from and against any and all claims,demands, losses, costs, expenses, deficiencies, liabilities or causes of action of any kind or nature (including, without limitation, reasonable attorneys' fees and other costs and expenses of defense)based upon, arising out of or otherwise relating to:

(a) the use of the Licensed Patents during the Term;
(b) the production, use, practice, lease, or sale of any Licensed Product;
(c) any advertising or other promotional activities with respect to (a) and/or (b) above; or
(d) the Licensee's compliance with, and performance of the Licensee's representations and warranties given under, and the Licensee's obligations pursuant to, this Agreement;

provided, however, that such claims, demands, losses, costs, expenses, deficiencies, liabilities or causes of action of any kind or nature (including, without limitation, reasonable attorneys' fees and other costs and expenses of defense) are not based upon, arising out of or otherwise relating to UABRF, or the Other Owners, and/or their Representative(s)'s gross negligence or willful misconduct.

ARTICLE 12
MISCELLANEOUS

12.1 Entire Agreement. This Agreement is the sole and entire agreement by and between the Parties regarding the subject matter set forth in this Agreement, and this Agreement supersedes all prior agreements and understandings with respect thereto. All previous negotiations, statements and preliminary instruments by the Parties with respect to the subject matter hereofare superseded by this Agreement.

12.2 No Inducement. Each Party hereby acknowledges that in executing this Agreement, such Party has not been induced, persuaded or motivated by any promise or representation made by any other Party, unless expressly set forth in this Agreement.

12.3 Independent Contractors. The relationship between the Parties is that of independent contractors. No Party has the authority to bind or act on behalf of the other Party without obtaining such other Party's prior written consent. The Parties do not intend to create an employer/employee relationship.

12.4 No Third Party Beneficiaries. This Agreement is entered into by and among the Parties for the exclusive benefit of the Parties and their successors and permitted assignees. This Agreement is expressly not intended for the benefit of any creditor of a Party, or any other person. Except and only to the extent provided by applicable statute, no such creditor or Third Party shall have any rights under this Agreement or any other agreement between the Parties.

12.5 Assignment. Neither Party shall sell, assign, transfer or otherwise dispose of this Agreement including by operation of law to a Third Party without the prior written consent of theother, which consent shall not be unreasonably withheld, conditioned or delayed; provided, however, that either Party may assign this Agreement to a Third Party that acquires, by merger,

sale of assets or otherwise, all or substantially all of the business of the assigning Party to which the subject matter of this Agreement relates without the prior written consent of the other Party. Any attempted assignment of this Agreement not in compliance with the terms of this subsectionwill be null and void. No assignment will relieve any Party of the performance of any accrued obligation that such Party may then have pursuant to this Agreement.

12.6 Amendments. Any and all modifications to this Agreement shall only be effective and binding if in writing and signed by a duly authorized representative of each Party.

12.7 Notices. Any notice, request, approval or consent required to be given under this Agreement will be sufficiently given if in writing and delivered to a Party in person, by recognized overnight courier or mailed in the United States Postal Service, postage prepaid to theaddress appearing below such Party's signature on the last page of this Agreement, or at such other address as each Party so designates in accordance with these criteria. Notice shall be deemed effective upon receipt if delivered in person or by overnight courier or five (5) business days after mailing with the United States Postal Service.

12.8 Disputes.

(a) *Equitable Relief* Either Party may seek equitable and legal relief in the event of a breach or threatened breach by the other Party of its obligations under this Agreement, without the requirement to post a bond.

(b) *Internal Resolution.* In the event of any dispute arising out of or relating to this Agreement or to a breach thereof, including its interpretation, performance or termination, the Parties shall try to settle such conflicts amicably between themselves. In the event that the conflict is not resolved within [**] after one Party notifies the other Party in writing concerning a dispute or conflict, then the dispute or conflict shall be referred to executive officers of each Party involved for resolving by negotiation in good faith as soon as practicable but no later than [**] after its referral.

(c) *Mediation.* In the event the Parties are still unable to resolve the dispute or conflict by negotiation, the dispute or conflict may then be submitted by a Party toa mediator, mutually agreed to by the Parties, for nonbinding mediation. The Parties shall cooperate with the mediator in an effort to resolve such dispute.

(d) *Arbitration.* If the dispute is not resolved within [**] of its submission to the mediator, either Party may submit the dispute for binding arbitration. The arbitration shall be conducted by three (3) arbitrators, one to be appointed by UABRF, one to be appointed by the Licensee and the third to be appointed by the other two arbitrators. The arbitration shall be conducted in accordance with the commercial rules of the American Arbitration Association, which shall administer the arbitration. The arbitration, including the rendering of the award, shall take place in Birmingham, Alabama and shall be the exclusive forum for resolving such dispute. The decision of the arbitrators shall be final and binding upon the Parties and the expense of the arbitration, including, without limitation, the award of attorneys' fees to the prevailing Party, shall be paid as the arbitrators determine.

12.9 Rights and Remedies. The rights and remedies provided by this Agreement are cumulative, and the use of any one right or remedy by any Party shall not preclude or waive the right to use any or all other remedies. Such rights and remedies are given in addition to any other rights the

Parties may have by law, statute, ordinance or otherwise.

12.10 Waiver. No waiver of a provision, breach or default shall apply to any other provision orsubsequent breach or default or be deemed continuous, nor will any single or partial exercise of aright or power preclude any other further exercise of any rights or remedies provided by law or equity.

12.11 Severability. In the event that any covenant, condition, or other provision contained in this Agreement is determined to be invalid, void or illegal, such covenant, condition or other provision shall be deemed deleted from the Agreement and shall not affect the validity of the remaining provisions of this Agreement.

12.12 Force Majeure. Neither Party shall be liable for any failure to perform as required by this Agreement to the extent such failure to perform is due to circumstances reasonably beyond such Party's control, including, without limitation, labor disturbances or labor disputes of any kind; accidents; acts, omissions or delays in acting by any Governmental Authority; civil disorders; insurrections; riots; war; acts of war (whether war be declared or not); terrorism; acts of aggression; acts of God; fire; floods; earthquakes; natural disasters; energy or other conservation measures imposed by law or regulation; explosions; failure of utilities; mechanical breakdowns; material shortages; disease or other such occurrences; provided that the affected Party uses reasonable efforts to overcome or avoid the effects of such cause and continues to perform its obligations to the extent possible.

12.13 Survivability. All rights and obligations of the Parties which by intent or meaning have validity beyond or by their nature apply or are to be performed or exercised after the termination or expiration of this Agreement shall survive the termination or expiration of this Agreement for the period so specified, if any, or for perpetuity.

12.14 Jurisdiction. The Licensee consents to the personal jurisdiction of the federal and state courts located in the State of Alabama with respect to all claims or other causes of action arising out of this Agreement.

12.15 Interpretation. Whenever used in this Agreement and when required by the context, the singular number shall include the plural and the plural the singular. Pronouns of one gender shall include all genders, masculine, feminine and neuter.

12.16 Captions. The captions as to contents of particular sections or paragraphs contained in this Agreement are inserted for convenience and are in no way to be construed as part of this Agreement or as a limitation on the scope of the particular sections or paragraphs to which they refer.

12.17 Counterparts. This Agreement may be executed in counterparts, each of which shall be deemed an original but all of which shall constitute one and the same instrument.

[The remainder of this page intentionally left blank]

IN WITNESS WHEREOF, the Licensee and UABRF have each caused its duly authorizedrepresentative to execute this Agreement, effective as of the Effective Date.

UABRF
The UAB Research Foundation

By: **/s/** David Winwood, Ph.D.
Name: David Winwood, Ph.D.
Title: CEO, UABRF

Address for Notices
The UAB Research Foundation
Attention: The Chief Executive Officer
701 20th Street South, AB 770
Birmingham, Alabama 35233

THE LICENSEE
Complexa, Inc.

By: **/s/** Joshua M. Tarnoff
Name: Joshua M. Tarnoff
Title**:** CEO, Complexa

Address for Notices
Complexa, Inc.
100 Technology Drive
Suite 400
Pittsburgh, PA 15219

With a copy to:
Raymond A. Miller, Esq.
Pepper Hamilton LLP
Suite 500
500 Grant St.
Pittsburgh, PA 15219-2507

Exhibit 10.11

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

NON-EXCLUSIVE LICENSE AGREEMENT

This Agreement is made and entered into as of May 27, 2021 ("Effective Date"), by and between the University of Pittsburgh – Of the Commonwealth System of Higher Education, a non-profit corporation, organized and existing under the laws of the Commonwealth of Pennsylvania, having an office at 1st Floor Gardner Steel Conference Center, 130 Thackeray Avenue, Pittsburgh, Pennsylvania 15260 ("University"), and Imara Inc. having its principal office at 116 Huntington Ave, Sixth Floor, Boston, MA 02116 ("Licensee"). University and Licensee each may be referred to herein individually as a "Party" or collectively as the "Parties."

WHEREAS, University is the owner by assignment from the inventors of certain Patent Rights (as defined below), including those entitled "Nitrated Fatty Acids for the treatment of Diabetes and Related Cardiovascular Diseases," developed by Bruce Freeman and Francisco Schopfer of University faculty, and University has the right to grant licenses under such Patent Rights;

WHEREAS, University desires to have the Patent Rights utilized in the public interest;

WHEREAS, University and Complexa, Inc. ("Complexa") entered into an Exclusive License Agreement, dated as of August 18, 2014 (the "Complexa License Agreement"), pursuant to which Complexa licensed from the University certain rights related to the Patent Rights;

WHEREAS, Complexa entered into an Assignment for the Benefit of Creditors under Delaware law, pursuant to which Complexa assigned all of its assets to Complexa (assignment for the benefit of creditors), LLC (the "Assignee"), a special purpose entity established to liquidate the assets of Complexa, compile claims, and distribute proceeds, if any, to creditors according to the priority established in under Delaware law;

WHEREAS, Licensee purchased certain assets from Assignee;

WHEREAS, for the avoidance of any doubt, each Party (on behalf of itself and its Affiliates) hereby acknowledges and agrees that the Complexa License Agreement (the "Complexa Agreement") terminated in its entirety, effective as of November 20, 2020;

WHEREAS, Licensee has represented to University, to induce University to enter into this Agreement, that Licensee is experienced in the development, production, manufacture, marketing and sale of products and/or the use of similar products to the Licensed Technology and that Licensee shall exploit the Patent Rights so that public utilization results therefrom; and

WHEREAS, Licensee desires to obtain a non-exclusive license under the Patent Rights upon the terms and conditions hereinafter set forth.

