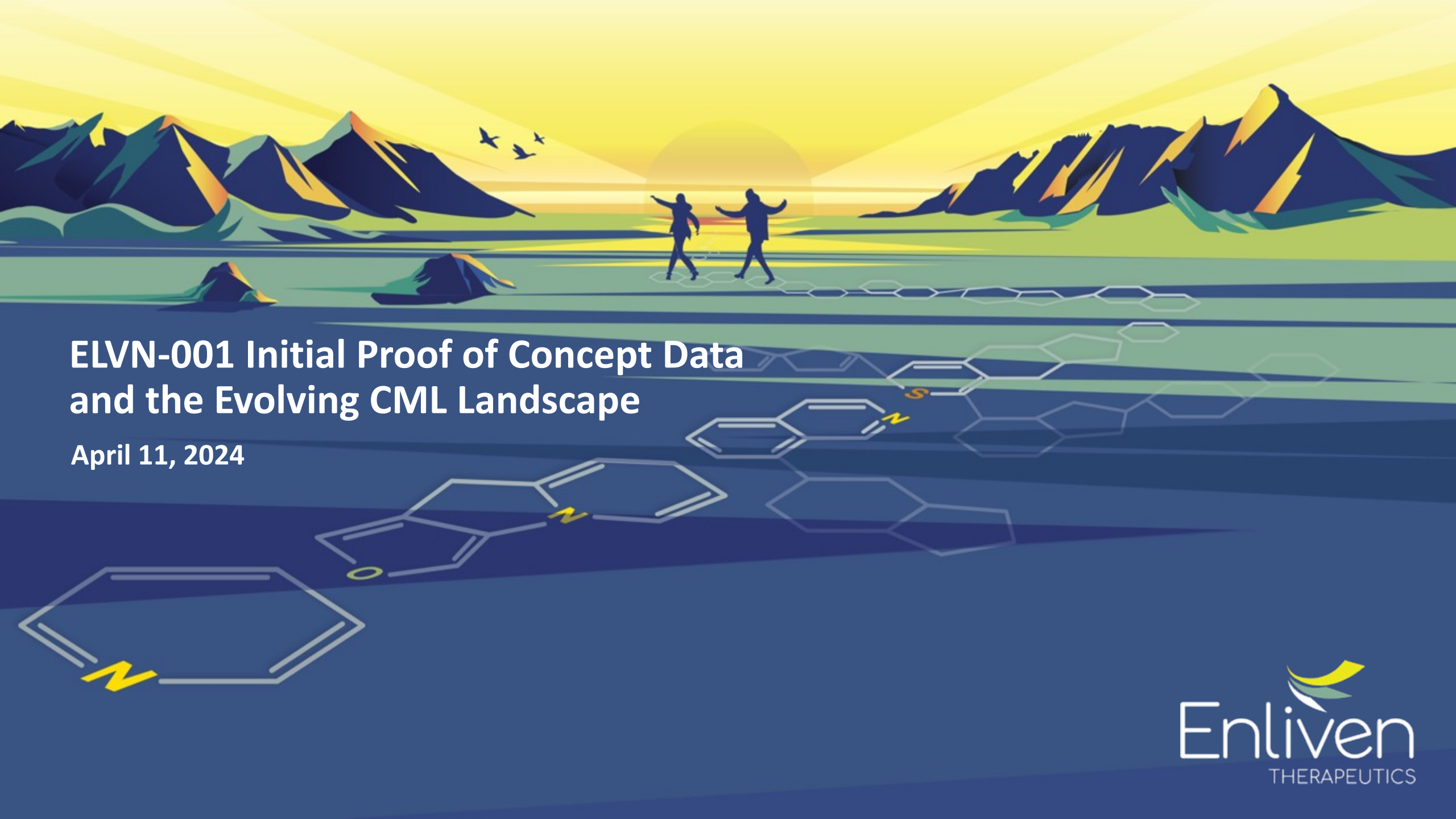


ELVN-001 Initial Proof of Concept Data and the Evolving CML Landscape

April 11, 2024

Enliven THERAPEUTICS

Disclaimer

This presentation contains forward-looking statements that involve substantial risks and uncertainties of Enliven Therapeutics, Inc. ("Enliven" or the "Company"). All statements other than statements of historical facts contained in this presentation, including statements regarding our future financial condition, results of operations, business strategy and plans, and objectives of management for future operations, as well as statements regarding industry trends, are forward-looking statements. Such forward-looking statements include, among other things, statements regarding the potential of, and expectations regarding Enliven's product candidates and programs, including ELVN-001 and ELVN-002; Enliven's ability to advance additional programs; the expected milestones and timing of such milestones including for ELVN-001, ELVN-002 and its discovery programs; and statements regarding Enliven's financial position, including its liquidity, cash runway and the sufficiency of its cash resources. In some cases, you can identify forward-looking statements by terminology such as "estimate," "intend," "may," "plan," "potentially" "will" or the negative of these terms or other similar expressions.

We have based these forward-looking statements largely on our current expectations and projections about future events and trends that we believe may affect our financial condition, results of operations, business strategy and financial needs. These forward-looking statements are subject to a number of risks, uncertainties and assumptions, including, among other things: the limited operating history of Enliven; the significant net losses incurred since its inception; the ability to advance product candidates through preclinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, product candidates; the outcome of preclinical testing and early clinical trials for product candidates and the potential that the outcome of preclinical testing and early clinical trials may not be predictive of the success of later clinical trials; Enliven's limited resources; the risk of failing to demonstrate safety and efficacy of product candidates; Enliven's limited experience as a company in designing and conducting clinical trials; potential delays or difficulties in the enrollment or maintenance of patients in clinical trials; developments relating to Enliven's competitors and its industry, including competing product candidates and therapies; the decision to develop or seek strategic collaborations to develop Enliven's current or future product candidates in combination with other therapies and the cost of combination therapies; the ability to attract, hire, and retain highly skilled executive officers and employees; the ability of Enliven to protect its intellectual property and proprietary technologies; the scope of any patent protection Enliven obtains or the loss of any of Enliven's patent protection; reliance on third parties, including contract manufacturing organizations, contract research organizations and strategic partners; general market or macroeconomic conditions; Enliven's ability to obtain additional capital to fund Enliven's general corporate activities and to fund Enliven's research and development; and other risks and uncertainties, including those more fully described in Enliven's filings with the Securities and Exchange Commission (SEC), including additional risks which may be found in the section entitled "Risk Factors" in Enliven's Annual and Quarterly Reports on Form 10-K and 10-Q filed with the SEC and in Enliven's future reports to be filed with the SEC. These risks are not exhaustive. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the impact of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. You should not rely upon forward-looking statements as predictions of future events. Although we believe that the expectations reflected in the forward-looking statements are reasonable, we cannot guarantee future results, levels of activity, performance or achievements. Except as required by law, we undertake no obligation to update publicly any forward-looking statements for any reason after the date of this presentation.

This presentation also contains estimates and other statistical data made by independent parties and by us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions, and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

Today's Agenda

1 Introduction

2 The Evolving Chronic Myeloid Leukemia (CML) Landscape & ELVN-001 Preclinical Profile

3 Understanding Clinical Benefit in CML

4 ELVN-001 Phase 1a Initial Proof of Concept Data

5 Discussion with Leading CML Investigator KOLs

6 Q&A

The Enliven Story: a Clinical-Stage Precision Oncology Company

Discovery process rooted in **validated biology**, **differentiated chemistry**, and **disciplined trial design**

+

Capital-efficient approach on **high potential programs** aiming to develop **first-in-class** or **best-in-class** candidates

+

ELVN-001 and ELVN-002 supported by **preclinical evidence** of an **improved therapeutic index**

+

Multiple **near-term milestones** in lead programs targeting **large** and **attractive markets**

+

Experienced team with a track record of inventing and developing **multiple FDA-approved cancer therapies**

Strong balance sheet expected to provide cash runway into late 2026

Pipeline & Discovery Programs Address New and Emerging Unmet Needs

Parallel lead product candidates:

Program	Target	Differentiation	Disease	Regimen	Discovery	IND-Enabling	Phase 1	Phase 2	Phase 3	Next Milestone	Milestone Expected
ELVN-001	BCR-ABL	Highly selective active site inhibitor w/activity against asciminib emergent mutations	CML	Monotherapy	monotherapy					Phase 1a Safety/Efficacy	April 11, 2024
ELVN-002	HER2 & HER2 mutants	Irreversible, highly selective, CNS penetrant	NSCLC, other solid tumors	Monotherapy	monotherapy					Phase 1 Safety/Efficacy	2025
			HER2+ MBC and CRC	Combination	+ trastuzumab +/- chemotherapy					Phase 1a Safety/Efficacy	

Multiple discovery stage efforts ongoing at various stages

CML = Chronic myeloid leukemia. CNS = Central nervous system. CRC = Colorectal cancer. IND = Investigational new drug. MBC = Metastatic breast cancer. NSCLC = Non-small cell lung cancer.

On Today's Call

Fabian Lang, M.D.
Senior Physician of Hematology/Oncology at Goethe University Hospital & CML Trial Investigator for ELVN-001

Michael J. Mauro, M.D.
Leader of the Myeloproliferative Neoplasms Program, Leukemia Service at Memorial Sloan Kettering Cancer Center & CML Trial Investigator for ELVN-001

Sam Kintz, M.B.A.
Co-founder, Chief Executive Officer of Enliven Therapeutics

Helen Collins, M.D.
Chief Medical Officer of Enliven Therapeutics

Damiette Smit, M.D.
VP of Clinical Development of Enliven Therapeutics

CML Landscape &
ELVN-001 Introduction

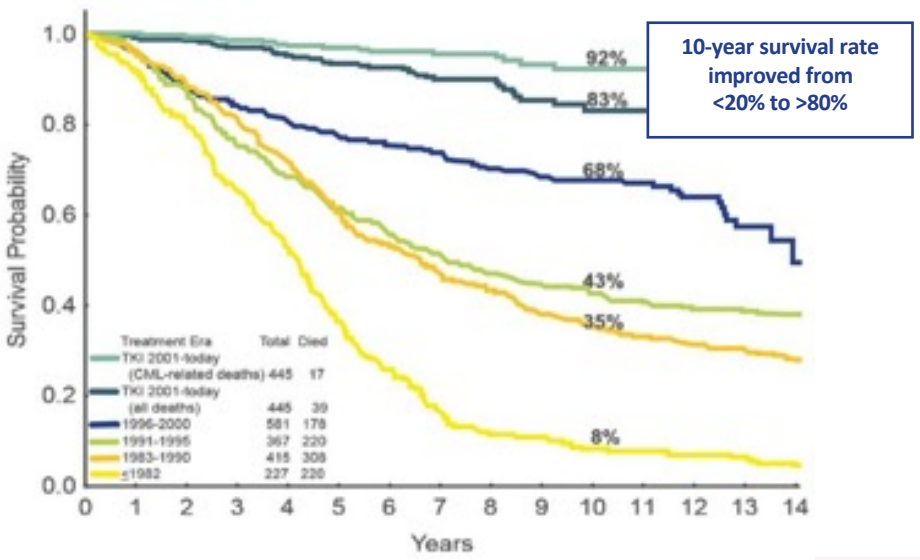
CML is Now a Long-Term Condition

As patients live longer on treatment, **quality of life** and **tolerability** have become important treatment goals

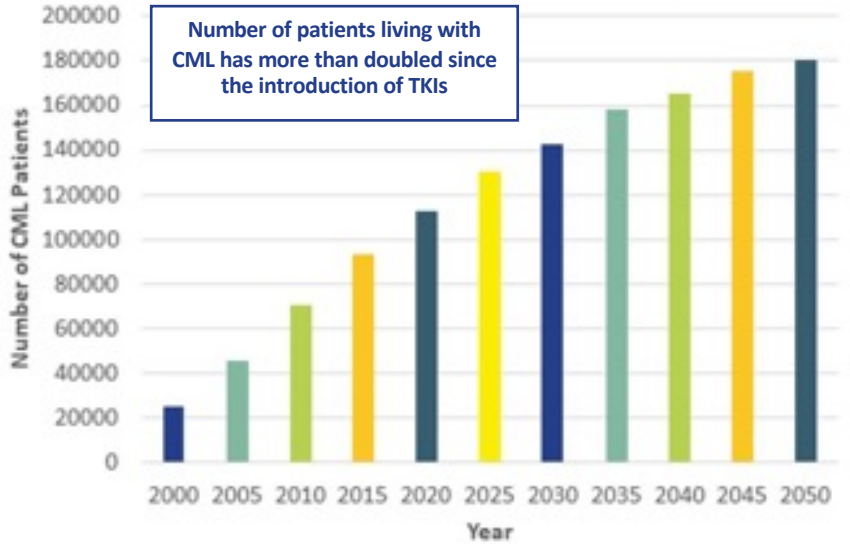
Prior to imatinib, the annual CML survival rate was

<20%

CML 10-Year Survival Rate Over Time



Estimated Prevalence of CML in the US Over Time



- Prevalence is increasing globally with expected overall survival approaching age-matched controls
- CML has become a chronic disease that can require life-long TKI-treatment

Top Treatment Goals for Physicians and Patients*

1st **Maintain or improve quality of life**

2nd **Manageable side effects**

CML = Chronic myeloid leukemia. FIH = First-in-human. MMR = Major molecular response. TFR = Treatment-free reemission. TKI = Tyrosine kinase inhibitors.

References: Huang X et al. Cancer. 2012;118:3213-3127; Kantarjian et al. Chronic Myeloid Leukemia, In: Harrison's Principles of Internal Medicine. 2014.; Lang et al, EHA 2023.

*For patients who have received two prior therapies.