NOW, THEREFORE, in consideration of the premises and the mutual covenants contained herein, the Parties hereto, intending to be legally bound, agree as follows:

ARTICLE 1 – DEFINITIONS

For purposes of this Agreement, the following words and phrases shall have the following meanings:

1.1 "Affiliate" shall mean, with respect to University, any clinical or research entity that is operated or managed as a facility under the UPMC Health System, whether or not owned by University and with respect to Imara, shall mean any entity over which it owns or controls more than 50% of the equity securities.

1.2 "Complexa Data" shall mean data related to the Compound that is Controlled by Licensee and that was acquired by Licensee directly from Complexa, Inc.

1.3 "Compound" shall mean CXA-10 (or IMR-261) the structure which is set forth in Exhibit B.

1.4 "Control" or "Controlled" means with respect to any patent, possession of the ability (whether by sole or joint ownership, license or otherwise), other than pursuant to this Agreement, by a Party to grant, without violating the terms of any agreement with a Third Party, a license, access or other right in, to or under such patent.

1.5 "Covered" means, as to a compound or product and patent, that, in the absence of a license granted under, or ownership of, such patent, the making, using, keeping, selling, offering for sale or importation of such compound or product would infringe such patent or, as to a pending claim included in such patent, the making, using, keeping, selling, offering for sale or importation of such compound or product would infringe such patent if such pending claim were to issue in an issued patent without modification.

1.6 [**] shall mean [**] a Pennsylvania corporation with an address at [**].

1.7 "Field" shall mean use of the Compound for the treatment of hemoglobinopathies and use of the Compound for the treatment of asthma in the Denver clinical trial only.

1.8 "Licensee IP" shall mean any and all intellectual property, including, without limitation, patents and/or patent applications, owned or Controlled by Licensee during the Term (other than the Patent Rights).

1.9 "Licensed Technology" shall mean any product or part thereof or service which includes the Compound in the Field and which is:

(a) Covered by a Valid Claim in the country in which any such product or part thereof is made, used or sold or in which any such service is used or sold; or

(b) Manufactured by using a process or is employed to practice a process which is Covered by a Valid Claim in the country in which any such process is used or in which such product or part thereof or service is used or sold.

1.10 [Reserved].

1.11 “Net Sales” shall mean Licensee’s [**] for Licensed Technology sold by Licensee, its Affiliates or Sublicensees (other than the University of Colorado Denver) to Third Parties in the Territory, less the sum of the following:

[**].

1.12 “Non-Commercial Research and Education Purposes” shall mean use of the Patent Rights (including distribution of biological materials Covered by the Patent Rights) for academic research or other not-for-profit scholarly purposes which are undertaken at a non-profit or governmental institution that does not use the Patent Rights in the production or manufacture of products for sale or the performance of services for a fee.

1.13 “Non-Royalty Sublicense Income” shall mean all non-royalty consideration, including, execution fees, maintenance fees and milestone fees received by Licensee from its Third Party sublicensees pursuant to any sublicense granted pursuant to this Agreement, but excluding any reimbursable expenses (e.g., government fees and taxes, intellectual property costs, etc.) paid by such sublicensee to Licensee.

1.14 “Patent Rights” shall mean University intellectual property described below that covers the Compound in the Field:

(a) The United States patents and/or patent applications listed in Exhibit A;

(b) Any non-provisional United States patent applications that claim priority to any provisional patent application listed in Exhibit A;

(c) Any and all divisionals, continuations, reissues, re-examinations, renewals, substitutions, and extensions of the foregoing; and

(d) Any and all patents issuing from the foregoing.

1.15 “Term” shall have the meaning set forth in Section 11.1.

1.16 “Territory” shall mean worldwide.

1.17 “Third Party” means any individual, partnership, corporation, limited liability company, joint venture or similar entity or organization, other than University, Licensee or their respective Affiliates.

1.18 “Valid Claim” means a claim (a) of any issued, unexpired patent included in the Patent Rights, which has not, in the country of issuance, been donated to the public, disclaimed, held invalid or unenforceable by a court of competent jurisdiction in an unappealed or unappealable decision, or (b) of any patent application included in the Patent Rights, which has not, in the country in question, been cancelled, withdrawn, or abandoned. Notwithstanding the foregoing, a patent application pending for more than [**] will not be considered to have any Valid Claim for purposes of this Agreement unless and until a patent that meets the criteria set forth in clause (a) above with respect to such application issues.

ARTICLE 2 – GRANT

2.1 Subject to the terms and conditions of this Agreement, University hereby grants to Licensee, to the extent it may lawfully do so, a non-exclusive license under the Patent Rights to make, have made, manufacture, research, develop, use, sell, offer for sale and commercialize the Licensed Technology in the Field and in the Territory for the Term. The license granted hereby is subject to the rights of the United States government, if any, as set forth in 35 U.S.C. §200, et seq. Licensee, its Affiliates and sublicensees shall not practice the Patent Rights outside of the Field.

2.2 University reserves the royalty-free, non-exclusive right to practice under the Patent Rights and to use the Licensed Technology for its own Non-Commercial Research and Education Purposes.

2.3 Licensee may grant sublicenses of any rights granted to it under this Agreement through multiple tiers of sublicenses to one or more sublicensees with the prior written consent of University, such consent not to be unreasonably withheld. Licensee agrees that any sublicense granted by it to a third party shall be on terms not less stringent than the terms of this Agreement and provide that the sublicensee shall comply with all applicable terms of this Agreement. Each sublicense granted by Licensee pursuant to this Agreement shall include an audit right by University of sublicensee of the same scope as provided in Article 6.2 with respect to Licensee. Licensee shall be fully responsible and liable for any acts or omissions of any Affiliate or sublicensee under such sublicense agreement as if such activities were conducted by Licensee.

2.4 Licensee agrees to forward to University a copy of any and all sublicense agreements promptly upon execution thereof, but in no event later than [**] after each such sublicense agreement has been executed by both parties thereto, provided however, such sublicense or amendment may be redacted with respect to the sublicensee’s scientific and technical information.

2.5 The license granted hereunder shall not be construed to confer any rights upon Licensee by implication, estoppel or otherwise as to any intellectual property not specifically set forth herein.

ARTICLE 3 – DUE DILIGENCE

3.1 Licensee (acting directly or through one or more Affiliates or Sublicensees) shall use Commercially Reasonable Efforts to develop and obtain FDA approval for the Licensed Technology.

“Commercially Reasonable Efforts” shall mean:

[**].

3.2 Licensee shall notify University of the achievement of the milestones in Section 3.1 within [**] upon the achievement of the applicable milestone.

3.3 Licensee's failure to perform in accordance with Section 3.1 hereof shall be grounds for University to terminate this Agreement and upon termination all rights and interest to the Patent Rights shall revert to University.

ARTICLE 4 – COVENANTS

4.1 To the extent requested by [**], Licensee will consider in good faith the terms pursuant to which it would grant access to all or a portion of the Complexa Data to [**]. For clarity, this provision and Agreement shall not be construed to confer any rights upon [**] or University by implication, estoppel or otherwise as to the Complexa Data and/or Licensee IP unless and until Licensee and [**] or University enter into a definitive agreement with respect to the Complexa Data and/or Licensee IP and after such point, such rights shall be limited to the extent of the rights granted under the definitive agreement.

ARTICLE 5 – LICENSE CONSIDERATION

5.1 In consideration of the rights, privileges and license granted by University hereunder, Licensee shall pay monetary consideration as follows:

(a) An initial one-time, nonrefundable license fee of Seven Thousand Five Dollars ($7,500) due immediately and payable within ten (10) business days from the Effective Date of this Agreement;

(b) An annual maintenance fee in the amount of [**], with the first annual maintenance fee due on the first anniversary of the Effective Date, and unless this Agreement is earlier terminated in accordance with its terms, each additional maintenance fee shall be due on each subsequent anniversary of the Effective Date during the Term.

(c) Royalties during the Term in an amount equal to [**] of aggregate Net Sales due each calendar quarter within [**] of delivery of the report set forth in Section 6.1.

(d) Beginning with the first commercial sale of Licensed Technology by Licensee, its Affiliates or Sublicensees to Third Parties, minimum annual royalty of [**] but only to the extent such minimum royalty is greater than the aggregate annual royalty computed in accordance with Section 5.1(c) above.

(e) A share of Non-Royalty Sublicense Income equal to [**] of such Non-Royalty Sublicense Income.

(f) Milestone payments shall be due and paid by Licensee to the University as follows:

[**].

These milestone payments are payable only once, regardless of the number of products for which the Licensed Technology achieves the relevant milestone.

5.2 All payments pursuant to this Agreement shall be made by check or by wire transfer in United States dollars without deduction or exchange, collection or other charges and

directed to the address or, in the case of wire transfer, to the bank, set forth in Article 12. With respect to the milestone payments in Section 5.1(f), Licensee will provide University with written notice upon the achievement of the milestone within [**] after such achievement. Following receipt of such written notice, University will promptly invoice Licensee for the milestone and Licensee will make the appropriate milestone payment within [**] after receipt of such invoice. Non-Royalty Sublicense Income payments pursuant to Article 5.1(e) hereof shall by paid within [**] after receipt of payment by Licensee (or as applicable, its Affiliates) from sublicensee.

5.3 The balance of any payments due pursuant to this Agreement which are overdue shall bear interest, compounded monthly, calculated from the due date until payment is received at the rate of [**] per annum. Payment of such interest by Licensee shall not waive the University's right to seek any other remedy, legal or equitable, to which it may be entitled because of the delinquency of any payment, including, but not limited to, termination of this Agreement as set forth in Article 11. In addition, Licensee shall reimburse University for any costs and expenses incurred in connection with collecting any overdue balance of payments from Licensee with respect to its payment obligations under this Agreement, including the costs of engaging counsel or a collection agency for such purpose.

5.4 Taxes imposed by any foreign governmental agency on any payment to be made to University by Licensee shall be paid by Licensee without deduction from any payment due to University hereunder.

5.5 Licensee shall sell products and/or services resulting from Licensed Technology to University and its Affiliates at such price(s) and on such terms and conditions as such products and/or services are made available to Licensee's most favored customer.

ARTICLE 6 – REPORTS AND AUDIT

6.1 Within thirty [**] after each March 31, June 30, September 30 and December 31 of each year during the term of this Agreement beginning in the year of first commercial sale of Licensed Technology, Licensee shall deliver to University true, accurate and detailed reports of the following information in substantially the form as illustrated in Exhibit D:

(a) Number of Licensed Technology products manufactured and sold by Licensee and all sublicensees;

(b) Total billings for all such products;

(c) Accounting for all Licensed Technology services used or sold by Licensee and all sublicensees;

(d) Deductions set forth in Section 1.11; and

(e) Total royalties due

(f) Name and address of sublicensees; and

(g) Total Non-Royalty Sublicense Income received during such calendar quarter and total amounts of payment due pursuant to Article 5.1 (e).

6.2 Licensee shall keep full, true and accurate books of account, in accordance with generally accepted accounting principles, containing all information that may be necessary for the purpose of showing the amounts payable to University hereunder. Such books of account shall be kept at Licensee's principal place of business. The relevant portions of such books of account shall be open to the University at all reasonable times for [**] following the end of the calendar year to which they pertain, and for [**] after the expiration or termination of this Agreement, for inspection by University or its agents for the purpose of verifying Licensee's royalty statement. The fees and expenses of University's representatives performing any such audit shall be borne by University, however, if an error of more than [**] of the total payments due or owing for any calendar year is discovered, then Licensee shall bear the University's fees and expenses.

6.3 No later than [**] after December 31 of each calendar year during the Term (beginning with the year ending December 31, 2021), Licensee shall provide to University a written annual progress report, in substantially the form as illustrated in Exhibit C, describing progress of Licensee, it's Affiliates and sublicensees on research and development, regulatory approvals, manufacturing, sublicensing, marketing and sales during the preceding twelve-month period ending December 31.

6.4 Notwithstanding the above, University shall have the right, [**] during the term of this Agreement, to inspect the applicable technical and other information from Licensee sufficient to evidence whether and to what extent Licensee is meeting its diligence obligations under Article 3 above. The fees and expenses of University's representatives performing any such inspection shall be borne by University.

6.5 Licensee shall report to the University the date of the first commercial sale of a Licensed Technology within [**] of occurrence in each country with a Valid Claim.

ARTICLE 7 – PATENT PROSECUTION AND INFRINGEMENT ACTIONS

7.1 As between the Parties, University will control the prosecution and maintenance of the Patent Rights during the Term. In the event University desires to abandon all or a portion of the Patent Rights, University shall provide Licensee with written notice thereof, which notice shall be provided to Licensee at least [**] before the date such abandonment would become effective. In the event University desires to cease paying maintenance fees for any of the Patent Rights in any country, University shall provide Licensee with written notice thereof, which notice shall be provided to Licensee at least [**] before the maintenance fees in question are due. In such event, Licensee shall have the right, but not the obligation, to pay any such maintenance fees on behalf of University.

7.2 In any infringement suit University may institute to enforce the Patent Rights pursuant to this Agreement, Licensee shall, at the request of University, provide reasonable cooperation and assistance to University in connection with University's enforcement action.

7.3 Licensee shall be responsible for [**] of all fees and costs, including attorneys' fees, relating to the filing, prosecution maintenance, and post-grant proceedings relating to the Patent Rights (collectively, the "Patent Costs") during the Term. Licensee's share of Patent Costs shall be paid by Licensee within [**] after receipt of University's invoice therefor, which invoice shall contain reasonable documentary support for the amounts being invoice to Licensee. Additionally, Licensee shall be liable to University for its share of Patent Costs that are taken by patent counsel after the term of this Agreement but in response to any instructions that were sent from University to patent counsel relating to the Patent Rights prior to the earlier of (i) Licensee providing notice of termination pursuant to Section 11.3 and (ii) expiration of the Term. Payments pursuant to this Section 7.3 are not creditable against royalties or any other payment due to University under this Agreement.

ARTICLE 8 - CONFIDENTIALITY

8.1 University shall maintain in confidence all Confidential Information (as defined below) of Licensee and shall not use or disclose such Confidential Information, except as expressly authorized by this Agreement. "Confidential Information" shall mean (i) the terms and existence of this Agreement, (ii) all information and reports due to University under Article 6 which are disclosed in writing and marked "Confidential" and (iii) all information of Licensee reviewed by University in the course of conducting an audit or inspection under Article 6 hereof. For the avoidance of doubt, Licensee may disclose the terms of this Agreement to the extent necessary to accountants, banks, investors and financing sources and their respective advisors and to any third party (and its affiliates, accountants, bankers, investors and advisors) in connection with a proposed merger, acquisition, licensing, collaboration or similar transaction.

8.2 The Confidentiality set forth above shall not apply to any information to the extent that (a) the University can show by written record that it possessed the information prior to its receipt from Licensee; (b) the information was, at the time of disclosure, available to the public or became so through no fault of the University; or (c) the information is subsequently disclosed to the University free of any obligations of confidentiality by a third party that has the right to disclose it. Notwithstanding any other provisions of this Article 8, the University may disclose Confidential Information of Licensee (i) on a need-to-know basis and in connection with University's performance or its obligations and/or exercise of its rights under this Agreement to its Affiliates, employees, consultants, or agents provided that such individuals or entities are bound by non-disclosure and non-use obligations at least equivalent in scope to those set forth in this Article 8; (ii) in confidence to its trustees, directors and professional advisors who are bound by non-disclosure and non-use obligations at least equivalent in scope to those set forth in this Article 8; and (iii) to the extent that such disclosure is required by a court order, or in order to comply with applicable laws or regulations, but provided that University will, except where impracticable, give reasonable advance notice to Licensee of such required disclosure and use efforts to secure, or to assist the other party in securing, a protective order relating to, or confidential treatment of such information.

ARTICLE 9 – INDEMNIFICATION/INSURANCE/LIMITATION OF LIABILITY

9.1 Licensee shall at all times during the Term and thereafter indemnify, defend and hold University, its trustees, officers, faculty members, employees and Affiliates ("Indemnified Parties") harmless against any liability, loss, damage or expense (including reasonable attorneys' fees and expenses), that the Indemnified Parties may incur or otherwise be required to pay to one or more Third Parties in connection with any Third Party suit, investigation, claim or demand resulting from or arising out of (i) any claims arising out of the research, development, manufacture, commercialization or use of the Licensed Technology (or practice of the Patent Rights) by, on behalf of, or under the authority of, Licensee or any of its sublicensees, (ii) the breach by Licensee of this Agreement, or (iii) the negligence or willful misconduct by or on behalf of Licensee or any of its sublicensees, except, in each case, to the extent such claims are caused by (as finally determined by a court of competent jurisdiction) the material breach by University of this Agreement or the gross negligence or willful misconduct of University.

9.2 If any proceeding is instituted against University with respect to which indemnity may be sought pursuant to Section 9.1, University will give prompt written notice of the indemnity claim to Licensee and provide Licensee with a copy of any complaint, summons or other written notice that University receives in connection with any such claim. Licensee shall have the right to control any litigation relating to such claim and the disposition of such claim by negotiated settlement or otherwise. Licensee will act reasonably and in good faith with respect to all matters relating to such claim and will not settle or otherwise resolve such claim without University's prior written consent, which will not be unreasonably withheld, conditioned or delayed; provided that such consent will not be required with respect to any settlement involving only the payment of monetary awards for which Licensee will be fully responsible. University will reasonably cooperate with Licensee in the Licensee's defense of any claim for which indemnity is sought under this Agreement, at Licensee's cost and expense.

9.3 During the Term, Licensee shall obtain and carry in full force and effect liability insurance which shall protect Licensee and University in regard to events covered by Section 9.1 above, as provided below:

(a) Commercial General Liability
   a. Coverage: Commercial General Liability, including, but not limited to, Products, Contractual, Fire, Legal and Personal Injury
   b. Limits: [**]

(b) Products Liability
   a. Coverage: Products Liability
   b. Limits: [**]

The University of Pittsburgh is to be named as an additional insured with respect to insurance policies identified in Sections 9.3(a) and 9.3(b) above. Certificates of insurance evidencing the coverage required above shall be filed with University's Innovation Institute, 1st Floor Gardner Steel Conference Center, 130 Thackeray Avenue, Pittsburgh, PA 15260, within [**] from the Effective Date of this Agreement and on or before July 1 of each subsequent year during the Term of this Agreement. Such certificates shall provide that the insurer will give University not less than [**] advance written notice of any cancellation of coverage or change in coverage that would result in Licensee no longer satisfying the coverage required herein.