Significant Need Remains for Better Treatment Options for CML

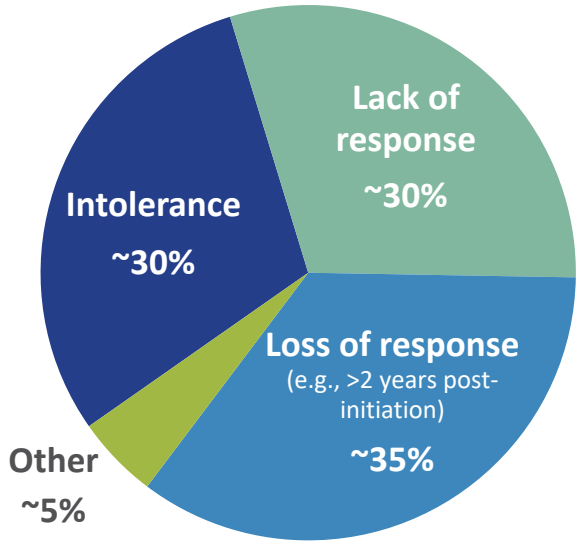
Challenges with Current Standard of Care

- Approximately **1 in 5 patients switch therapy** within the first year and **~40%** of patients switch in the first 5 years (1L & 2L)
- **Growing 3L+** patient population (>25% of CP-CML) with **limited treatment options**
- Except for asciminib, approved TKIs have **poor kinase selectivity,** resulting in tolerability issues that can impact efficacy
- **Long-term use of 2nd generation TKIs is associated with adverse events** such as pleural effusions, GI and cardiovascular events
- Adverse events, comorbidities, restrictions with concomitant medications, and specific administration requirements may **impede long-term patient adherence**
- **Fewer than 10%** of patients successfully achieve sustained treatment-free remission (TFR)

77% of HCPs indicated need for more effective, safe, and tolerable agents for CML

Switching Dynamics Demonstrate Unmet Need

Rationale for Switching Treatment



In the US and EU3, majority of treatment switches across lines of therapy and TKIs are driven by intolerance or initial lack of molecular response (~60% combined)

1L = First line. 2L = Second line. 3L+ = Third line or later. 2nd Generation TKIs = Nilotinib, Dasatinib, Bosutinib. CML = Chronic Myeloid Leukemia. CP-CML = Chronic phase CML. GI = Gastrointestinal. TKI = Tyrosine kinase inhibitors. HCP = Healthcare professional. EU3 = France, UK, Germany.

References: HCP Qualitative & Quantitative Interviews (ClearView); Hochhaus A et al. ASH 2015; Hochhaus A et al. *Leukemia.* 2017; 31(7):1525-1531; Osorio S et al. *Ann Hematol.* 2018; 97(11):2089-2098; Rea et al. *Blood.* 2021; blood.2020009984; Baccarani M and Gale RP. *Leukemia.* 2021; 35:2199-2204; Iclusig® (ponatinib) USPI; Sprycel® (dasatinib) USPI; Tasigna® (nilotinib) USPI.; Bosulif® (bosutinib) USPI.

Poor Selectivity Limits Tolerability & Efficacy of 1st, 2nd & 3rd Gen Agents

	Compound	Company	T315I Coverage	Off Target(s) & Treatment-Emergent, Non-Hematologic Adverse Events (All Gr / Gr 3+)		1L Efficacy	Drug & Administration Requirements	Annualized Sales (USD)‡
	Imatinib (Gleevec®)	Novartis	**X**	c-KIT, CSFR-1, PDGFR	Peripheral Edema (20% / 0%) Nausea (41% / 2%)	28% MMR 3% MR4.5	Avoid strong CYP3A inhibitors or inducers	**$500M**
2nd Gen	**Dasatinib (Spyrcel®)**	BMS	**X**	SRC family, c-KIT, PDGFR-αβ	Fluid Retention (38% / 5%) Pleural Effusions (28% / 3%) Diarrhea (22% / 1%)	46% MMR 5% MR4.5	Avoid strong CYP3A inhibitors or inducers, PPIs, antacids, and H2 blockers	**$2.1B**
2nd Gen	**Nilotinib (Tasigna®)**	Novartis	**X**	c-KIT, PDGFR, CSFR-1, DDR-1 (hERG Channel)	Rash (38% / <1%) Headache (32% / 3%) Nausea (22% / 2%); Diarrhea (19% / 1%) **Black Box:** QT Prolongation/Sudden Deaths	44% MMR 11% MR4.5	Avoid strong CYP3A inhibitors or inducers and PPIs; avoid food 2 hours before and 1 hour after each dose	**$1.8B**
2nd Gen	**Bosutinib (Bosulif®)**	Pfizer	**X**	SRC family	Hepatic dysfunction (45% / 27%) Diarrhea (75% / 9%) Abdominal Pain (39% / 2%)	41% MMR 7.5% MR4.5	Avoid strong CYP3A inhibitors or inducers, PPIs, antacids, and H2 blockers	**$725M**
3rd Gen	**Ponatinib (Iclusig®)**	Takeda	✓	KDR, FGFR, c-KIT, RET, FLT3, PDGFR	**Black Box:** Arterial Occlusive Events, Heart Failure, VTE, Hepatoxicity	N/A	Avoid strong CYP3A inhibitors or inducers	**$500M**
	Asciminib (Scemblix®)	Novartis	✓ **(US, high dose only)**	N/A	Hypersensitivity (32% / 2%) Hypertension (19% / 9%) Cardiovascular (13% / 3.4%)	Expected 2024	Avoid CYP2C9 substrates and certain statins; avoid food 2 hours before and 1 hour after each dose	**$500M**

A selective BCR-ABL inhibitor could yield enhanced target coverage, leading to greater efficacy and better long-term tolerability

1L = Front line. GI = Gastrointestinal. Gr = Grade. FY = Fiscal Year. MMR = Major Molecular Response. MR4.5 = Deep Molecular Response. PPI = Proton pump inhibitors. MMR and MR4.5 at 12 months. VTE = Venous thromboembolism.
‡ Represents calendar year 4th quarter 2023 annualized sales (USD); B = billions, M = millions; numbers in the billions have been rounded to the 1/10th of a billion and sales numbers in the millions have been rounded to the nearest $25 million increment from Company Investor Reports.

References: 1. Gleevec® (imatinib) USPI; 2. Sprycel® (dasatinib) USPI; 3. Kantarjian H et al. *NEJM*, 2010; 362(24):2260-70; 4. Cortes JE et al. *J Clin Oncol*. 2016; 34(20):2333-40; 5. Tasigna® (nilotinib) USPI; 6. Saglio G et al. *NEJM* 2010; 362(24):2251-9; 7. Hochhaus A et al. *Leukemia*. 2016; 30(5):1044-54; 8. Bosulif® (bosutinib) USPI. 9. Cortes JE et al. *J Clin Oncol*, 2012; 30(28):3486-92; 10. Iclusig® (ponatinib) USPI; 12. Scemblix® (asciminib) USPI.

Review of Asciminib (Scemblix®), 4th Generation Allosteric TKI

Observations

- Asciminib's **strong launch** demonstrates the **large market** size and **need for better agents**
- However, unmet needs still exist. In ASCEMBL, only **1.2% of patients discontinued due to PD/death, but due to lack of efficacy/AE:**
  - ~30% of patients discontinue by week 48
  - **~50% of patients discontinue** by week 96
- Asciminib has limitations:
  - **Resistance mutations** in both the allosteric binding site and the ATP pocket result in loss of activity
  - **Drug-drug interactions** require avoiding drugs that are CYP2C9 substrates (up to 20% of commonly prescribed medications)
  - **Requires fasting** 2 hours before and 1 hour after each dose
  - **Substrate for efflux transporters** (PgP & BCRP), which may contribute to **lack of efficacy**
  - Treatment of **T315I mutations requires 5x dose** resulting in more dose reductions (23%), increased pancreatic & liver enzyme elevation

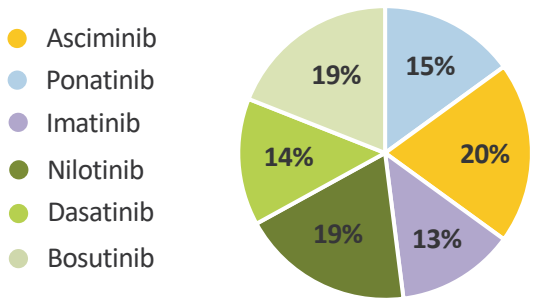
Scemblix's Robust Launch Continues to Demonstrate Patient Need for More Effective and Tolerable Agents

US 3L+ Approval	Q4 2021
EU 3L+ Approval	Q3 2022
1L Data Readout	H1 2024

$125M
4Q23 Sales

$500M of annualized sales

Current 3L+ Market Dynamics

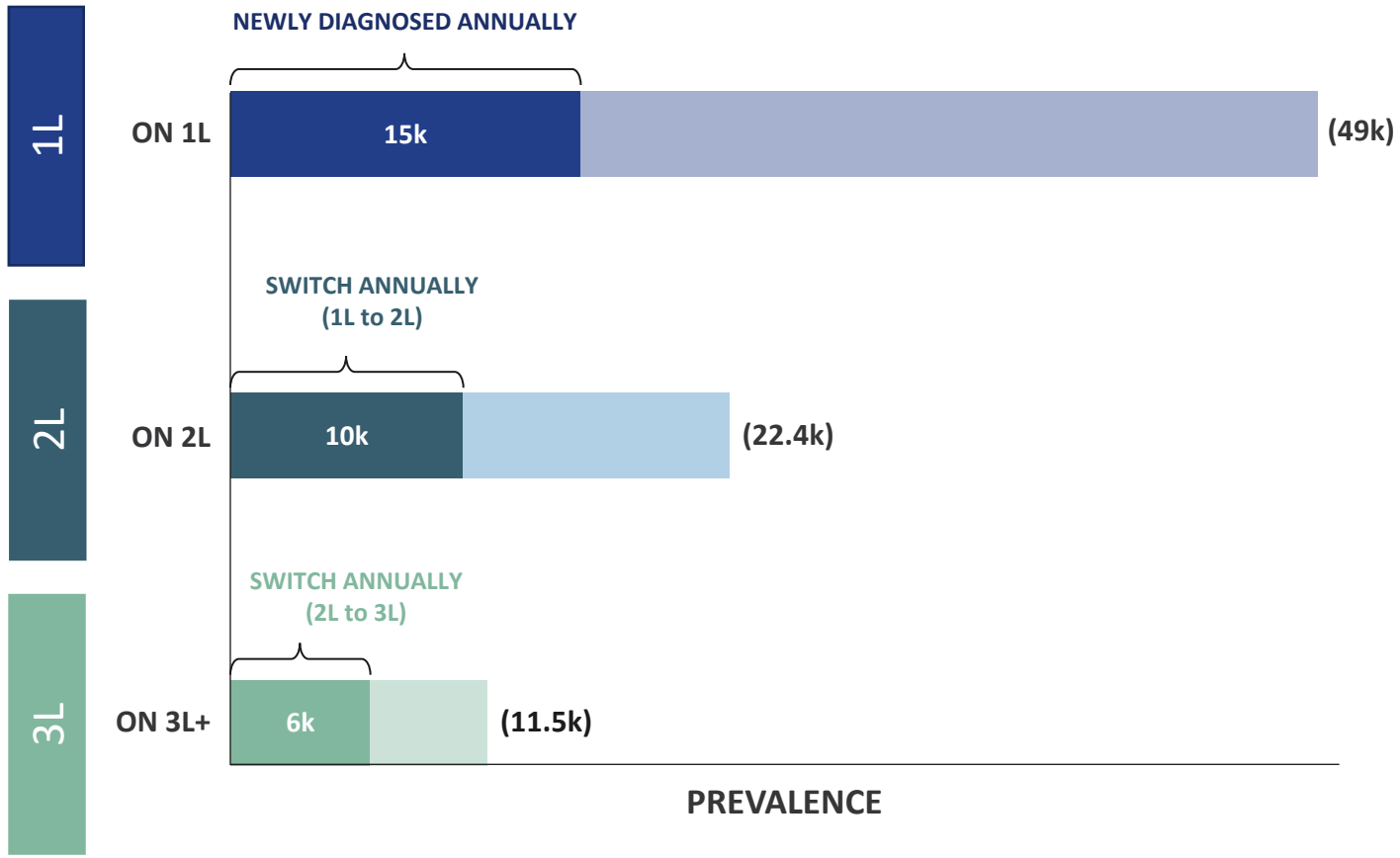


~$2B
implied market size in 3L+ alone

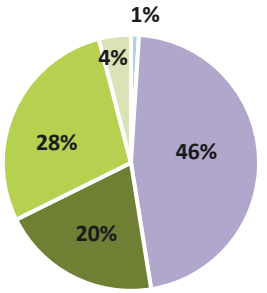
AE = Adverse event. ATP = Adenosine triphosphate. PD = Progressive disease. TKI = Tyrosine kinase inhibitor. ASCEMBL: A phase 3, open-label, randomized study of asciminib vs bosutinib in CML after 2 or more prior TKIs.
References: Hochhaus et al. ASH 2020; Cortes et al. ASH 2020; ASH 2021; Scemblix (Asciminib) USPI; ASCO 2022; Eadie et al Oncotarget 2018; Pharmaceogent Genomics, 2010 Apr; 20(4):277-281]; November 2023 Novartis R&D Investor Event. HCP Qualitative & Quantitative Interviews (ClearView).
Note: Current Scemblix information and 3L+ markey dynamics based on November 2023 Novartis R&D Investor Event. Estimated 3L+ market size calculated using Scemblix Q3 23 annualized sales and 20% market penetrance. Sales numbers in the billions have been rounded to the nearest billion.

Asciminib has the Potential to Disrupt Early Line Standard of Care

CML Patient Population

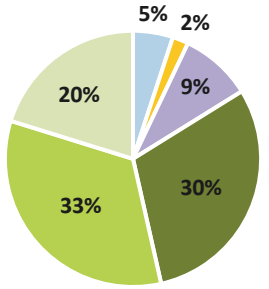


CML Treatment Landscape



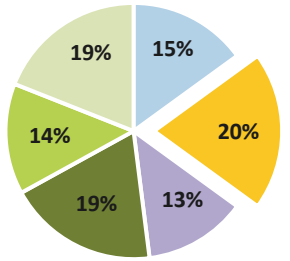
1L

~50% of patients are treated with imatinib, and the other ~50% with 2nd Gen TKIs



2L

Nearly all patients receive 2nd Gen TKIs (mainly nilotinib or dasatinib)



3L+

>50% of patients receive 2nd Gen TKIs

Asciminib · Ponatinib · Imatinib

2nd Generation TKIs: Nilotinib · Dasatinib · Bosutinib

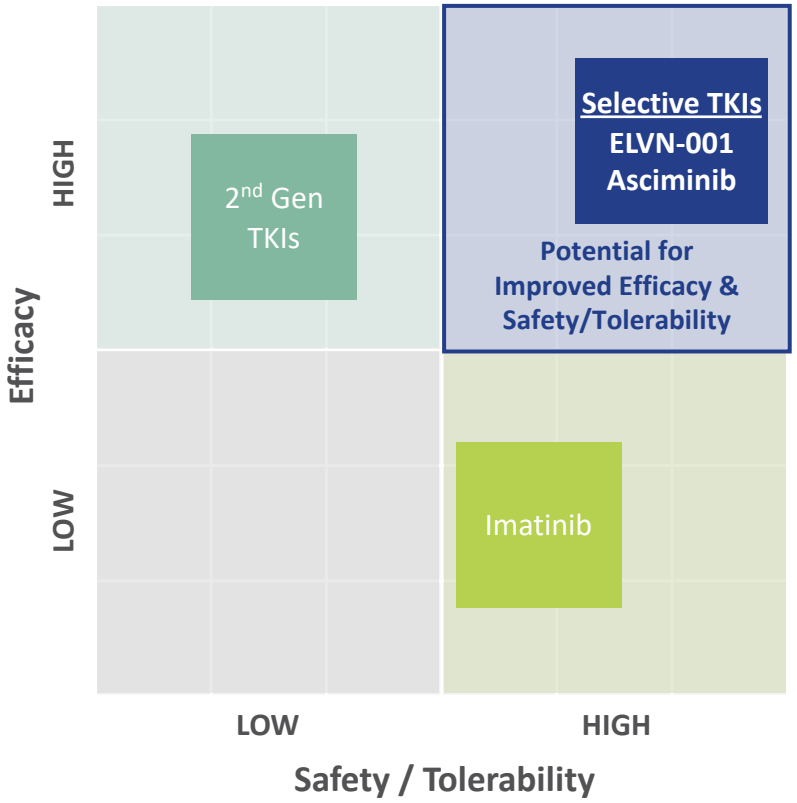
1L = First line. 2L = Second line. 3L+ = Third line or later. CML = Chronic myeloid leukemia. Gen= Generation. TKI = Tyrosine kinase inhibitor.

References: November 2023 Novartis R&D Investor Event. HCP Qualitative & Quantitative Interviews (ClearView).

ELVN-001 is Well Positioned to Follow Asciminib in Future CML Treatment Paradigm

Limitations of Current Treatment Paradigm

(if data supports)



Future Treatment Paradigm

(if data supports)

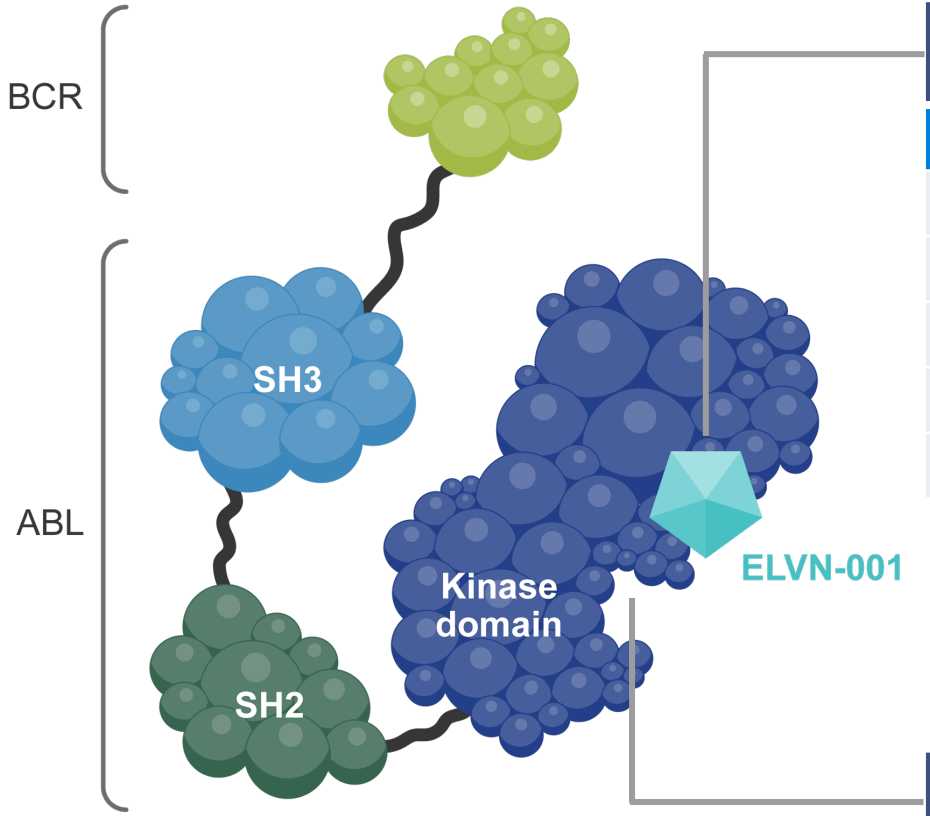
1L	1st Gen TKI Imatinib	4th Gen TKI Asciminib	**Asciminib could capture significant 1L market share** given potentially superior efficacy compared to imatinib & **improved tolerability compared to 2nd Gen TKIs**
2L	4th Gen TKI Asciminib	ELVN-001	**ELVN-001 is well positioned** to follow asciminib given its **unique binding mode and complementary MoA** (ATP-site/active form vs. allosteric/inactive form)
3L+	ELVN-001		With more early line use of asciminib, there may be a significant **need for treatment options with improved efficacy & tolerability** in later lines

Market Insights & Assumptions

- **Initial opportunity to address the ~16k patients** who switch therapies annually in 2L+ CML
- Additionally, an **opportunity may exist to compete directly with asciminib across lines of therapy** based on differentiated efficacy, tolerability or administration requirements

1L = First line. 2L = Second line. 2L+ = Second line or later. 3L+ = Third or later line. Gen = Generation. 2nd Gen TKIs = Nilotinib, Dasatinib, Bosutinib. CML = Chronic myeloid leukemia. MoA = Mechanism of action. TKI = Tyrosine kinase inhibitor.
Note: Illustrative current and future treatment paradigm.
References: HCP Qualitative & Quantitative Interviews (ClearView).

ELVN-001 is a Selective Active Site, Active Form Inhibitor of BCR::ABL1



ATP-BINDING SITE

DRUG	BINDING CONFORMATION
ELVN-001	**Active**
BOSUTINIB	Active
DASATINIB	Active
IMATINIB	Inactive
NILOTINIB	Inactive
PONATINIB	Inactive

MYRISTOYL POCKET

DRUG	BINDING CONFORMATION
ASCIMINIB	**Inactive**

Key Attributes of ELVN-001:

- Type 1 small molecule inhibitor of BCR::ABL1 targeting the ATP-binding site of the ABL1 kinase domain that binds to a unique P-loop "folded-in" active conformation of ABL1
- Unique binding mode confers exquisite selectivity against the broader kinome
- Broad activity against multiple clinically important BCR::ABL1 mutations, including T315I, and those that confer resistance to asciminib
- Unlike all the approved TKIs, ELVN-001 is not a substrate for the common drug efflux transporters, P-gp and BCRP, which may play a role in resistance to TKIs in CML

ATP = Adenosine triphosphate. CML = Chronic myeloid leukemia. BCRP = Breast cancer resistance protein. P-gp = P-glycoprotein. TKI = Tyrosine kinase inhibitors.

References: Braun T. et al. *Cancer Cell* 2020 2020 Apr 13;37(4):530-542; Qiang W et al., Mechanisms of Resistance to the BCR-ABL1 Allosteric Inhibitor Asciminib; Leukemia 2017.

ELVN-001 is Highly Selective for ABL1

- ELVN-001 has a **very selective kinase profile**
  - Clean against key off-target kinases in cells compared to 2nd and 3rd Gen TKIs
  - 372 kinases screened at 1 µM compound (100 µM ATP)
  - Kinases with >50% inhibition selected for IC_{50} determination
  - >100x window vs. all but 2 kinases profiled
- ELVN-001 is also very clean (>10 µM) in an *in vitro* safety panel of >130 receptors

Cellular Phosphorylation IC_{50} (nM)

	cKIT	FLT3wt	PDGFRb	VEGFR2	cSRC
ELVN-001	>10,000	>10,000	>10,000	>10,000	>10,000
Ponatinib	30	3.8	89	4.8	630
Nilotinib	200	>10,000	720	2,900	>10,000
Dasatinib	0.6	>1,000	7.1	>1,000	10
Bosutinib	1,000	4,700	7,900	>10,000	16

ELVN-001 (100 µM ATP)

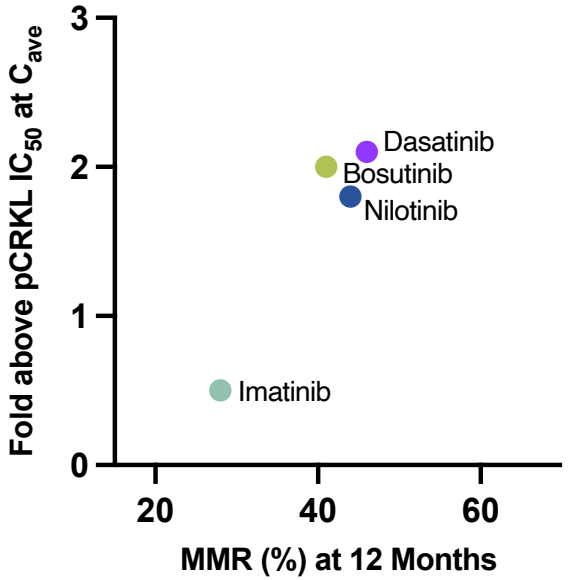
Kinase	IC_{50} (nM)
ABL1	**1**
ABL2/ARG	31
TRKC	41
TNIK	110
LOK/STK10	183
LRRK2	486
FGR	550
ACK1	698
FYN	725
HGK/MAP4K4	973
LCK	>1,000

Large window for ABL2/ARG may result in a favorable safety profile

2nd Gen = Nilotinib, Dasatinib, Bosutinib. 3rd Gen = Ponatinib. ATP = Adenosine triphosphate. TKI = Tyrosine kinase inhibitors.
Note: IC values used to calculate fold shift represent an average derived from multiple runs internally with a minimum of two independent experiments.
Reference: Abl kinases are required for vascular function, Tie2, and angiopoietin-1-mediated survival. Pendergast et al. *PNAS*. 2013;110(30):12432-7.

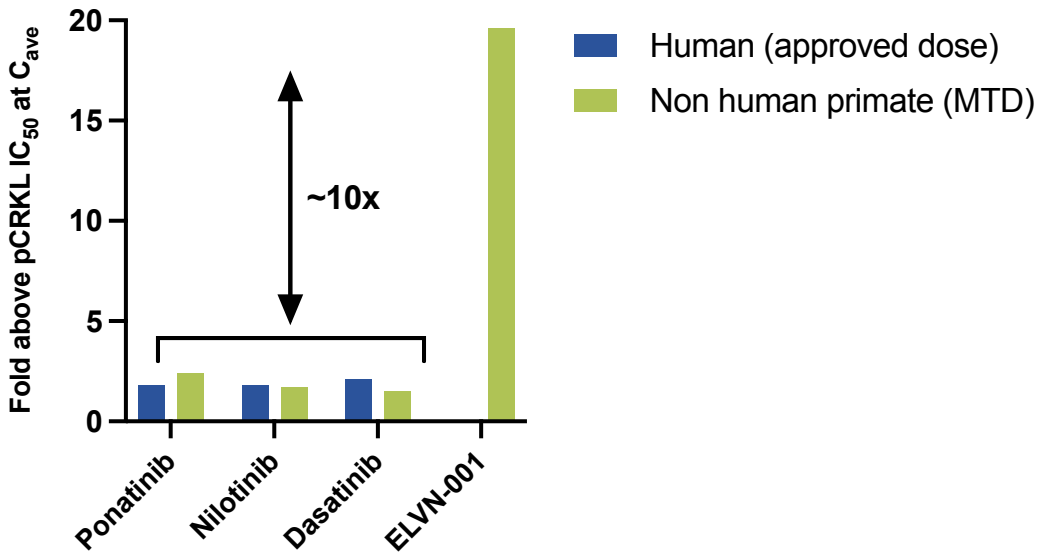
ELVN-001 Potentially Affords an Improved Therapeutic Index

Target Coverage at C_{ave} vs. 1L MMR



- Clear correlation between target coverage of the approved active site agents and 1L MMR at 12 months (from H2H pivotal studies)
- Phosphorylated CRKL or pCRKL IC_{50} represents a robust pharmacodynamic marker for BCR::ABL1 inhibition

Therapeutic Index vs. NHP Safety Margin



- Toxicology studies with other ABL TKIs show that the maximum tolerated drug exposure is similar between non-human primates and humans*
- Data suggests ELVN-001 has the potential for a significantly greater therapeutic index than approved active site TKIs

1L = First line. CRKL = Crk like protein. H2H = Head-to-head. MMR = Major molecular response. MTD = Maximum tolerated dose. NHP = Non-human primate.
NHP data for ponatinib, nilotinib, and dasatinib were obtained from the data reported for the maximum tolerated dose (MTD) in their respective New Drug Applications. NHP data from 28-day GLP tox study for ELVN-001 at 5 mg/kg, a well tolerated, no adverse event dose (NOAEL).
*No data for bosutinib in NHPs available.
y-axis: mean C_{ave} plasma concentration at the human approved dose (or NHP MTD) divided by K562 pCRKL IC_{50} in 100% human serum; C_{ave} = steady state plasma exposure area under the curve, AUC (ng*hr/mL), divided by 24 hours
Note: IC values represent an average derived from multiple runs internally with a minimum of three independent experiments.
References: Human PK References: (Imatinib) Peng et al. *J Clin Oncol*. 2004; 22:935-942.; (Nilotinib) Tasigna® USPI; (Bosutinib) Bosulif® USPI; (Dasatinib) Spyrcel® USPI; (Ponatinib) Iclusig® USPI.
MMR References: (Bosutinib) Cortes JE et al. *J Clin Oncol*. 2012; 30(28):3486-92; (Nilotinib and Imatinib) Saglio G et al. *NEJM*. 2010; 362(24):2251-9; (Dasatinib) Kantarjian H et al. NEJM, 2010; 362(24):226.

BCR::ABL1 Mutations Conferring Resistance to Asciminib (ASCEMBL)

ELVN-001 maintains activity against the emerging BCR::ABL1 mutations known to confer resistance to asciminib and activity against T315I similar to ponatinib

Emerging BCR-ABL mutations upon discontinuation due to lack of efficacy or progressive disease

	Asciminib (n=39)	Bosutinib (n=30)
No Mutations	22 (56%)	20 (67%)
ATP Binding Site	M244V (n=3), E355G, F359V, T315I	T315I, V299L
Myristoyl Binding Pocket	A337T (n=3), P465	None

Fold Shift from BCR::ABL1 wt (Ba/F3 Cells)

	T315I	M244V	A337T	E355G	F359C	F359V	P465S
Asciminib	96	611	173	>2380	>2380	>2380	>2380
ELVN-001	4	2	1	4	3	2	2
Dasatinib	2935	2	1	3	4	2	2
Bosutinib	113	3	1	4	5	5	4
Ponatinib	3	2	1	3	5	5	2
Imatinib	>20	3	1	8	18	10	4
Nilotinib	>341	2	1	5	33	21	3
Vodobatinib	445	2	1	3	10	7	2
Olverembatinib	5	2	1	3	6	6	2

Most frequent mutation at baseline and end of treatment in patients that switched off asciminib in ASCEMBL*

*ASCEMBL: A phase 3, open-label, randomized study of asciminib vs bosutinib in CML after 2 or more prior TKIs. CML = Chronic myeloid leukemia. TKI = Tyrosine kinase inhibitor.
Note: IC values represent an average derived from multiple runs internally with a minimum of two independent experiments.
References: Rea et al., Blood (2021) 138 (21): 2031–2041.