9.4 UNIVERSITY, AND ITS AGENTS AND/OR EMPLOYEES, MAKE NO REPRESENTATION AND EXTEND NO WARRANTIES OF ANY KIND, EITHER EXPRESS OR IMPLIED, INCLUDING BUT NOT LIMITED TO WARRANTIES OF MERCHANTABILITY, FITNESS FOR A PARTICULAR PURPOSE, AND VALIDITY OF PATENT RIGHTS CLAIMS, ISSUED OR PENDING. NOTHING IN THIS AGREEMENT SHALL BE CONSTRUED AS A REPRESENTATION OR WARRANTY THAT THE PRACTICE BY LICENSEE OF THE LICENSE GRANTED HEREUNDER SHALL NOT INFRINGE THE PATENT RIGHTS OF ANY THIRD PARTY. EXCEPT FOR (A) THIRD PARTY CLAIMS THAT ARE SUBJECT TO INDEMNIFICATION UNDER ARTICLE 9, OR (B) CLAIMS ARISING OUT OF A PARTY'S WILLFUL MISCONDUCT NEITHER PARTY WILL BE LIABLE TO THE OTHER PARTY IN CONNECTION WITH THIS AGREEMENT FOR ANY INDIRECT, SPECIAL AND CONSEQUENTIAL DAMAGES, (EVEN IF SUCH PARTY HAS BEEN ADVISED OF THE POSSIBILITY OF SUCH DAMAGES. LICENSEE ASSUMES ALL RESPONSIBILITY AND LIABILITY FOR LOSS OR DAMAGE CAUSED BY THE MANUFACTURE, USE OR SALE OF THE LICENSED TECHNOLOGY.

ARTICLE 10 – ASSIGNMENT

This Agreement is not assignable be either Party without the prior written consent of the other Party, such consent not to be unreasonably withheld, and any attempt to do so shall be null and void. In the event the University assigns or otherwise transfers any of the Patent Rights to a Third Party during the Term, any such assignment or transfer shall be made subject to the terms of this Agreement.

ARTICLE 11 – TERM AND TERMINATION

11.1 Term. Unless earlier terminated in accordance with Sections 11.2 or 11.3, this Agreement shall expire upon the expiration of the last Valid Claim (the "Term").

11.2 University shall have the right to terminate this Agreement, upon written notice, if:

(a) Licensee defaults in the performance of any of the obligations herein contained and such default has not been cured within [**] after receiving written notice thereof from University;

(b) The practice of the Patent Rights by Licensee is outside of the Field; or

(c) Licensee ceases to carry out its business, becomes bankrupt or insolvent, applies for or consents to the appointment of a trustee, receiver or liquidator of its assets or seeks relief under any law for the aid of debtors.

11.3 Licensee may terminate this Agreement upon ninety (90) days prior written notice to University. Upon termination of this Agreement, neither Party shall be released from any obligation that accrued prior to the effective date of such termination.

11.4 Section 5.1, Article 8, Section 9.1, Section 9.2, Article 10, Section 11.3, Section 11.4, Article 12 and Article 13 shall survive expiration or termination of this Agreement.

ARTICLE 12 – NOTICES

12.1 Any notice or communication pursuant to this Agreement shall be sufficiently made or given if sent by certified or registered mail, postage prepaid, or by overnight carrier, with proof of delivery by receipt, addressed to the address below or as either Party shall designate by written notice to the other Party, or if in accordance with Section 12.3.

In the case of University:

Innovation Institute
University of Pittsburgh
1st Floor Gardner Steel Conference Center
130 Thackeray Avenue
Pittsburgh, PA 15260
ATTN: Director
Innovation Institute

In the case of Licensee:

Imara Inc.
116 Huntington Ave, Sixth Floor
Boston, MA 02116
Attention: Legal Department
Email: notices@imaratx.com

12.2 Any payments to University hereunder by wire transfer shall be directed as follows:

[***]

The Licensee shall be responsible for all applicable fees and costs relating to any wire transfer, to include translation fees, without any deduction of such fees from amounts due to the University pursuant to this Agreement.

12.3 All invoices to Licensee generated by University under this Agreement will be sent electronically via e-mail and in PDF format to: ap@imaratx.com.

ARTICLE 13– MISCELLANEOUS

13.1 This Agreement may not be amended or modified except by the execution of a written instrument signed by the Director of the University of Pittsburgh Innovation Institute, his successor, or other designated University employee having signatory authority, and Licensee's Chief Executive Officer or other designated Licensee employee having signatory authority.

13.2 This Agreement shall be construed and interpreted in accordance with the laws of the Commonwealth of Pennsylvania. The forum for any action relating to this Agreement, including those brought against individuals such as University employees or agents, shall be the Courts of Allegheny County, Pennsylvania, or, if in a federal proceeding, the United States District Court for the Western District of Pennsylvania.

13.3 The Parties acknowledge that this Agreement and the Exhibits hereto set forth the entire understanding and intentions of the Parties (including their respective Affiliates) hereto as to the subject matter hereof and supersedes all previous representations, negotiations, or understandings between the Parties (including their respective Affiliates) and/or their respective employees or agents, whether written or oral, regarding the subject matter of this Agreement. As of the Effective Date, this Agreement supersedes the Complexa Agreement and neither party shall have any further rights or obligations to the other party under the Complexa Agreement.

13.4 The Parties acknowledge that they consulted, or had the opportunity to investigate and/or consult, with their legal counsel and/or other advisors with respect to the Patent Rights and the terms of this Agreement.

13.5 The Parties agree that this Agreement constitutes an arm's length business transaction and does not create a fiduciary relationship.

13.6 Nothing contained in this Agreement shall be construed as conferring upon either Party any right to use in advertising, publicity or other promotional activities any name, trade name, trademark, or other designation of the other Party, including any contraction, abbreviation, or simulation of any of the foregoing. Without the express written approval of the other Party, neither party shall use any designation of the other party in any promotional activity associated with this Agreement. Except as may be required by applicable law or regulations, neither Party shall issue any press release or make any public statement in regard to this Agreement without the prior written approval of the other Party.

13.7 Licensee agrees that with respect to the performance of this Agreement or the practice of the rights granted by the University hereunder, it shall comply with any and all applicable United States export control laws and regulations, as well as any and all embargoes and/or other restrictions imposed by the Treasury Department's Office of Foreign Asset Controls.

13.8 Each Party agrees that in connection with this Agreement that it will abide by applicable laws and regulations. Neither Party will offer, promise or give, directly or indirectly, anything of value to any government official, political party official, political candidate, or employee thereof or to any Third-Party while knowing that such item of value or any portion thereof may be offered, promised, or given to a government official, political party official, political candidate, or employee thereof for the purpose of obtaining or retaining business. Each Party specifically agrees that in connection with this Agreement, it will take no action, or omit to take any action, which would cause the other Party to be in violation of the applicable laws of the United States, including the U.S. Foreign Corrupt Practices Act and/or any local laws regarding bribery as well as any US anti-boycott laws.

13.9 If during the Term Licensee challenges the validity or enforceability of University's Patent Rights or University's ownership of the Patent Rights anywhere in the world, the Licensee shall continue to pay to University all royalties and other financial obligations required under this Agreement, to include Patent Costs, during the period while such challenge is pending. If any such challenge is unsuccessful by Licensee, the royalty rates set forth in Article 5.1 above shall automatically double in value, to include all royalty minimums and floors; and Licensee shall reimburse the University for all fees and costs associated with defending such action, to include attorneys' and expert fees. The effective date of such increase in royalty rates shall be the date of the first court order or date of issuance of a re-examination certificate (or foreign equivalents thereof) declaring any claim of the Patent Rights as valid or enforceable.

13.10 If one or more of the provisions of this Agreement shall be held invalid, illegal or unenforceable, the remaining provisions shall not in any way be affected or impaired thereby. In the event any provision is held illegal or unenforceable, the parties shall use reasonable efforts to substitute a valid, legal and enforceable provision which, insofar as is practical, implements purposes of the provision held invalid, illegal or unenforceable.

13.11 Failure at any time to require performance of any of the provisions herein shall not waive or diminish a Party's right thereafter to demand compliance therewith or with any other provision. Waiver of any default shall not waive any other default. A Party shall not be deemed to have waived any rights hereunder unless such waiver is in writing and signed by a duly authorized officer of the Party making such waiver.

[*remainder of page intentionally left blank*]

IN WITNESS WHEREOF, the parties represent and warrant that each has the authority to bind the Party to this Agreement and have set their hands and seals as of the date set forth on the first page hereof.

UNIVERSITY OF PITTSBURGH – OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION

By /s/ Evan Facher, Ph.D., MBA
Evan Facher, Ph.D., MBA
Director, Innovation Institute
Vice Chancellor for Innovation and Entrepreneurship

IMARA INC.

By /s/ Rahul Ballal, Ph.D.
Rahul Ballal, Ph.D.
President and Chief Executive Officer

Exhibit 10.12

Certain identified information has been excluded from the exhibit because it is both (i) not material and (ii) is the type of information that the registrant treats as private or confidential. Double asterisks denote omissions.

Amendment No. 1
to
Non-Exclusive License Agreement

This Amendment No. 1 (the "***Amendment***") is made as of December 8, 2021 (the "***Amendment Effective Date***") by and between Imara Inc., a Delaware corporation having an address at 116 Huntington Avenue, 6th Floor, Boston, MA 02116 ("***Licensee***") and the University of Pittsburgh – Of the Commonwealth System of Higher Education, a non-profit corporation, organized and existing under the laws of the Commonwealth of Pennsylvania, having an office at 1st Floor Gardner Steel Conference Center, 130 Thackeray Avenue, Pittsburgh Pennsylvania 15260 ("***University***"). Licensee and University may be referred to herein individually as a "***Party***" or collectively as the "***Parties***."

WHEREAS, the Parties are party to that certain Non-Exclusive License Agreement dated May 27, 2021 (the "***Agreement***"); and

WHEREAS, the Parties desire to amend the Agreement as set forth in this Amendment.

NOW, THEREFORE, in consideration of the mutual covenants and undertakings contained herein, the Parties, intending to be legally bound, hereby agree as follows:

1. Defined Terms. Capitalized terms not otherwise defined herein shall have the meaning ascribed to such term in the Agreement.

2. Amendment to License Field. The Parties hereby agree that the defined term "Field" in Section 1.7 of the Agreement is hereby amended and restated in its entirety to read as follows:

   "1.7 "Field" shall mean use of the Compound for the diagnosis, treatment or prevention of the following indications:
   - Hemoglobinopathies, including sickle cell disease and beta-thalassemia;
   - Red cell anemias and iron disorders, including iron-refractory iron deficiency anemia (IRIDA), hereditary hemochromatosis and polycythemia vera; and
   - Asthma in the Denver clinical trial only."

3. Consideration. As consideration for modifications to the Agreement as set forth in this Amendment, Licensee shall:

   (a) pay monetary consideration in the form of a one-time, nonrefundable fee of [**], payable within [**] from the Amendment Effective Date ([**] of this amount reflecting an amount to be paid by Licensee on behalf of a third-party related to Invoice No. 432171); and

(b) simultaneous with execution of this Amendment, assign all of its right, title and interest in the patents and patent applications identified on Schedule A to this Amendment (the "***Assigned Patents***"), using the form of Assignment Agreement set forth on Schedule B to this Amendment; provided that, if at any point from and after the Amendment Effective Date, Licensee's manufacture, research, development, use, sale, offer for sale or commercialization of the Compound in the Field, is Covered by any patent or patent application claiming priority to one or more of the Assigned Patents (including any and all divisionals, continuations, reissues, re-examinations, renewals, substitutions, and extensions of the foregoing), then University agrees to grant and hereby grants to Licensee a non-exclusive, fully-paid, royalty-free, perpetual, irrevocable, sublicensable (solely to the extent of Section 2.3 of the Agreement) license under University's right, title and interest to the Assigned Patents to make, have made, manufacture, research, develop, use, sell, offer for sale and commercialize the Compound in the Field and in the Territory.

4. Amendment Effective Date. This Amendment shall be effective as of the Amendment Effective Date.

5. Survival. Section 3(b) of this Amendment shall be part of the Agreement and survive expiration or termination of the Agreement (as amended hereby).

6. No Other Amendments. Except as amended by this Amendment, the Agreement is hereby ratified and confirmed and all other terms of the Agreement shall remain in full force and effect, unaltered by this Amendment.

IN WITNESS WHEREOF, the Parties hereto have duly executed this Amendment as of the Amendment Effective Date.

IMARA INC.

By: **/s/** Rahul D. Ballal, PhD
Name: Rahul D. Ballal, PhD
Title: Chief Executive Officer

UNIVERSITY OF PITTSBURGH – OF THE COMMONWEALTH SYSTEM OF HIGHER EDUCATION

By: **/s/** Evan Facher, Ph.D., MBA
Name: Evan Facher, Ph.D., MBA
Title**:** Director, Innovation Institute, Vice Chancellor for Innovation and Entrepreneurship

Exhibit 10.17

Imara, Inc.
116 Huntington Ave, 6th Floor
Boston, MA 02116 USA

Info@Imaratx.com
+1 617 206 2038

www.imaratx.com

December 4, 2020

Kenneth M. Attie, MD

Dear Ken:

On behalf of IMARA Inc., a Delaware corporation (the "**Company**"), I am very pleased to offer you employment with the Company, subject to the terms and conditions set forth below and contingent upon satisfactory completion of a references check and the Company's standard background check:

1. Position. You will be employed to serve as the Sr. Vice President, Chief Medical Officer of the Company. In that position, you will have the duties, authorities and responsibilities that are customarily associated with such position, and such other the duties, authorities and responsibilities the Board of Directors of the Company (the "**Board**") and the Chief Executive Officer of the Company (the "**CEO**") (including any designee of the CEO) designate from time to time. You will report to the Chief Executive Officer. You will perform such duties to the Company primarily at the Company's headquarters in Boston, Massachusetts, subject to such travel as the position requires. While an employee of the Company, you will devote substantially all of your full professional time and efforts to the business of the Company. You may engage in a reasonable amount of volunteer work so long as that work does not conflict with your duties to the Company, however any other outside professional or other business activity you engage in must be approved in advance by the Board and must not conflict with your duties to the Company.

2. Start Date. The start date for your new position with the Company is January 19, 2021 (the "**Start Date**") or such other date as may be mutually agreed upon by you and the Company. Notwithstanding the foregoing, if prior to the Start Date either you or the Company reasonably believes that your commencement of employment with the Company would be likely to result in a dispute between or among Acceleron Pharma Inc. **("Acceleron")**, you, and/or the Company pertaining to your post-employment obligations to Acceleron (including, without limitation, a claim being brought in litigation or arbitration by Acceleron against you and/or the Company), you may withdraw your acceptance of this offer or the Company may rescind this offer of employment, in which event you would not be entitled to commence employment with the Company or receive any compensation from the Company.

3. Compensation.

a. *Base Salary*. Commencing on the Start Date, your base salary will be at the rate of $17,500.00 semi-monthly (i.e. a gross aggregate amount of $420,000 per annum assuming continuing service over a 12-month period), subject to tax and other withholdings as required

by law. Your salary shall be reviewed annually by the Company's Board of Directors (the "**Board**").

b. *Hiring Bonus.* You will receive a lump sum payment of $50,000 less regular withholdings, payable within the first two pay periods following your start date. If you terminate your employment before the end of the first twelve months of employment you will be required to repay a portion of the Hiring Bonus to the Company in full that is calculated as the product of the full hiring bonus multiplied by a ratio, the numerator of which is twelve minus the number of complete months you worked for the Company prior to your departure and the denominator of which is twelve.

c. *Discretionary Bonus Program*. You will be eligible for an annual discretionary bonus of up to thirty-five percent (35%) of your annualized base salary to allow you to participate in the success of the Company based upon a combination of Company achievements and your performance, both as determined in the sole discretion of the Board. Any annual bonus shall be paid no later than March 15th of the year immediately following the year to which the applicable annual bonus relates, and you must be an active employee of the Company on the date any bonus is paid to be eligible for and to earn a bonus award. No bonus shall be considered to be earned until it is paid, as it also serves as an incentive to remain employed by the Company. Any bonus will be prorated based on actual days of service for the year in which the Start Date occurs.

d. *Option.* Subject to the approval of the Board, the Company will grant to you a stock option (the "**Option**") under the Company's 2020 Equity Incentive Plan, (as amended from time to time the "**Plan**"), for the purchase of 110,000 shares of Common Stock of the Company. The exercise price for the Option shall be equal to the closing price per share of Common Stock of the Company on the Nasdaq Global Select Market on the date of grant. The Option shall be subject to all terms and other provisions set forth in the Plan and in a separate option agreement ("**Option Agreement**"), which will provide for (i) vesting of shares subject to the Option as follows so long as you have been continuously providing services to the Company as an employee, consultant or advisor through each vesting date: (A) 25% of such shares will vest on the first anniversary of your commencement of employment (the "**First Vesting Date**") and (B) the remainder of such shares will vest in equal quarterly installments over the three year period following the First Vesting Date; and (ii) the acceleration of vesting on all unvested shares subject to the Option if the Company terminates your employment for any reason other than Cause (except for termination due to your death or Disability) or you resign for Good Reason (in either case, a "**Qualifying Termination**"), in either case within 12 months after a Change of Control (as defined below), so long as you have been continuously providing services as an employee, consultant or advisor to the Company up to and including such Change of Control through the date of such termination without Cause or such resignation for Good Reason.

e. *Withholdings.* The Company shall withhold from any compensation or benefits payable under this letter agreement or the Restrictive Covenants Agreement (as defined below) any federal, state and local income, employment or other similar taxes and withholdings as may be required to be withheld pursuant to any applicable law or regulation.

4. Benefits.

a. *Vacation & Holidays.* You will be eligible for four (4) weeks of paid vacation each year, to be accrued and used consistent with the Company's vacation policy. You will also be eligible for Company-paid holidays in accordance with Company policy.

b. *Other.* You may participate in any and all benefit programs that the Company establishes and makes available to its employees from time to time, provided that you are eligible under (and subject to all provisions of) the plan documents that govern those programs. Benefits are subject to change at any time in the Company's sole discretion. The Company will also reimburse 100% of the parking/commuting cost of one of the following; Monthly Parking at a designated parking garage lot, Charlie Card T-Pass, or Commuter Rail.

c. *Expenses.* The Company shall reimburse you for all ordinary and reasonable out-of-pocket business expenses incurred by you in furtherance of the Company's business in accordance with the Company's policies with respect thereto as in effect from time to time. In order to be eligible for any expense reimbursement hereunder, you must (i) submit reasonable documentation evidencing the nature and amount of any such business expenses incurred by you and (ii) submit any request for reimbursement no later than ninety (90) days following the date that such business expense is incurred.

5. At-Will Employment. Your employment with the Company is and shall at all times during your employment hereunder be "at-will" employment. The Company or you may terminate your employment at any time for any reason, with or without Cause or Good Reason, and with or without notice. You agree that although your title, duties, compensation or benefits may change from time to time, such changes will not change the "at-will" nature of your employment during your tenure as an employee of the Company, and may only be changed by an express written agreement that is signed by you and an officer duly authorized by the Board (other than you).