ELVN-001 Clinical Focus and Target Product Profile

Our Opportunity

Drive Deeper Responses | **Improve Tolerability** | **Enhance Safety & Convenience**

Target Product Profile

- Activity against native BCR::ABL1, T315I, and known asciminib-resistant mutations
- **Highly selective:** No/minimal clinically relevant off-target toxicity
- **Efficacy**: MMR greater than approved TKIs driven by an enhanced therapeutic window
- **Tolerability**: Fewer dose reductions & discontinuations
- **Safety**: No black box warnings; no edema, effusions, reduced GI toxicity
- **No restrictions** with concomitant medications

Phase 1a/b: Dose Escalation in Late Line

- Patients with CML who have exhausted all available treatment options
- Seek to demonstrate improved therapeutic window & efficacy (BCR::ABL1 transcript level reductions) in highly resistant/intolerant disease

Phase 1b: Expansions

- Begin enrolling earlier lines of patients
- Seek to demonstrate the potential for improved tolerability and efficacy compared to 2nd Gen TKIs
- Generate data supportive of an early line pivotal study

Current Goal: Early Line H2H vs Physician's Choice

- Superiority based on 6m and 12m MMR in CP-CML
- Better overall tolerability, fewer dose reductions & discontinuations vs. approved agents

Optionality: 4L+ and T315I mutation

- Single-arm study; precedent for approval in late line based on CCyR/MR2 (ponatinib, OPTIC trial)
- T315I mutation in ponatinib or asciminib progressed, intolerant or ineligible

CCyR = Complete cytogenetic response. CML = Chronic myeloid leukemia. CP-CML = Chronic phase CML. H2H = Head-to-head. m = Month. MMR = Major molecular response. MR2 = BCR::ABL1 ≤ 1%. TKI = Tyrosine kinase inhibitor. 2nd Gen TKIs = nilotinib, dasatinib, bosutinib.

Understanding Clinical Benefit in CML

The Standard Clinical Endpoint in CML is Molecular Response

1

Hematologic Response

- Measured by blood test and physical examination
- Normalization of white blood cell and platelet count without immature cells, such as blasts, in peripheral blood
- No signs or symptoms of disease, including resolution of palpable splenomegaly

2

Cytogenetic Response

- Best measured by bone marrow sample
- Percent of bone marrow cells with Philadelphia chromosome by FISH/karyotype (cytogenetic test)

3

Molecular Response

- Measured by blood test
- Number of copies of the BCR::ABL1 transcript in blood (qPCR)
- **Evolving into the standard of care in assessing treatment response in CML**

CML = Chronic myeloid leukemia. FISH = Fluorescence *in situ* hybridization. qPCR = Quantitative reverse transcriptase polymerase chain reaction.

References: Hochhaus et al. Leukemia 2020.

Molecular Response Milestones

≥ 1 log reduction in BCR::ABL1 transcript levels is a meaningful indication of efficacy

BCR::ABL1 Transcript Level	Molecular Response	Relevance
≤ 10%	MR1	• Even in 3L+ setting insufficient for optimal survival
≤ 1%	MR2	• Equivalent to complete cytogenetic remission (absence of Philadelphia chromosome) by bone marrow biopsy
≤ 0.1%	MR3	• ≥ MR3 is also known as a **major molecular response (MMR)** • Has become a key regulatory endpoint as this predicts close to 100% CML-specific survival
≤ 0.01%	MR4	• MR4/4.5 lasting ≥ 2 years has been used as a benchmark to stop treatment (typically in earlier line treatment), which is the ultimate goal
≤ 0.0032%	MR4.5	
≤ 0.001%	MR5	

There is no standard definition of an acceptable response to third, fourth or fifth-line treatment

3L+ = Third line or later. CML = Chronic myeloid leukemia. Molecular response in CML is measured by the ratio of BCR::ABL1/ABL1.

References: Hochhaus, et al. Leukemia 2020; NCCN Guidelines 2.2024.

Switching TKIs is Usually Due to Lack of Efficacy or Intolerance

Lack of Efficacy (LOE)

- Often used interchangeably with resistance or loss of efficacy, is assessed based on molecular parameters
  - 1L/2L: switching is recommended after failure to meet specific molecular milestones at 3, 6 and 12 months, loss of an already achieved milestone (e.g., loss of MMR), or development of resistance mutations or high-risk chromosomal abnormalities
  - 3L+: no standard recommendation of when to switch therapies

Intolerance

- Inability to take TKI due to side effects that do not respond to dose reduction or medical management
  - Hematologic side effects, such as cytopenias (low blood cell counts), occur with all TKIs and are rarely a cause of treatment changes
  - Non-hematologic side effects are the most common reason to switch (due to medical necessity or reduction in quality of life)
- Tolerability is an increasingly important consideration as therapy is often lifelong and multiple TKIs are available

Disease Progression

- Progression to blast crisis, which is rare in CML, and is associated with a change in the treatment paradigm

Treatment goal for late-line patients is often to achieve MMR and/or maintain MMR with a good quality of life

1L = First line. 2L= Second line. 3L+ = Third line or later. CML = Chronic myeloid leukemia. TKI = Tyrosine kinase inhibitor. MMR = Major molecular response.

References: 1. Hochhaus, NEJM 2018; 2. Hochhaus Leukemia 2020; 3. Saxena 2021 J. of Heme Onc; 4. Ibrahim, 2011 Bood; 5. Hehlmann 2014 JCO.

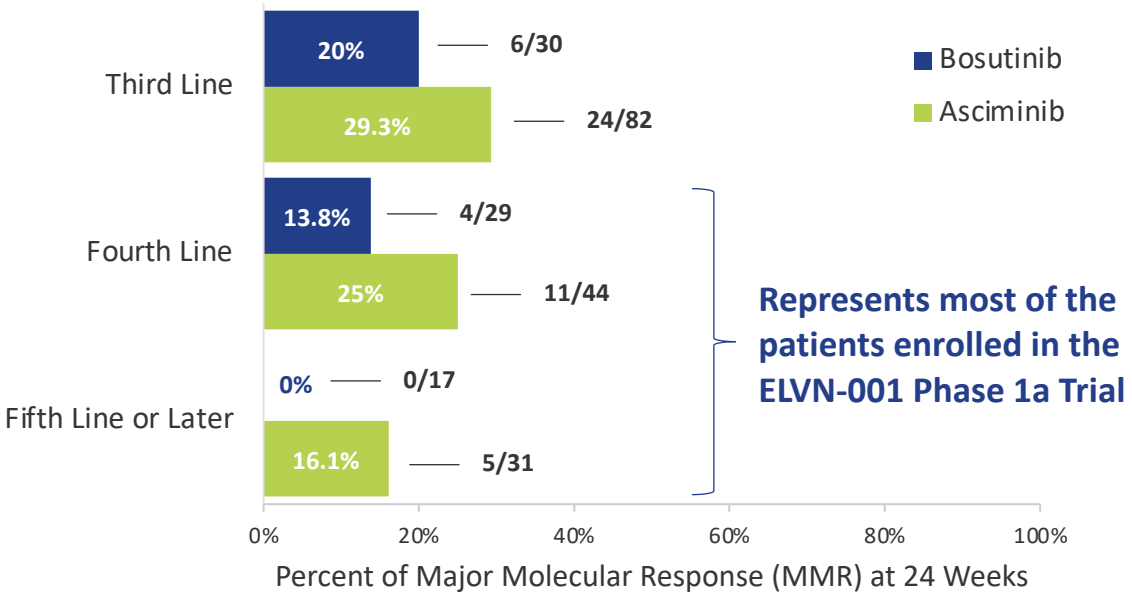
Phase 1 Data in Late-Line CML from Most Recently Approved TKIs

	Asciminib Phase 1 (2019)		Bosutinib Phase 1 (2012)	
Demographics (Prior TKIs)	1	2 (2%)	1	0%
	2	30 (27%)	2	**115 (97%)**
	≥ 3	**81 (72%)**	≥ 3	3 (3%)
Efficacy (Non-T315I)	**Cumulative MMR by 6 months**	**37/99 (37%)**	**Cumulative MMR (median f/up 28 mo.)**	**16/105 (15%)**
	TKI-Resistant (other than ponatinib*)	3/28 (11%)	TKI-Resistant (dasatinib or nilotinib)	3/54 (6%)
	Response Achieved	19/80 (24%)		
	Response Maintained	18/19 (95%)		
Safety / Tolerability	6% discontinued due to adverse event (median follow-up 13.7 months)		20% discontinued due to adverse event (median follow-up 28.5 months)	
	Although asciminib achieved an overall MMR rate of 37% by 6 months, the response rate was only 11% in TKI-resistant patients		**Despite a less heavily pre-treated patient population and longer follow-up, bosutinib only achieved an overall MMR of 15%**	

CML = Chronic myeloid leukemia. MMR = Major molecular response. TKI = Tyrosine kinase inhibitor. f/up = Follow-up. Mo. = Months.
*Asciminib in ponatinib-resistant patients: MMR by 6 mo. = 0% (n=4). These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, conclusions from cross-trial comparisons cannot be made.
References: Hughes et al., NEJM 2019; Khoury HJ et al. Blood. 2012.

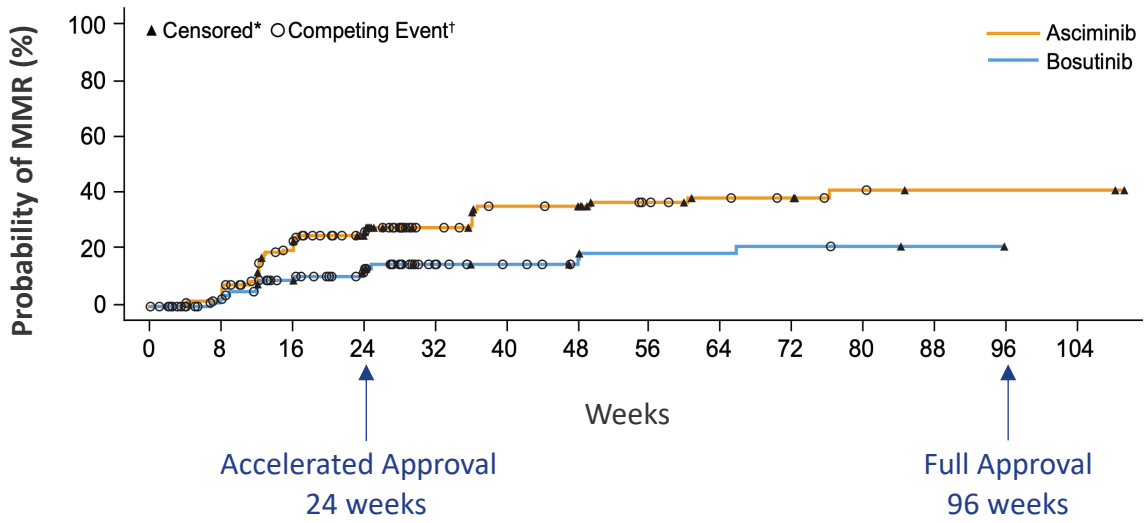
Phase 1 Data Predicted Pivotal Trial Data
Asciminib vs. Bosutinib in Late-Line CML (ASCEMBL)

Percent MMR at 24 Weeks



MMR rate decreased with increasing number of prior TKIs

Probability of MMR Over Time



MMR rate increased over time for both drugs

- Cumulative MMR at 24 weeks for asciminib vs. bosutinib was 25% vs. 12%
- Dose reductions due to adverse events: 21% asciminib vs. 42% bosutinib*

CML = Chronic myeloid leukemia. MMR = Major molecular response. TKI = Tyrosine kinase inhibitor.
*Median duration of exposure of 23.7 months for asciminib and 7 months for bosutinib. Note: overall MMR by 24 weeks was 25.5% for asciminib and 13.2% for bosutinib.

References: Rea D et al., Blood. 2021.

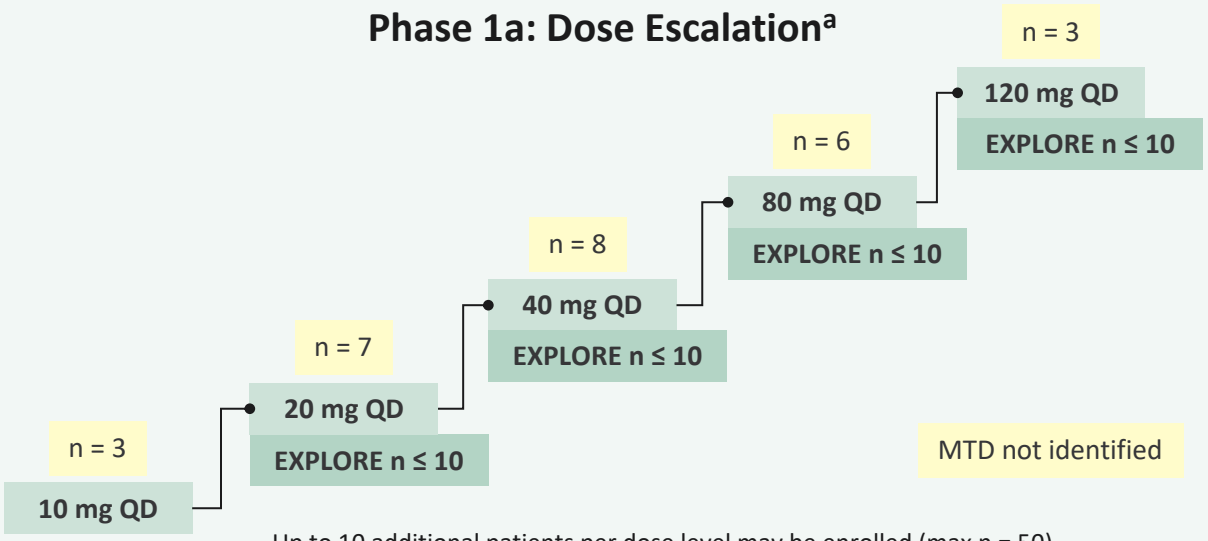
ELVN-001 Phase 1a Initial Proof of Concept Data in CML

ELVN-001 Phase 1 Trial Design

Key eligibility criteria:

- Chronic Phase CML (CP-CML)
- Failed, intolerant to, not a candidate for, available therapies known to be active for treatment of their CML

Phase 1a: Dose Escalation[a]



Up to 10 additional patients per dose level may be enrolled (max n = 50)

Phase 1b: Dose Expansion

RANDOMIZE		
Dose level 1 Phase 1b expansion in CP-CML no T315I mutations; n=20	**Dose level 2** Phase 1b expansion in CP-CML no T315I mutations; n=20	**T315I** Phase 1b expansion in CP-CML with T315I mutations; n=20

Additional (non) randomized expansion cohorts may be opened for patients based on emerging data

Primary endpoint:

- Safety[b]

Key secondary endpoints (Phase 1a[c]):

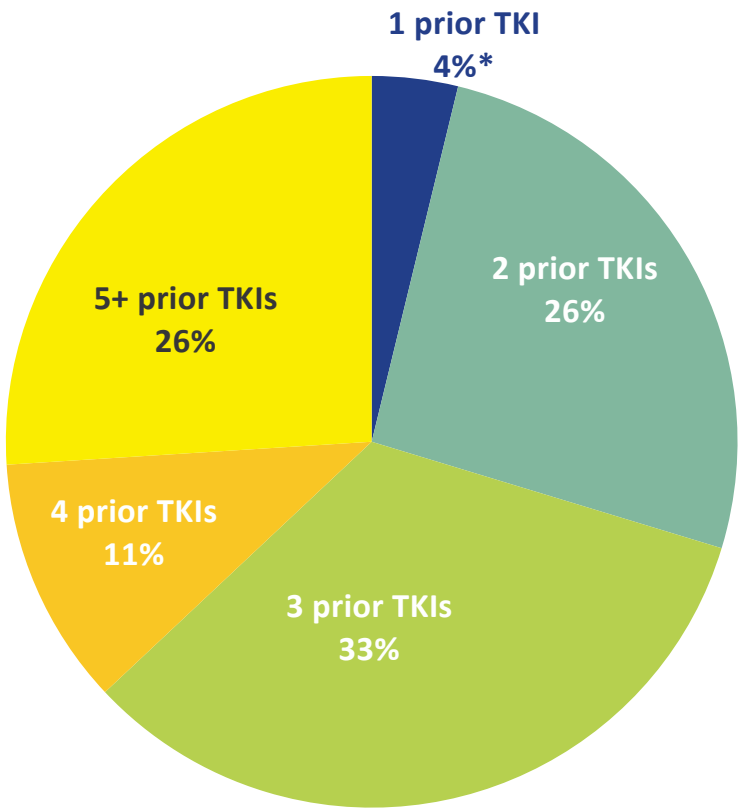
- Pharmacokinetics parameters
- Molecular response (MR) by central qPCR (measured every 4 weeks x 6, then every 12 weeks)

QD = Once daily. CML = Chronic myeloid leukemia. CP = Chronic phase. qPCR = quantitative reverse transcriptase polymerase chain reaction. MTD = Maximum tolerated dose.
a. Re-enrollment and intra-subject dose escalation allowed if meeting specific criteria; b. incidence of dose limiting toxicities, adverse events, clinically significant laboratory abnormalities and ECG abnormalities; c. Phase 1b secondary endpoints: duration of MR, BCR::ABL1 qPCR ≤ 1%, complete hematological response.

ELVN-001 Phase 1a Enrolled a Heavily Pretreated Patient Population

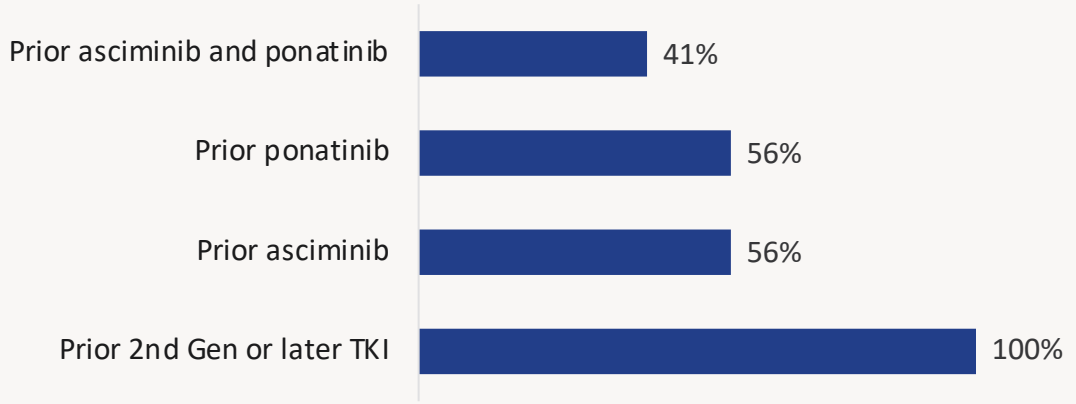
70% of patients had ≥ 3 prior TKIs

Number of different prior TKIs (% of patients enrolled)



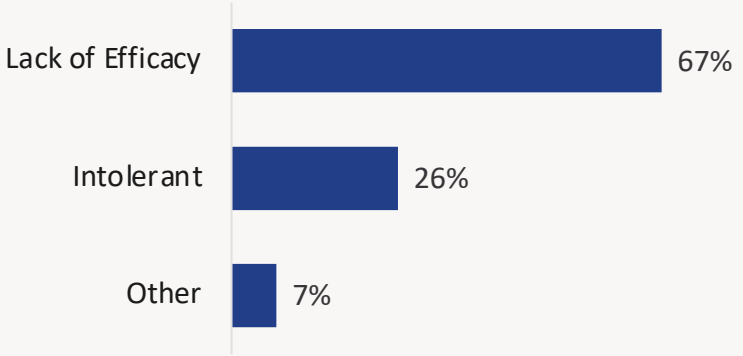
70% patients have received prior ponatinib and/or prior asciminib

Patient treatment status by previous TKI (% of patients enrolled)



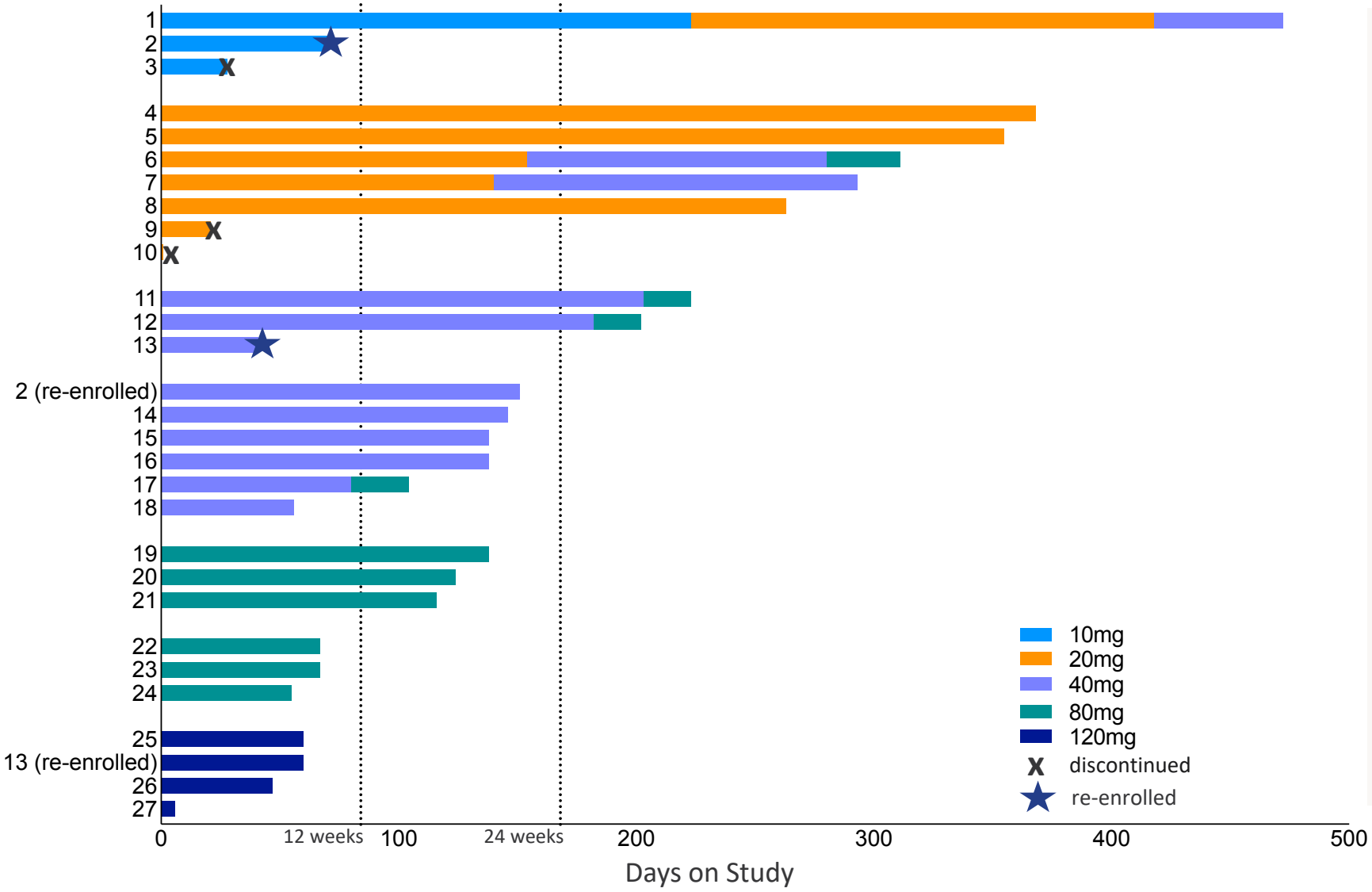
The most common reason for discontinuing prior TKI was lack of efficacy

Reason for discontinuation of last therapy (% of patients enrolled)



TKI = Tyrosine kinase inhibitor. 2nd Gen = 2nd Generation = dasatinib, nilotinib/radotinib, bosutinib.
*1 patient identified as ineligible after 1 dose. Also, 1 patient recategorized from 1 to 3 prior lines of therapy based on data received after data extraction date.

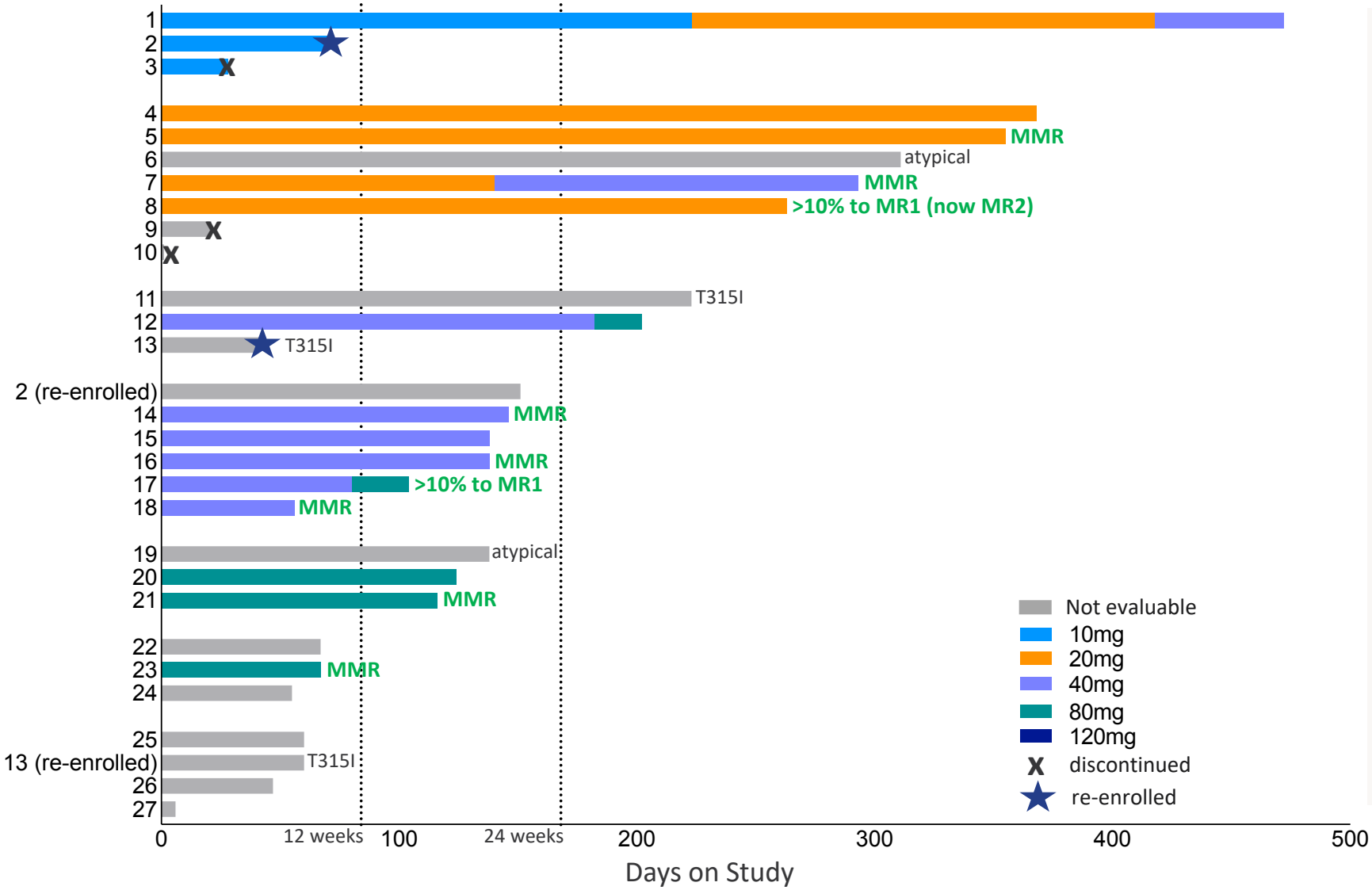
Median Time on ELVN-001 at Cutoff was 18 Weeks (~4 months)
89% (24/27) of Patients Remain on Treatment



- Protocol allows re-enrollment and intra-subject dose escalation*
  - 6 patients had intra-subject dose escalation
  - 2 patients re-enrolled at higher dose levels
- No progressive disease
- No dose reductions
- 3 discontinuations
  - 2 due to adverse events (10mg and 20mg)
  - 1 due to protocol deviation

*If certain protocol specific criteria are met.