6. Termination of Employment.

a. If you resign your employment with the Company without Good Reason or the Company terminates your employment for Cause you will receive no additional compensation other than: (i) any unpaid base salary for services rendered through the last day of your employment (the "**Termination Date**"); (ii) reimbursement of any un-reimbursed business expenses incurred as of the Termination Date in accordance with the Company's reimbursement policy, (iii) payment for any accrued but unused vacation time (if applicable) earned through the Termination Date; and (iv) all other earned payments, vested benefits or vested or earned fringe benefits to which you shall be entitled under the terms of any applicable compensation arrangement or benefit, equity or fringe benefit plan or program or grant or this letter agreement (collectively, clauses (i) through (iv) shall be referred herein as the "**Accrued Benefits**"). The Accrued Benefits will be paid to you consistent with applicable law.

b. If a Qualifying Termination occurs, you will receive the Accrued Benefits, and, based upon satisfaction of the criteria in Section 6(d) below, including without limitation your execution and delivery of the separation and release agreement described therein and the lapse of any applicable revocation period without the release being revoked, you shall be eligible to receive the following severance benefits: (i) severance pay in the form of continuation of your base salary in effect as of the Termination Date for a period of nine (9) months, less standard

deductions, payable in accordance with the Company's then regular pay policies commencing on or before the sixtieth (60th) day following the Termination Date ("**Severance Pay**"), provided, that the first such payment shall include any amounts that would have been paid to you hereunder had the release become effective upon the Termination Date; and (ii) following the Termination Date, if you are eligible for and elect to continue your health insurance coverage pursuant to your rights under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended, or any state equivalent ("**COBRA**"), then the Company shall reimburse you for your premiums under COBRA on a monthly basis until the earlier of (x) nine (9) months following the Termination Date, or (y) the date upon which you commence full-time employment (or employment that provides you with eligibility for healthcare benefits substantially comparable to those provided by the Company) with an entity other than the Company. Notwithstanding any of the foregoing, if the 60-day period following the Termination Date would end in a calendar year subsequent to the year in which the Termination Date occurs, (i) the payments under this Section 6(b) will not be paid or commence before the first payroll of the subsequent calendar year; and (ii) any Severance Pay received in any calendar year shall be reduced by the amount of Garden Leave Pay you receive in the same such calendar year under, and as defined in, the Restrictive Covenants Agreement; provided that in no event shall the Severance Pay be reduced below $1000. In addition, if you experience a Qualifying Termination within 12 months after a Change of Control, and subject to Section 6(d), the Company shall pay you fifty percent (50%) of your annual bonus target amount for the year in which the Termination Date occurred in a lump sum on the date the first installment of Severance Pay is paid.

c. If your employment terminates because of your death or Disability, then you will receive the Accrued Benefits. For purposes of this letter agreement, "**Disability**" shall be defined as your inability to have performed your material duties hereunder due to a physical or mental injury, infirmity or incapacity for a consecutive one hundred eighty (180) days (including weekends and holidays) in any 365-day period. Notwithstanding the foregoing, in the event that as a result of earlier absence because of mental or physical incapacity you incur a "separation from service" within the meaning of such term under Section 409A of the Internal Revenue Code and the rules and regulations promulgated thereunder ("**Code Section 409A**") you shall on such date automatically be terminated from employment as a Disability termination.

d. Eligibility for receipt of the severance benefits and other pay and benefits in Section 6(b) shall be conditioned on your (i) returning to the Company all of its property and confidential information that is in your possession or control, and (ii) prior to the date provided in the Release, but in no event later than the 60-day period following the Termination Date, signing and not revoking a separation and release of claims agreement in a form provided by the Company (the "**Release**") that contains, among other provisions, a 12-month post-employment noncompetition restriction and a seven (7) business day revocation period, provided, that such Release shall (A) not expand the scope of prohibited competitive activity greater than as described in the Restrictive Covenants Agreement, (B) not terminate any of your rights to indemnification and defense which you will have given your role at the Company, (C) impact any rights that you may have as a stockholder in the Company, (D) not release your rights to the Accrued Benefits, and (E) contain, among other things, a general release of claims against the Company, its affiliates and each of its and their officers, directors, employees, agents and attorneys, and the following provisions:

(I) You agree that for the three (3)-year period following the Termination Date you, directly or indirectly, orally, in writing or through any medium (including, but not limited to, the press or other media, computer networks or bulletin boards, or any other form of communication) will not make any false statement, disparage or defame the goodwill or reputation of the Company, its affiliates or their respective directors, managers, officers, stockholders, members, agents and/or employees. Nothing herein shall prohibit you (i) from disclosing that you are no longer employed by the Company, (ii) from responding truthfully to subpoena, court order or other compulsory legal process, (iii) from rebutting in good faith statements made by the other party that are untrue or misleading or (iv) providing truthful information to a government entity; and

(II) You acknowledge your continuing obligations as set forth in the Restrictive Covenants Agreement.

e. For all purposes of this letter agreement, the term "**Cause**" shall mean; (i) a good faith finding by the Company that you have engaged in willful misconduct or gross negligence as to a material matter in connection with your duties; (ii) any act constituting fraud with respect to the Company; (iii) the indictment for, conviction of, or a plea of guilty or *nolo contendere* to, a felony under applicable law; (iv) a good faith finding by the Company that you have engaged in material violation of a material term of this letter agreement, the Restrictive Covenants Agreement or any written Company policy made available to you; (v) your failure to attempt in good faith to (A) perform your duties in all material respects or (B) follow a clear, lawful and reasonable directive of the Board; or (vi) material breach of a fiduciary duty owed to the Company that has caused or could reasonably be expected to cause a material injury to the Company; provided, that in no event shall your employment be terminated for Cause unless (A) an event or circumstance set forth in clauses (i) through (vi) has occurred and the Company provides you with written notice after Company has knowledge of the occurrence of existence of such event or circumstance, which notice reasonably identifies the event or circumstance that the Company believes constitutes Cause and (B) with respect to the events and circumstances set forth in clauses (iv) and (v) only, you fail to substantially cure the event or circumstance so identified within 30 days of the receipt of such notice, if the Board considers the situation to be reasonably correctable.

f. For all purposes of this letter agreement, the term "**Good Reason**" shall mean, each without your consent: (i) a material diminution in your authority, duties or responsibilities (other than temporarily while physically or mentally incapacitated or as required by applicable law); (ii) a material reduction by the Company in your annual base salary; (iii) relocation of your primary office at the Company's headquarters in the Boston, Massachusetts metropolitan area to another location by more than twenty (20) miles; or (iv) a material breach by the Company of a material term of this letter agreement. You shall provide the Company with a written notice detailing the specific circumstances alleged to constitute Good Reason within ninety (90) days after the first occurrence of such circumstances, and the Company shall have thirty (30) days following receipt of such notice to cure such circumstances in all material respects, provided, that, no termination for Good Reason shall occur unless you end your employment within 180 days after the first occurrence of any Good Reason event.

g. For all purposes of this letter agreement, the term "**Change of Control**" shall mean: (i) any merger, reorganization, consolidation, recapitalization or other transaction or

series of related transactions, including a transfer of shares of capital stock, whether or not the Company is the surviving or continuing corporation in such transaction, and whether or not the Company is a party thereto, that results in the holders of shares of capital stock immediately prior to such transaction or transactions holding, immediately after such transaction or transactions (whether by virtue of securities issued as consideration for the transaction or otherwise), less than 50% of the voting power and economic interest of the surviving, continuing or purchasing entity; or (ii) any sale, lease, exclusive license or other disposition of all or substantially all of the assets (tangible or intangible) of the Company and any subsidiaries taken as a whole.

7. Other Agreements. As an employee of the Company, you will have access to certain Company and third-party confidential information and you may during the course of your employment develop certain information or inventions, which will be the property of the Company. To protect the interest of the Company and as a condition of your employment with the Company, you agree to sign the Employee Confidentiality, Assignment and Noncompetition Agreement enclosed herewith (the "**Restrictive Covenants Agreement**"). The Restrictive Covenants Agreement is incorporated by reference herein.

8. Section 409A.

a. The intent of the parties is that payments and benefits under this letter agreement and the Restrictive Covenants Agreement (as applicable) comply with, or be exempt from, Code Section 409A and, accordingly, to the maximum extent permitted, this letter agreement shall be interpreted to be in compliance therewith or exempt therefrom. If you notify the Company (with specificity as to the reason therefor) that you believe that any provision of this letter agreement (or of any award of compensation, including equity compensation or benefits) would cause you to incur any additional tax or interest under Code Section 409A and the Company concurs with such belief or the Company independently makes such determination, the Company shall, after consulting with you, reform such provision to try to comply with Code Section 409A through good faith modifications to the minimum extent reasonably appropriate to conform with Code Section 409A. To the extent that any provision hereof is modified in order to comply with Code Section 409A, such modification shall be made in good faith and shall, to the maximum extent reasonably possible, maintain the original intent and economic benefit to you and the Company of the applicable provision without violating the provisions of Code Section 409A.

b. A termination of employment shall not be deemed to have occurred for purposes of any provision of this letter agreement providing for the payment of any amounts or benefits upon or following a termination of employment that are considered "nonqualified deferred compensation" under Code Section 409A unless such termination is also a "separation from service" within the meaning of Code Section 409A and, for purposes of any such provision of this letter agreement, references to a "termination," "termination of employment" or like terms shall mean "separation from service." Notwithstanding any provision to the contrary in this letter agreement, no payments or benefits that are considered "nonqualified deferred compensation" under Code Section 409A to which you otherwise become entitled under this letter agreement or the Restrictive Covenants Agreement in connection with your termination of employment, shall be made or provided to you prior to the earlier of (i) the expiration of the six (6) month period measured from the date of your "separation from service" with the Company (as such term is defined in Code Section 409A) or (ii) the date of your death, if you are deemed at the time

of such separation from service to be a "specified employee" under Code Section 409A. Upon the expiration of the applicable Code Section 409A(a)(2) deferral period, all payments and benefits deferred pursuant to this Section 8(b) (whether they would have otherwise been payable in a single sum or in installments in the absence of such deferral) shall be paid or reimbursed to you in a lump sum, and any remaining payments and benefits due under this letter agreement or the Restrictive Covenants Agreement shall be paid or provided in accordance with the normal payment dates specified for them herein.