Evaluation of Efficacy by Major Molecular Response by 12 Weeks (n=16)



- **43.8% (7/16)** cumulative MMR by 12 weeks
  - 2 additional patients with an improvement in molecular response level
- Excludes
  - Atypical transcripts, which cannot be measured by the central lab (excluded in asciminib Phase 1)
  - T315I mutated CML (note: both were resistant to ponatinib and asciminib, remain on study)

CML = Chronic myeloid leukemia. MMR = Major molecular response. MR1 = BCR::ABL1 ≤ 10%. MR2 = BCR::ABL1 ≤ 1%.
Evaluable for cumulative MMR by 12 weeks: patients who discontinued treatment and had at least one post-baseline assessment, or patients assessed at 12 weeks or achieved MMR prior to 12 weeks (same as asciminib Phase 1).

ELVN-001 Early Data Compares Favorably to Precedent Phase 1 Trials

		Asciminib Phase 1 (2019)	Bosutinib Phase 1 (2012)	ELVN-001 Phase 1a
Demographics (Prior TKIs)	1	2 (2%)	0%	1 (4%)
	2	30 (27%)	**115 (97%)**	7 (26%)
	3	41 (36%)	3 (3%)[1]	9 (33%)
	4	**32 (28%)**		**3 (11%)**
	≥ 5	**9 (8%)**		**7 (26%)**
Efficacy (Non-T315I)	**Cumulative MMR**	**37/99 (37%)**	**16/105 (15%)**	**7/16 (44%)**
	TKI-resistant[2]	3/32 (11%)	3/54 (6%)	4/10 (40%)
	Response Achieved[3]	19/80 (24%)		2/11 (18%)
	Response Maintained	18/19 (95%)		5/5 (100%)
	Time Frame	**by 24 weeks**	**median follow-up 28.5 mo.**	**by 12 weeks**

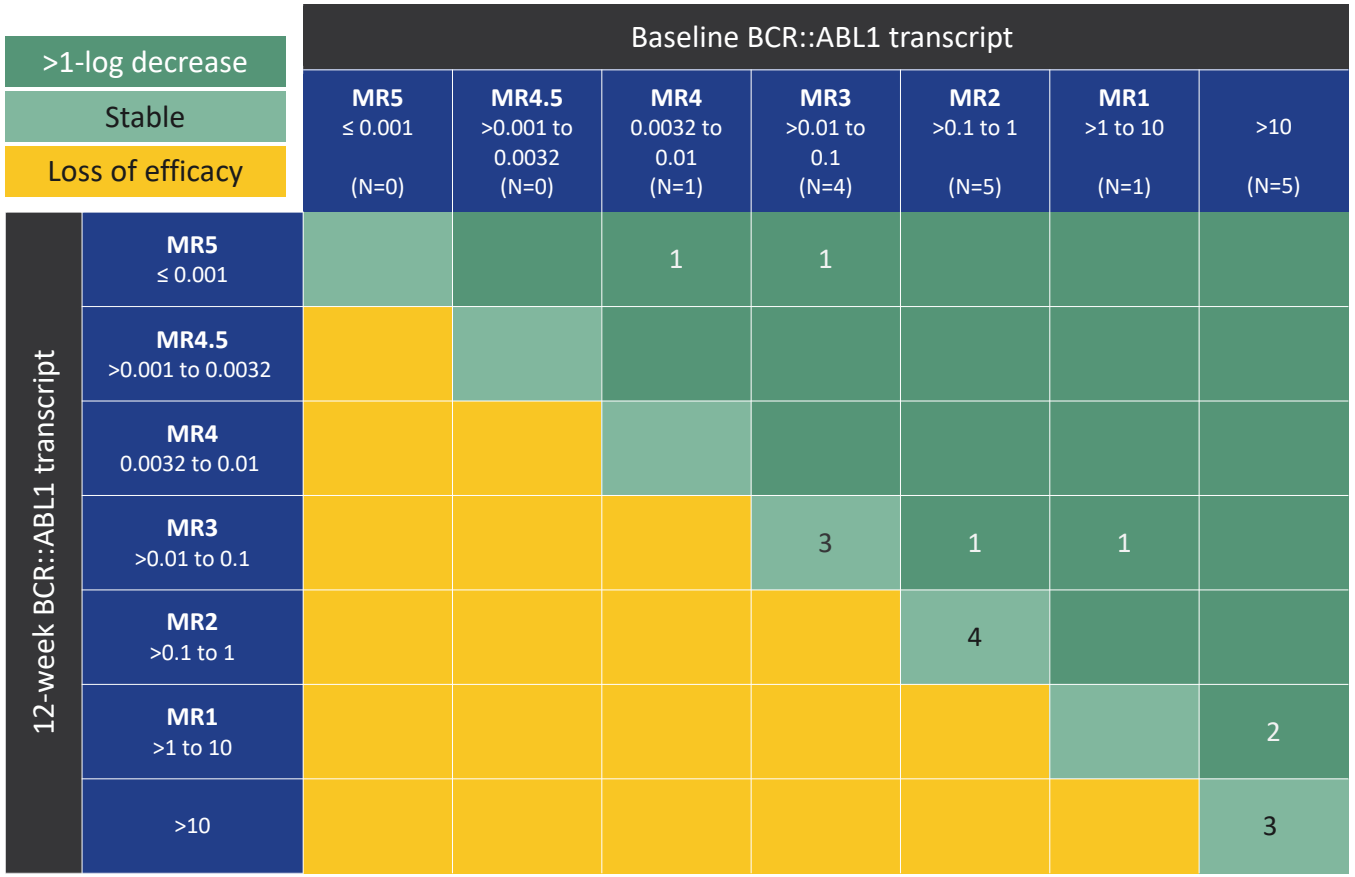
More heavily pre-treated patients

ELVN-001 in post-asciminib patients: 4/9 MMR by 12 wk.

ELVN-001's cumulative MMR rate compares favorably despite a more heavily pre-treated patient population & shorter time frame

CML = Chronic myeloid leukemia. MMR = Major molecular response. TKI = Tyrosine kinase inhibitor. f/up = Follow-up. Wk. = Weeks.
[1]Refers to ≥ 3 prior TKIs. [2]For asciminib, this does not include ponatinib-resistant patients (MMR by 6 mo. = 0%, n=4); for bosutinib, this includes patients that were resistant to nilotinib (n=27) or dasatinib (n=37). [3]For asciminib n=80 includes 4 patients that were resistant to ponatinib (subtracting these patients, achieved MMR rate: 19/76 (25%) by 24 weeks); for ELVN-001 n=11 includes 3 patients that were resistant to ponatinib (subtracting these patients, achieved MMR rate: 2/8 (25%) by 12 weeks).
These data are derived from different clinical trials at different points in time, with differences in trial design and patient populations. As a result, conclusions from cross-trial comparisons cannot be made, and no head-to-head clinical trials have been conducted.
References: Hughes et al., NEJM 2019; Khoury HJ et al. Blood. 2012.

Stable or Improved BCR::ABL1 Transcripts in all Evaluable Patients by 12 Weeks (n=16)



Within only 12 weeks of treatment:

- 7/16 patients achieved or maintained MMR
- **6/16 improved MR category**:
  - 3 improved by one MR level
  - 2 improved by 2 levels
  - 1 improved by 3 levels

- In precedent trials, **cumulative molecular response rates increased** over time

MR = Molecular response. MMR = Major molecular response and includes MR3, MR4, MR4.5 and MR5. Stable = transcript levels remain within listed category.

Safety and Tolerability of ELVN-001

- Well tolerated to date
  - Maximum tolerated dose has not been reached
  - No dose reductions
  - No ≥ Grade 3 non-hematologic treatment-related AEs; no Grade 1/2 >11%
  - No obvious relationship between dose/exposure and AEs

- 2 discontinuations due to AEs within the first 30 days of treatment
  - 10mg: 1 patient with Grade 2 asymptomatic pancreatitis
  - 20mg: 1 patient with Grade 3/4 hematologic cytopenias

AE = Adverse event.

Hematologic Treatment Emergent Adverse Events

Hematologic TEAE Regardless of Relatedness

Dose	10 mg		20 mg		40 mg		80 mg		120 mg		Total	
N	3		7		8		6		3		27	
Grade	1/2	3/4	1/2	3/4	1/2	3/4	1/2	3/4	1/2	3/4	1/2	3/4
Neutropenia		2 (66.7%)		2 (18.6%)								4 (14.8%)
Thrombocytopenia	1 (33.3%)			2 (28.6%)			1 (16.7%)				2 (7.4%)	2 (7.4%)
Anemia	1 (33.3%)		1 (14.3%)								2 (7.4%)	
Pancytopenia				1 (14.3%)								1 (3.7%)

- Grade 3/4 hematologic TEAEs were reported for 4/27 patients, which all occurred within the first 8 weeks
  - 1 patient (20mg), who discontinued their prior TKI for hematologic toxicity, discontinued due to an SAE of neutrophil count decrease, thrombocytopenia and pancytopenia
- No dose reductions due to cytopenias
- Hematologic toxicity expected as it is associated with all the CML TKIs with median time to Grade 3 of 6 weeks

CML = Chronic myeloid leukemia. TEAE = Treatment emergent adverse. SAE = serious adverse event. TKI = Tyrosine kinase inhibitor.
Note: patients are grouped in their original assigned dose. Neutropenia includes neutrophil count decreased; thrombocytopenia includes platelet count decreased.
References: Scemblix USPI 2022; Iclusig, USPI 2024.

Non-Hematologic Treatment-Related AEs Reported in ≥ 2 patients (5%)

Non-Heme TRAEs in ≥ 2 Patients

Dose	10mg		20mg		40mg		80mg		120mg		Total	
N	3		7		8		6		3		27	
Grade	1/2	3/4	1/2	3/4	1/2	3/4	1/2	3/4	1/2	3/4	1/2	3/4
Lipase increased	1 (33.3%)		1 (14.3%)		1(12.5%)						3 (11.1%)	
Headache			1 (14.3%)				1 (16.7%)				2 (7.4%)	
Hypertension			1 (14.3%)				1 (16.7%)				2 (7.4%)	
Nausea			1 (14.3%)						1 (33.3%)		2 (7.4%)	

- No ≥ Grade 3 non-hematologic TRAEs
- 1 patient (10mg) discontinued due to Grade 2 SAE of asymptomatic pancreatitis (Day 29)
- To date, no effusions, edemas or cardiovascular adverse events

The non-hematologic TRAE data to date is consistent with the selective kinase profile of ELVN-001

AE = Adverse event. TRAE = Treatment related adverse event. SAE = Serious adverse event.
Non-related AEs in ≥ 2 patients (any grade): diarrhea, arthralgia and oral herpes. The only Grade 3 non-related AEs reported were appendicitis and proctitis (both n=1, same patient).
Note: patients are grouped in their original assigned dose.

Summary

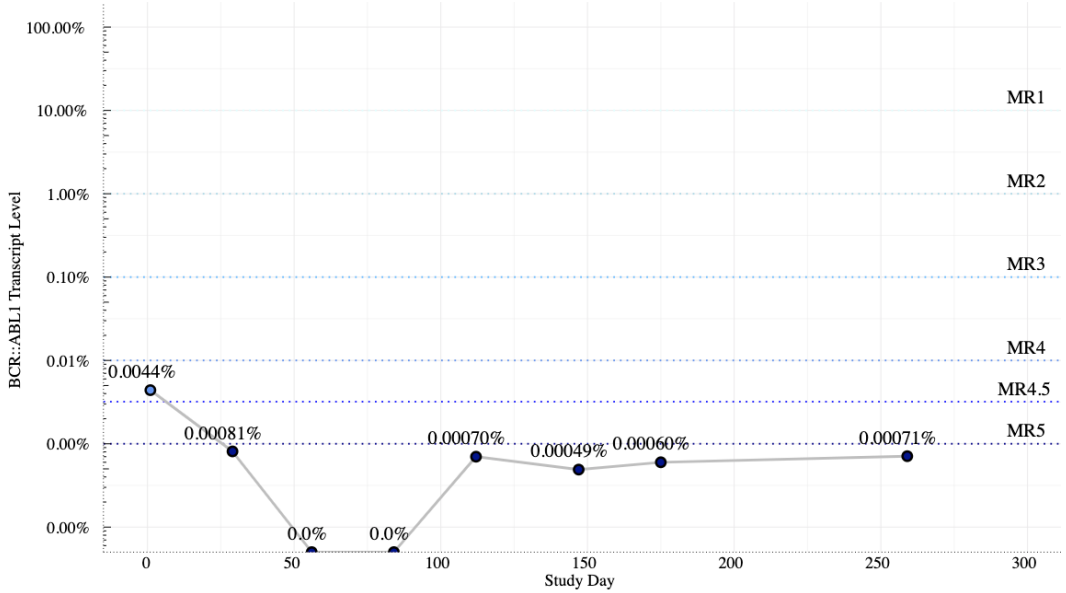
- Presented today is the initial clinical data from the Phase 1a portion of our ongoing ELVN-001 Phase 1 trial
- Early anti-CML activity was observed in this late line patient population
  - Cumulative MMR rate of 44% by 12 weeks is favorable compared to cumulative MMR rates observed in the Phase 1 trials of asciminib and bosutinib
- ELVN-001 has been well tolerated to date
  - Non-hematologic adverse events profile to date is encouraging, with no ≥ Grade 3 non-hematologic drug-related adverse events
  - Hematologic adverse events observed are consistent with other TKIs
  - Overall, the early safety profile is consistent with the selective kinase profile of ELVN-001

CML = Chronic myeloid leukemia. MMR= Major molecular response. TKI = Tyrosine kinase inhibitor.

Patient Vignettes

Deepening of Response in Heavily Pretreated Patient

MR5 after 7 prior TKIs @ 20mg QD ELVN-001



Patient Background

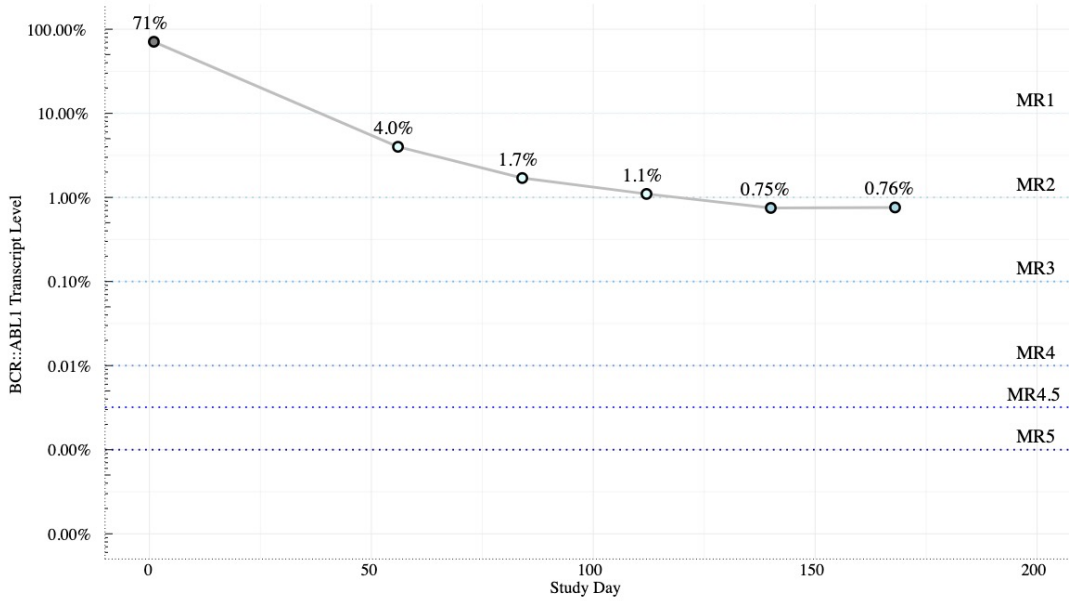
Relevant past medical history	Hypertension
Prior therapy (reason for switch)	Imatinib (LOE), nilotinib (pruritis), dasatinib (LOE), bosutinib (diarrhea), nilotinib (pruritis), asciminib (LOE), ponatinib (polyneuropathy), bosutinib (LOE), ponatinib (polyneuropathy/muscle/joint/bone pain)
Mutations	None
Safety	Worsening of hypertension G2 (R), G1/2 loss of appetite, pruritus, rhinitis, diarrhea, herpes simplex reactivation, headache, toothache, hyperlipidemia, arthralgia (all NR)
Efficacy	MR4 to MR5

Achieved and remains in a deep response 9 months after exhausting every other FDA approved TKI

G1/2 = Grade 1 or 2. QD = Once daily. LOE = Lack of efficacy. MR = Molecular response, NR = Not related to ELVN-001 per investigator, R = Related to ELVN-001 per investigator. TKI = Tyrosine kinase inhibitor.
Mutation not detected by central lab (transcript level too low at baseline); not performed at local lab. *Data extracted as of 18 March 2024; data from ongoing study and may change.*

Intolerant to 5 Prior TKIs, Including Asciminib: >10% → <1% by 6 Mo.

MR2 after 6 prior TKIs @ 20mg QD ELVN-001



Patient Background

Relevant past medical history	Young patient with no medical history
Prior therapy (reason for switch)	Imatinib (LOE), bosutinib (GI tox), nilotinib (heme/hepatic/pancreatic tox), dasatinib (heme tox), ponatinib (heme tox), asciminib (heme tox), imatinib (heme tox)
Mutations	None
Safety	G1-3 thrombocytopenia, anemia, neutropenia, G2 oral HSV, G1 influenza A (all R)
Efficacy	Non-CHR to CHR; molecular response = MR2

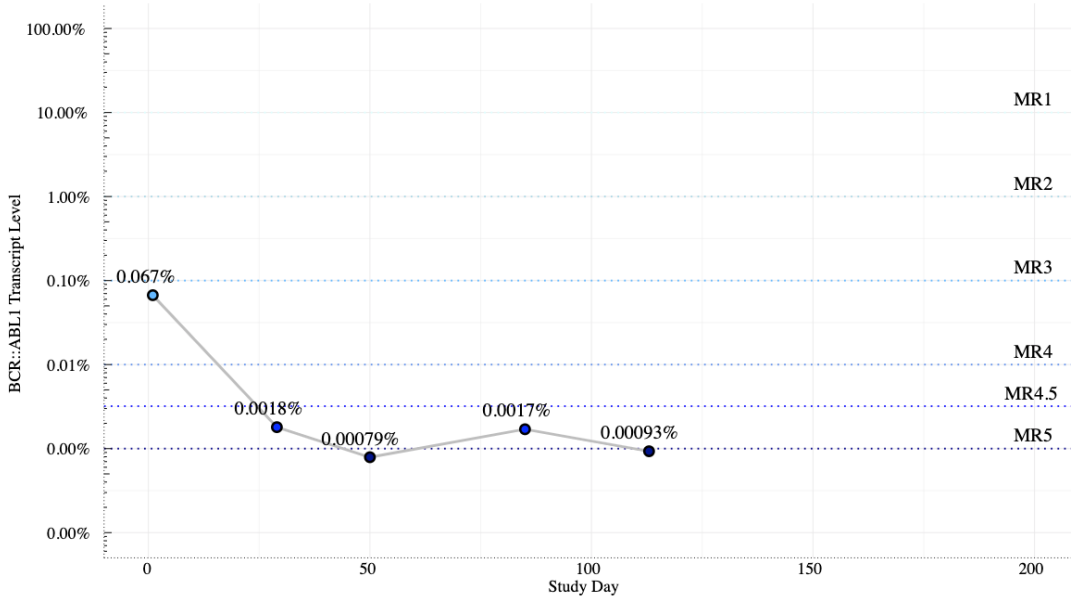
In asciminib's Phase 1 ~20% of patients with baseline BCR::ABL1 transcript levels >10% achieved levels <1% by 6 months

G1-3 = Grade 1, 2 or 3. QD = Once daily. LOE = Lack of efficacy. CHR = Complete hematological response. HSV = Herpes simplex virus. MR = Molecular response. R= Related to ELVN-001 per investigator. GI = Gastrointestinal. Tox = Toxicity. Heme = hematologic. TKI = Tyrosine kinase inhibitor. *Data extracted as of 18 March 2021; data from ongoing study and may change.*

References: Mauro, et al. Leukemia 2023.

1L Asciminib Resistant Patient: MR5 with > 1-log decrease

MR5 post-Asciminib @ 40mg QD ELVN-001



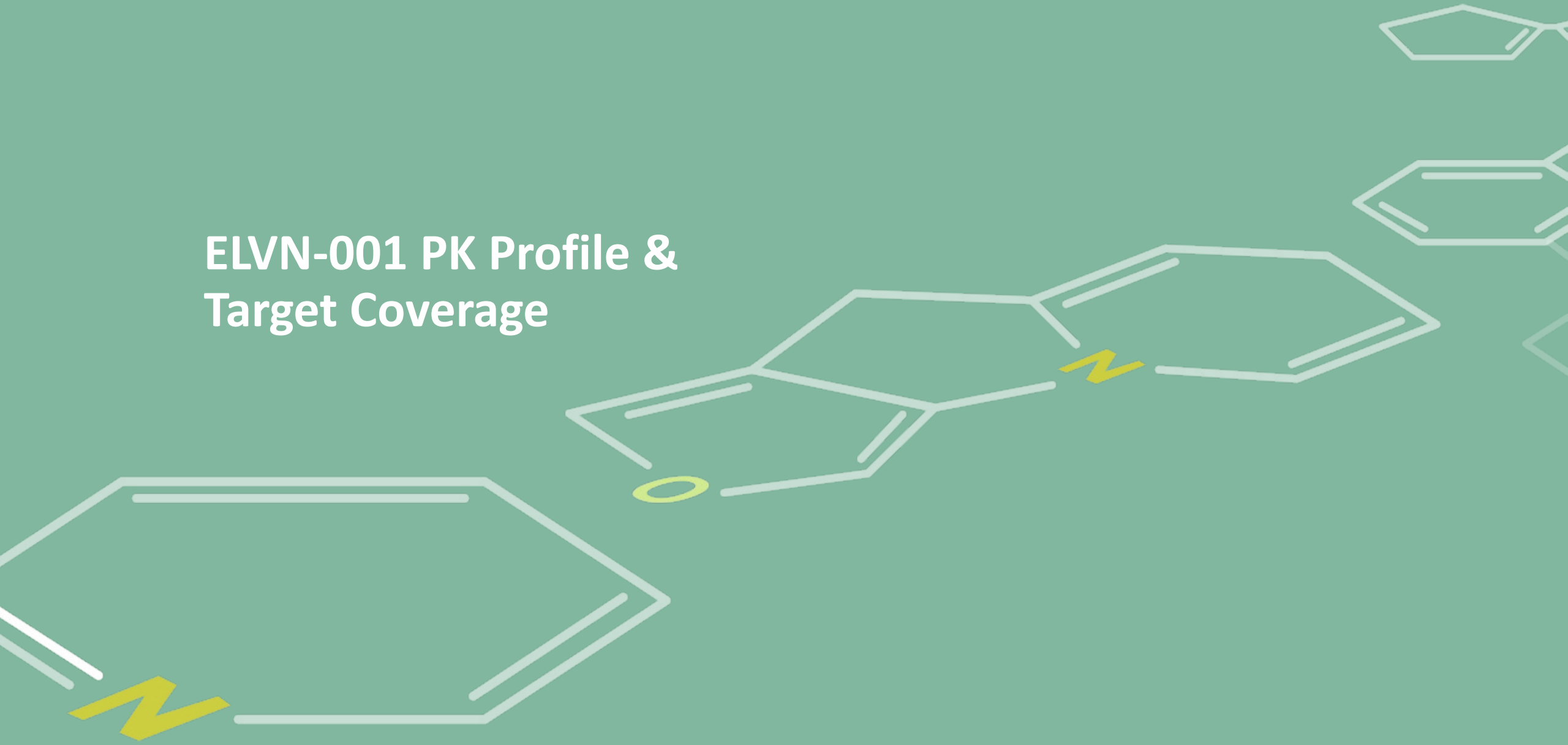
Patient Background

Relevant past medical history	Hyperlipidemia
Prior therapy (reason for switch)	Asciminib (LOE), ponatinib (LOE)
Mutations	A337T and V506M (mutation detected locally)
Safety	G1 rash (R) resolved by day 28 on study
Efficacy	Molecular response = MR5

A337T was the most common clinically emergent mutation that conferred resistance to asciminib on ASCEMBL

1L = First line. G1 = Grade 1. QD = Once daily. LOE = Lack of efficacy. MR = Molecular response. R = Related to ELVN-001 per investigator.
Mutation data not confirmed by central lab (transcript level too low at baseline). *Data extracted as of 18 March 2024; data from ongoing study-may change.*
References: Rea et al., Blood (2021) 138 (21): 2031–2041.

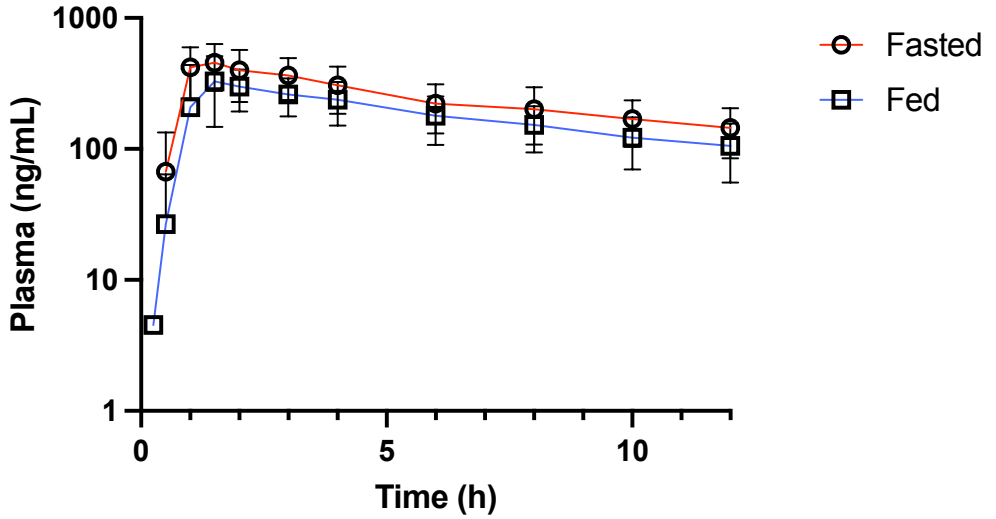
ELVN-001 PK Profile & Target Coverage



ELVN-001's PK Profile Supports Once Daily Dosing with Flexible Administration Requirements

- Linear PK observed in healthy volunteers (HV) and patients
  - No time-dependent PK observed in either HVs or cancer patients
  - Both C_{max} and AUC increased dose-proportionally
  - High concordance between HV and patient PK based on current data
- Fast and complete absorption with no significant food effect
- Mean terminal $t_{1/2}$ is ~12 hours in healthy volunteers
  - Similar effective $t_{1/2}$ observed in patients (10-20 hours)
  - Suitable for QD regimen
- Minimal risk of drug-drug interactions (DDIs)
  - Not an inhibitor (competitive or time-dependent) or inducer of major CYP enzymes, or of UGT1A1
  - Not a substrate for major CYP enzymes
  - Not a substrate of BCRP or P-gp
- No correlation between AEs and PK parameters in patients

120mg ELVN-001 (single dose)

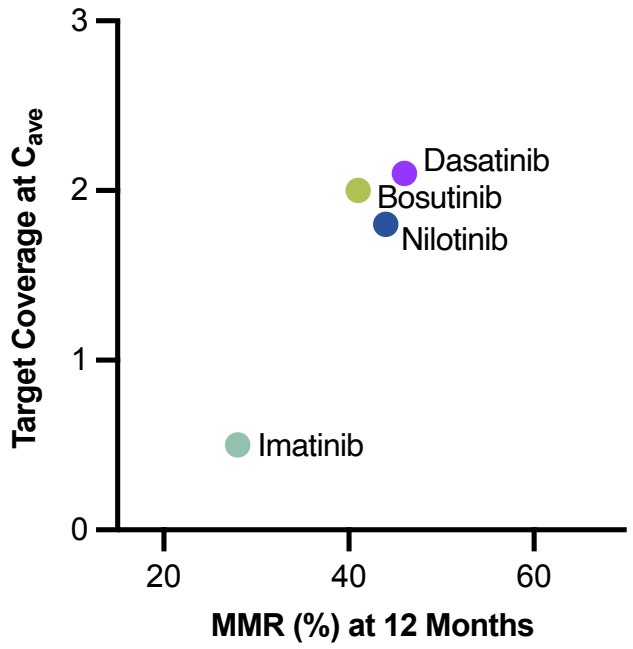


- Food effect study at 120mg single dose in HVs showed that:
  - AUC_{inf} under fasting conditions were similar to that under fed conditions, with a fed/fasted AUC ratio of 1.2.
  - C_{max} under fasting conditions were similar to that under fed conditions, with a fed/fasted C_{max} ratio of 0.8.