c. All expenses or other reimbursements under this letter agreement shall be made promptly following submission of required documentation, and in any case on or prior to the last day of the taxable year following the taxable year in which such expenses were incurred by you (provided that if any such reimbursements constitute taxable income to you, such reimbursements shall be paid no later than March 15th of the calendar year following the calendar year in which the expenses to be reimbursed were incurred), and (i) the right to reimbursement or in-kind benefits shall not be subject to liquidation or exchange for another benefit and (ii) no such reimbursement or expenses eligible for reimbursement in any taxable year shall in any way affect the expenses eligible for reimbursement in any other taxable year, provided, that the foregoing clause (ii) shall not be violated with regard to expenses reimbursed under any arrangement covered by Section 105(b) of the Internal Revenue Code solely because such expenses are subject to a limit related to the period the arrangement is in effect.

d. For purposes of Code Section 409A, your right to receive any installment payment pursuant to this letter agreement shall be treated as a right to receive a series of separate and distinct payments. Neither you nor the Company shall have the right to accelerate or defer the delivery of any payments or benefits under this letter agreement or the Restrictive Covenants Agreement except to the extent specifically permitted or required by Section 409A. Whenever a payment under this letter agreement or the Restrictive Covenants Agreement specifies a payment period with reference to a number of days (e.g., "payment shall be made within thirty (30) days following the date of termination"), the actual date of payment within the specified period shall be within the sole discretion of the Company. Notwithstanding any other provision of this letter agreement to the contrary, in no event shall any payment under this letter agreement or the Restrictive Covenants Agreement that constitutes "nonqualified deferred compensation" for purposes of Code Section 409A be subject to offset, counterclaim or recoupment by any other amount payable to you unless otherwise permitted by Code Section 409A.

9. Resolution of Disputes. Any controversy or claim arising out of or relating to your employment, this letter agreement, its enforcement or interpretation, or because of an alleged breach, default, or misrepresentation in connection with any of its provisions, shall be submitted to arbitration in Boston, Massachusetts before a single arbitrator (applying Massachusetts law), in accordance with the National Rules for the Resolution of Employment Disputes then in effect of the American Arbitration Association ("**AAA**") as modified by the terms and conditions of this Section 9; provided, however, that provisional injunctive relief (including without limitation under the Restrictive Covenants Agreement) may, but need not, be sought in a court of law before or while arbitration proceedings are pending, and any provisional injunctive relief granted by such court shall remain effective until the matter is finally determined by the arbitrator. The arbitrator shall be selected by mutual agreement of the parties or, if the parties cannot agree, by striking from a list of arbitrators supplied by AAA. The arbitrator shall issue a written opinion

revealing, however briefly, the essential findings and conclusions upon which the award is based. Final resolution of any dispute through arbitration may include any remedy or relief, which the arbitrator deems just and equitable. Any award or relief granted by the arbitrator hereunder shall be final and binding on the parties hereto and may be enforced by any court of competent jurisdiction.

The parties acknowledge that they are hereby waiving any rights to trial by jury in any action, proceeding or counterclaim brought by either of the parties against the other in connection with any matter whatsoever arising out of or in any way connected with this letter agreement or your employment.

The Company shall pay the arbitrator's fees and arbitration expenses and any other costs associated with the arbitration or arbitration hearing that are unique to arbitration. The Company and you each shall separately pay its or your own deposition, witness, expert and attorneys' fees and other expenses as and to the same extent as if the matter were being held in court unless otherwise provided by law. The arbitrator shall have the sole and exclusive power and authority to decide any and all issues of or related to whether this letter agreement or any provision of this letter agreement is subject to arbitration.

10. No Inconsistent Obligations. By accepting this offer of employment, you represent and warrant to the Company that you are under no obligations or commitments, whether contractual or otherwise, that are inconsistent with your obligations set forth in this letter agreement or that would be violated by your employment by the Company. You agree that you will not take any action on behalf of the Company or cause the Company to take any action that will violate any agreement that you have with a prior employer.

11. Section 280G.

a. Notwithstanding any other provision of this letter agreement, except as set forth in Section 11(b), in the event that the Company undergoes a "Change in Ownership or Control" (as defined below), the Company shall not be obligated to provide to you a portion of any "Contingent Compensation Payments" (as defined below) that you would otherwise be entitled to receive to the extent necessary to eliminate any "excess parachute payments" (as defined in Code Section 280G(b)(1)) for you. For purposes of this Section 11, the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Payments" and the aggregate amount (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-30 or any successor provision) of the Contingent Compensation Payments so eliminated shall be referred to as the "Eliminated Amount."

b. Notwithstanding the provisions of Section 11(a), no such reduction in Contingent Compensation Payments shall be made if (i) the Eliminated Amount (computed without regard to this sentence) exceeds (ii) 100% of the aggregate present value (determined in accordance with Treasury Regulation Section 1.280G-1, Q/A-31 and Q/A-32 or any successor provisions) of the amount of any additional taxes that would be incurred by you if the Eliminated Payments (determined without regard to this sentence) were paid to you (including, state and federal income taxes on the Eliminated Payments, the excise tax imposed by Section 4999 of the Code payable with respect to all of the Contingent Compensation Payments in excess of your "base amount" (as defined in Section 280G(b)(3) of the Code), and any withholding taxes). The

override of such reduction in Contingent Compensation Payments pursuant to this Section 11(b) shall be referred to as a "Section 11(b) Override." For purposes of this paragraph, if any federal or state income taxes would be attributable to the receipt of any Eliminated Payment, the amount of such taxes shall be computed by multiplying the amount of the Eliminated Payment by the maximum combined federal and state income tax rate provided by law.

c. For purposes of this Section 11 the following terms shall have the following respective meanings:

(I) "Change in Ownership or Control" shall mean a change in the ownership or effective control of the Company or in the ownership of a substantial portion of the assets of the Company determined in accordance with Section 280G(b)(2) of the Code.

(II) "Contingent Compensation Payment" shall mean any payment (or benefit) in the nature of compensation that is made or made available (under this letter agreement or otherwise) to a "disqualified individual" (as defined in Section 280G(c) of the Code) and that is contingent (within the meaning of Section 280G(b)(2)(A)(i) of the Code) on a Change in Ownership or Control of the Company.

d. Any payments or other benefits otherwise due to you following a Change in Ownership or Control that could reasonably be characterized (as determined by the Company) as Contingent Compensation Payments (the "Potential Payments") shall not be made until the dates provided for in this Section 11(d). Within 30 days after each date on which you first become entitled to receive (whether or not then due) a Contingent Compensation Payment relating to such Change in Ownership or Control, the Company shall determine and notify you (with reasonable detail regarding the basis for its determinations) (i) which Potential Payments constitute Contingent Compensation Payments, (ii) the Eliminated Amount and (iii) whether the Section 11(b) Override is applicable. Within 30 days after delivery of such notice to you, you shall deliver a response to the Company (the "Executive Response") stating either (A) that you agree with the Company's determination pursuant to the preceding sentence, or (B) that you disagree with such determination, in which case you shall set forth (i) which Potential Payments should be characterized as Contingent Compensation Payments, (ii) the Eliminated Amount, and (iii) whether the Section 11(b) Override is applicable. In the event that you fail to deliver an Executive Response on or before the required date, the Company's initial determination shall be final. If and to the extent that any Contingent Compensation Payments are required to be treated as Eliminated Payments pursuant to this Section 11, then the payments shall be reduced or eliminated, as determined by the Company, in the following order: (i) any cash payments, (ii) any taxable benefits, (iii) any nontaxable benefits, and (iv) any vesting of equity awards in each case in reverse order beginning with payments or benefits that are to be paid the farthest in time from the date that triggers the applicability of the excise tax, to the extent necessary to maximize the Eliminated Payments. If you state in the Executive Response that you agree with the Company's determination, the Company shall make the Potential Payments to you within three business days following delivery to the Company of the Executive Response (except for any Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). If you state in the Executive Response that you disagree with the Company's determination, then, for a period of 60 days following delivery of the Executive Response, you and the Company shall use good faith efforts to resolve such dispute. If such dispute is not resolved within such 60-day period, such dispute shall be settled exclusively

by arbitration in the Commonwealth of Massachusetts, in accordance with the rules of the American Arbitration Association then in effect. Judgment may be entered on the arbitrator's award in any court having jurisdiction. The Company shall, within three business days following delivery to the Company of the Executive Response, make to you those Potential Payments as to which there is no dispute between the Company and you regarding whether they should be made (except for any such Potential Payments which are not due to be made until after such date, which Potential Payments shall be made on the date on which they are due). The balance of the Potential Payments shall be made within three business days following the resolution of such dispute. Subject to the limitations contained in Sections 11(a) and 11(b) hereof, the amount of any payments to be made to you following the resolution of such dispute shall be increased by the amount of the accrued interest thereon computed at the prime rate announced from time to time by The Wall Street Journal, compounded monthly from the date that such payments originally were due.

e. The provisions of this Section 11 are intended to apply to any and all payments or benefits available to you under this letter agreement or any other agreement or plan of the Company under which you may receive Contingent Compensation Payments.

12. Verification of Status. You agree to provide to the Company, within three days of your Start Date, documentation of your eligibility to work in the United States. You may need to obtain a work visa to be eligible to work in the United States. If that is the case, your employment with the Company will be conditioned upon your obtaining a work visa in a timely manner as determined by the Company. The Company's offer of employment is contingent upon your authorization and successful completion of background and reference checks.

13. Miscellaneous.

a. This letter agreement may be executed in counterparts, each of which shall be deemed to be an original but all of which together will constitute one and the same instrument.

b. The Company may only assign this letter agreement to a successor (whether direct or indirect, by purchase, merger, consolidation or otherwise) to all or substantially all of the business and/or assets of the Company, provided, that such successor expressly agrees to assume and perform this letter agreement in the same manner and to the same extent that the Company would have been required to perform it if no such assignment had taken place, and the term "Company" shall include any such successor that assumes and agrees to perform this letter agreement, by operation of law or otherwise.

c. No provision of this letter agreement may be modified, waived or discharged unless such waiver, modification or discharge is agreed to in writing and signed by you and such officer as may be designated by the Board (other than you). No waiver by either party hereto at any time of any breach by the other party hereto of, or compliance with, any condition or provision of this letter agreement to be performed by such other party shall be deemed a waiver of similar or dissimilar provisions or conditions at the same or at any prior or subsequent time.

d. The validity, interpretation, construction and performance of this letter agreement shall be governed by the laws of the Commonwealth of Massachusetts without regard to the choice of law principles thereof.

e. This letter agreement, the Restrictive Covenants Agreement, the Plan and any Option Agreement embody the entire agreement and understanding between the parties hereto with respect to the subject matter hereof and supersede all prior oral or written agreements, discussions and/or understandings relating to the subject matter hereof.

f. Please accept all of the terms as set forth herein by signing and returning this letter agreement and the Restrictive Covenants Agreement by January 4, 2021.

I look forward to your joining the Company to create a successful company, and I am confident that your employment with the Company will prove mutually beneficial. If you have any further questions or require additional information, please feel free to contact me.

Sincerely,

Sincerely,

IMARA INC.

By: /s/ Rahul D. Ballal, Ph.D.
Name: Rahul D. Ballal, Ph.D.
Title: President and CEO

AGREED:

By: /s/ Kenneth M. Attie, MD
Name: Kenneth M. Attie, MD

Exhibit 10.18

IMARA Inc.
116 Huntington Avenue, 6th Floor
Boston, MA 02116 USA

Info@Imaratx.com
+1 617 202-2020

www.imaratx.com

November 5, 2021

Kenneth M. Attie, MD

Dear Ken,

You are a key member of the senior management team of Imara Inc. (the "***Company***"). As a result, the Company would like to amend that certain letter agreement (the "***Letter Agreement***"), dated December 4, 2020, setting forth the terms of your employment with the Company.

This first amendment (the "***First Amendment***") to the Letter Agreement, is effective as of the date set forth above (the "***Amendment Effective Date***") and shall update the terms of your employment with the Company as set forth below.

1. Defined Terms. Capitalized terms not otherwise defined herein shall have the meaning ascribed to such term in the Letter Agreement.

2. Termination of Employment. Section 6(b) of the Letter Agreement is hereby amended and restated in its entirety to read as follows:

"(b) (I) If you experience a Qualifying Termination and such Qualifying Termination does not occur within 12 months after a Change of Control, you will receive the Accrued Benefits, and, based upon satisfaction of the criteria in Section 6(d) below, including without limitation your execution and delivery of the separation and release agreement described therein and the lapse of any applicable revocation period without the release being revoked, you shall be eligible to receive the following severance benefits: (i) continuation of your base salary in effect as of the Termination Date for a period of nine (9) months, less standard deductions, payable in accordance with the Company's then regular pay policies commencing on or before the sixtieth (60th) day following the Termination Date ("***Severance Pay***"), provided, that the first such payment shall include any amounts that would have been paid to you hereunder had the release become effective upon the Termination Date; and (ii) following the Termination Date, if you are eligible for and elect to continue your health insurance coverage pursuant to your rights under the Consolidated Omnibus Budget Reconciliation Act of 1985, as amended, or any state equivalent ("***COBRA***"), then the Company shall reimburse you for your premiums under COBRA on a monthly basis until the earlier of (x) nine (9) months following the Termination Date, or (y) the date upon which you commence full-time employment (or employment that provides you with eligibility for healthcare benefits substantially comparable to those provided by the Company) with an entity other than the Company. Notwithstanding any of the foregoing, (i) if the 60-day period following the Termination Date would end in a calendar year subsequent to the year in which the Termination Date occurs, the payments

under this Section 6(b) will not be paid or commence before the first payroll of the subsequent calendar year; and (ii) any Severance Pay received in any calendar year shall be reduced by the amount of Garden Leave Pay you receive in the same such calendar year under, and as defined in, the Restrictive Covenants Agreement; provided that in no event shall the Severance Pay be reduced below $1000.

(II) If you experience a Qualifying Termination and such Qualifying Termination occurs within 12 months after a Change of Control, you will receive the Accrued Benefits, and, based upon satisfaction of the criteria in Section 6(d) below, including without limitation your execution and delivery of the separation and release agreement described therein and the lapse of any applicable revocation period without the release being revoked, you shall be eligible to receive the following severance benefits: (i) continuation of your base salary in effect as of the Termination Date for a period of twelve (12) months, less standard deductions, payable in accordance with the Company's then regular pay policies commencing on or before the sixtieth (60th) day following the Termination Date ("***COC Base Salary Severance***"), provided, that the first such payment shall include any amounts that would have been paid to you hereunder had the release become effective upon the Termination Date, (ii) one hundred percent (100%) of your annual bonus target amount for the year in which the Termination Date occurred in a lump sum on the date the first installment of COC Base Salary Severance is paid ("***COC Bonus Severance***") and (iii) following the Termination Date, if you are eligible for and elect to continue your health insurance coverage pursuant to your rights under COBRA, then the Company shall reimburse you for your premiums under COBRA on a monthly basis until the earlier of (x) twelve (12) months following the Termination Date, or (y) the date upon which you commence full-time employment (or employment that provides you with eligibility for healthcare benefits substantially comparable to those provided by the Company) with an entity other than the Company. Notwithstanding any of the foregoing, (i) if the 60-day period following the Termination Date would end in a calendar year subsequent to the year in which the Termination Date occurs, the payments under the prior sentence will not be paid or commence before the first payroll of the subsequent calendar year and (ii) any COC Base Salary Severance and COC Bonus Severance received in any calendar year shall be reduced by the amount of Garden Leave Pay you receive in the same such calendar year under, and as defined in, the Restrictive Covenants Agreement, provided that in no event shall the aggregate COC Base Salary Severance and COC Bonus Severance be reduced below $1000."

3. No Other Amendments. Except as amended by this First Amendment, the Letter Agreement remains unaltered and all other terms of the Letter Agreement shall remain in full force and effect.

4. Counterparts. This First Amendment may be executed in any number of counterparts, each of which shall be deemed an original and all of which taken together shall be deemed to constitute one and the same instrument. An executed signature page of this First Amendment delivered by facsimile transmission (with transmission confirmed) or in .pdf format via e-mail shall be as effective as an original executed signature page.

Please accept all of the terms as set forth herein by signing and returning this First Amendment.

Sincerely,

IMARA INC.

By: /s/ Rahul D. Ballal, Ph.D.
Name: Rahul D. Ballal, Ph.D.
Title: President and CEO

AGREED:

By: /s/ Kenneth M. Attie, MD
Name: Kenneth M. Attie, MD

Exhibit 21.1

List of Subsidiaries

Name	Jurisdiction of Incorporation
IMARA Security Corporation	Massachusetts

Exhibit 23.1

Consent of Independent Registered Public Accounting Firm

We consent to the incorporation by reference in the following Registration Statements:

(1) Registration Statement (Form S-3 No. 333-254978) of IMARA Inc., and
(2) Registration Statements (Form S-8 Nos. 333-237117 and 333-258538) pertaining to the stock incentive plan, equity incentive plans and employee stock purchase plan of IMARA Inc.

of our report dated March 15, 2022, with respect to the consolidated financial statements of IMARA Inc. included in this Annual Report (Form 10-K) of IMARA Inc. for the year ended December 31, 2021.

/s/ Ernst & Young LLP

Boston, Massachusetts
March 15, 2022

Exhibit 31.1

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Rahul D. Ballal, certify that:

1. I have reviewed this Annual Report on Form 10-K of IMARA Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2022

By: /s/ Rahul D. Ballal

Rahul D. Ballal, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

CERTIFICATION PURSUANT TO
RULES 13a-14(a) AND 15d-14(a) UNDER THE SECURITIES EXCHANGE ACT OF 1934,
AS ADOPTED PURSUANT TO SECTION 302 OF THE SARBANES-OXLEY ACT OF 2002

I, Michael P. Gray, certify that:

1. I have reviewed this Annual Report on Form 10-K of IMARA Inc.;

2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;

3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;

4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:

   (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;

   (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;

   (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and

   (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and

5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):

   (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and

   (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: March 15, 2022

By: /s/ Michael P. Gray

Michael Gray
Chief Financial Officer and Chief Operating Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of IMARA Inc. (the "Company") for the year ended December 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 15, 2022

By: /s/ Rahul D. Ballal

Rahul D. Ballal, Ph.D.
President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 32.2

CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350, AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002

In connection with the Annual Report on Form 10-K of IMARA Inc. (the "Company") for the year ended December 31, 2021, as filed with the Securities and Exchange Commission on the date hereof (the "Report"), I certify, pursuant to 18 U.S.C. § 1350, as adopted pursuant to § 906 of the Sarbanes-Oxley Act of 2002, that:

(1) The Report fully complies with the requirements of section 13(a) or 15(d) of the Securities Exchange Act of 1934; and

(2) The information contained in the Report fairly presents, in all material respects, the financial condition and result of operations of the Company.

Date: March 15, 2022

By: /s/ Michael P. Gray

Michael Gray
Chief Financial Officer and Chief Operating Officer
(Principal Financial Officer)