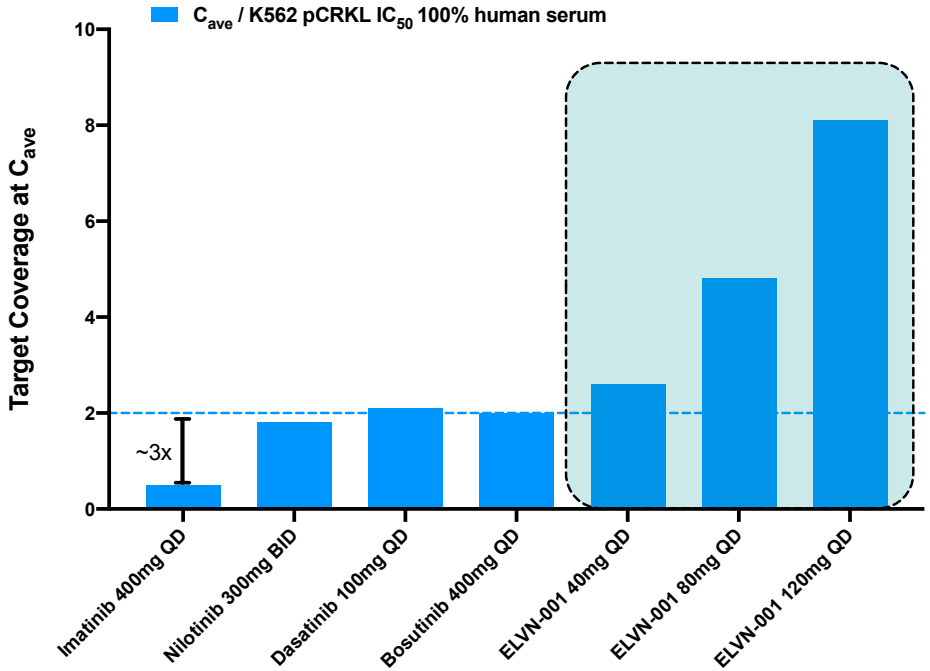
AEs = Adverse events. PK = Pharmacokinetics. HV = Healthy volunteers. C_{max} = Maximum serum concentration. AUC = Area under the curve. AUC_{inf} = AUC extrapolated to infinity. QD = Once daily. CYP = Cytochromes P450. BCRP = Breast cancer resistance protein. P-gp = P-glycoprotein. UGT1A1 = UDP Glucuronosyltransferase Family 1 Member A1.

ELVN-001 Achieved Superior Target Coverage Compared to 2nd Gen TKIs

C_{ave} Target Coverage vs. 1L MMR at 12 mo.



C_{ave} Target Coverage vs. Active Site TKIs (1L)

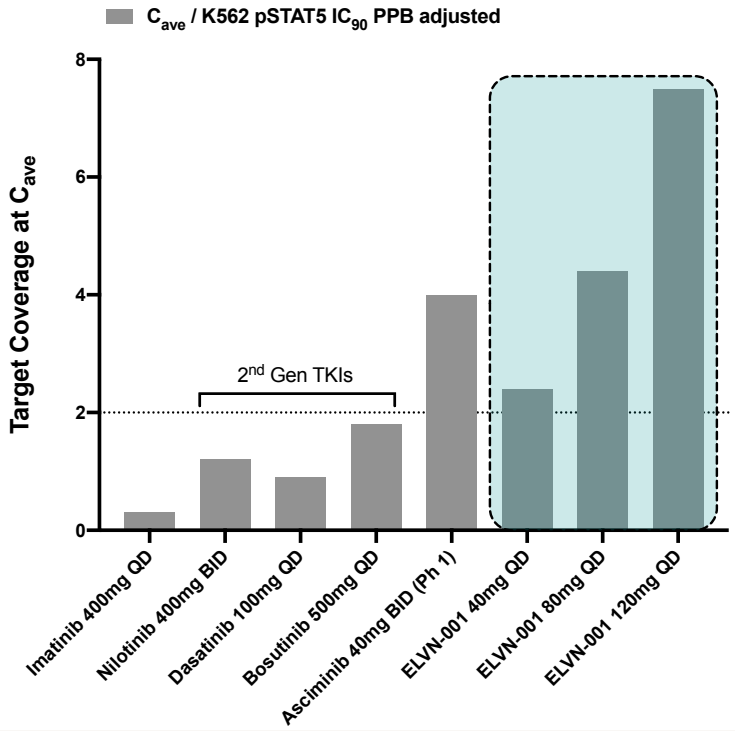


At doses ≥ 40mg QD, **ELVN-001 achieved better target coverage** compared to 2nd Generation TKIs

1L = First line. CRKL = Crk like protein. MMR = Major molecular response. QD = Once daily. TKI = Tyrosine kinase inhibitor. 2nd Gen TKIs = bosutinib, dasatinib, nilotinib.
References: 1. Imatinib clin pharm in CML pts: Peng et al, Clin Pharmacokinet 2005. 2. Imatinib NDA. 3. Nilotinib USPI. 4. Dasatinib USPI. 5. Bosutinib USPI.
MMR References: (Bosutinib) Cortes JE et al. *J Clin Oncol*. 2012; 30(28):3486-92; (Nilotinib and Imatinib) Saglio G et al. *NEJM*. 2010; 362(24):2251-9; (Dasatinib) Kantarjian H et al. NEJM, 2010; 362(24):226.
Notes: Cave = Area under the curve (AUC) divided by 24 hours. For the approved drugs, human pharmacokinetic (PK) values were obtained from population PK (popPK) simulation data reported in respective USPIs or from Ref 1 (imatinib). ELVN-001 human PK values are the mean values from a preliminary popPK simulation based on PK from 78 healthy volunteer subjects; to date, there has been no significant difference between ELVN-001 PK in cancer patients and healthy subjects. In vitro cell pharmacodynamic measurements were performed head-to-head and represent the average value from multiple experiments (n≥3). K562 cells were employed for these experiments. pCRKL IC_{50} measurements were performed in the presence of 100% human serum.

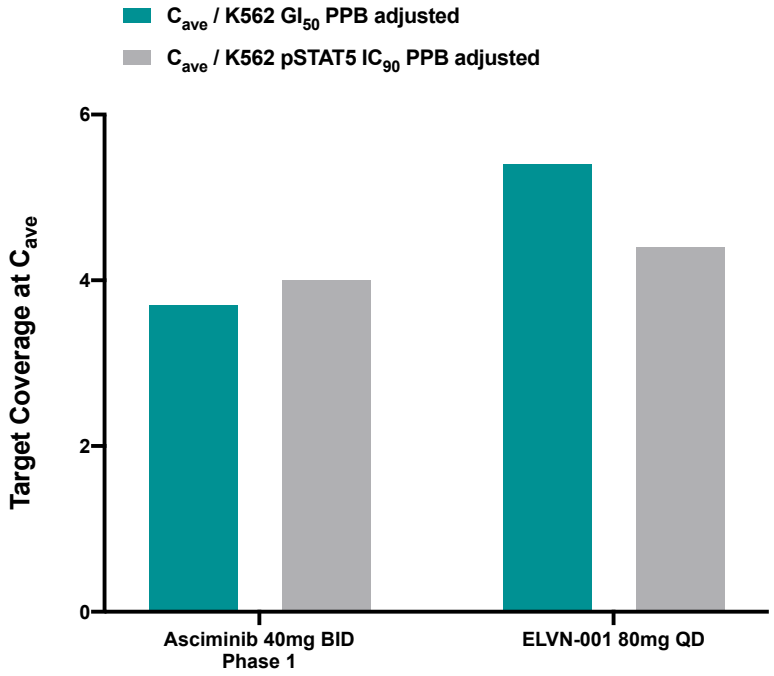
ELVN-001 Achieved Similar Target Coverage Compared to Asciminib

C_{ave} Target Coverage vs. All TKIs (Late Line)



- ELVN-001 had better target coverage based on plasma protein binding adjusted pSTAT5 IC_{90} at ≥ 40mg QD compared to 2nd Gen TKIs, and similar target coverage as asciminib at 80mg QD

C_{ave} Target Coverage vs. Asciminib (Phase 1)



- Novartis referenced preclinical 90% inhibitory concentration for phosphorylated STAT5 or pSTAT5 IC_{90} and anti-proliferation GI_{50} as the key target coverage metrics supporting an optimal asciminib dose of 40mg BID or 80mg QD for CML patients without T315I mutations

CML = Chronic myeloid leukemia. CRKL = CRK like protein. STAT5 = Signal transducer and activator of transcription 5. QD = Once daily. BID = Twice daily. PPB = Plasma protein binding. TKI = Tyrosine kinase inhibitor. 2nd Gen TKIs = bosutinib, dasatinib, nilotinib.

References: 1. Imatinib clin pharm in CML pts: Peng et al, Clin Pharmacokinet 2005. 2. Imatinib NDA. 3. Nilotinib USPI. 4. Dasatinib USPI. 5. Bosutinib USPI. 6. Hughes TP et al. *NEJM.* 2019;381(24):2315-2326. 7. Asciminb NDA.

Notes: Cave = Area under the curve (AUC) divided by 24 hours. For the approved drugs, human pharmacokinetic (PK) values were obtained from population PK (popPK) simulation data reported in respective USPIs or from Ref 1 (imatinib) and Ref 6 (asciminib Phase 1). ELVN-001 human PK values are the mean values from a preliminary popPK simulation based on PK from 78 healthy volunteer subjects; to date, there has been no significant difference between ELVN-001 PK in cancer patients and healthy subjects. Human plasma protein binding values were obtained from the respective NDAs or measured in house (ELVN-001). In vitro cell pharmacodynamic measurements were performed head-to-head and represent the average value from multiple experiments (n≥3). K562 cells were employed for these experiments. pSTAT5 IC_{90} and GI_{50} measurements were performed in 10% FBS and the values were adjusted to account for human plasma protein binding by dividing by the unbound fraction for each drug.

Summary & Next Steps

Summary

CML Opportunity

- CML is a chronic condition, often requiring decades of daily therapy
- Despite generics, the commercial market supports ~$6B in sales from six approved BCR::ABL1 TKIs, which are used interchangeably across lines of therapy
- Clear need for better agents, demonstrated by the recent asciminib (Scemblix) launch that is already generating $500M in annualized sales with only ~20% penetration into 3L+
- Based on recently announced positive topline 1L Phase 3 data, asciminib is poised to penetrate early lines of therapy
- We believe an opportunity exists to become the preferred active site TKI option post-asciminib, as well as to compete directly with asciminib based on differentiated efficacy, tolerability and/or administration requirements across lines of therapy

ELVN-001 Initial Proof of Concept Data

- As a highly selective, active site, active form inhibitor of BCR::ABL1, ELVN-001 represents a complimentary MOA compared to asciminib
- Based on initial Phase 1a data, ELVN-001:
  - Achieved initial cumulative MMR rates in heavily pre-treated patients, including post-asciminib patients, that are favorable when compared to historical Phase 1 MMR rates from other TKIs
  - Has been well-tolerated with no ≥ Grade 3 and low incidence of drug-related Grade 1 or 2 non-hematologic toxicities
  - Has a PK profile that supports once daily dosing with flexible administration requirements
  - Achieved target coverage superior to 2nd Gen TKIs and similar to asciminib at well-tolerated doses

1L = First line. 3L+ = Third line or later. 2nd Gen TKIs = nilotinib, dasatinib, bosutinib. CML = Chronic myeloid leukemia. MOA = Mechanism of action. MMR = Major molecular response. PK = Pharmacokinetic. TKI = Tyrosine kinase inhibitor.

Next Steps for ELVN-001

2Q 2024

Initiate Phase 1b and continue ongoing exploration in Phase 1a

2025

Phase 1b data with ~60-100 patients across various lines of therapy with significant follow-up

2025 Year End

Initial regulatory interactions with the aim of achieving regulatory path clarity regarding the first head-to-head pivotal trial

Appendix

5 Patients that Maintained MMR by 12 Weeks

		Reason for Discontinuation					
ELVN-001 Dose	# Prior TKIs	Ponatinib	Asciminib	Last Prior TKI	Resistant to other prior TKIs	Baseline MR Status	By 12 Weeks
20mg	6	Intolerant	LOE	Intolerant (P)	I, D, B	MR4	MR5
40mg	2	LOE	LOE	LOE (P)		MR3	MR5
40mg	2			Intolerant (I)	D	MR3	MR3
80mg	3		LOE (A+D)	LOE (A+D)	N, D	MR3	MR3
80mg	3		LOE	LOE (A)	N, D	MR3	MR3

2/5 patients improved MR category by 12 weeks

- 4/5 patients were resistant to ponatinib and/or asciminib
- 3/5 patients were resistant to last prior TKI

A = Asciminib, B = bosutinib, D = dasatinib, I = imatinib, N = Nilotinib, P = ponatinib. A+D = asciminib + dasatinib combination. LOE = Lack or loss of efficacy. MR = Molecular response. MMR = Major molecular response = MR3, MR4, MR5. MR1 ≤ 10%. MR2 ≤ 1%. MR3 ≤ 0.1%. MR4 ≤ 0.01%. MR5 ≤ 0.001%.

Scemblix (asciminib) USPI: Warnings and Precautions

- Myelosuppression: Severe thrombocytopenia and neutropenia events may occur. Monitor complete blood counts regularly during therapy and manage by treatment interruption or dose reduction.
- Pancreatic Toxicity: Monitor serum lipase and amylase. Interrupt, then resume at reduced dose or discontinue SCEMBLIX based on severity. Evaluate for pancreatitis when lipase elevation is accompanied by abdominal symptoms.
- Hypertension: Monitor blood pressure and manage hypertension as clinically indicated. Interrupt, dose reduce, or stop SCEMBLIX if hypertension is not medically controlled.
- Hypersensitivity: May cause hypersensitivity reactions. Monitor patients for signs and symptoms and initiate appropriate treatment as clinically indicated.
- Cardiovascular Toxicity: Cardiovascular toxicity may occur. Monitor patients with history of cardiovascular risk factors for cardiovascular signs and symptoms. Initiate appropriate treatment as clinically indicated. (5.5)
- Embryo-Fetal Toxicity: Can cause fetal harm. Advise females of reproductive potential of the potential risk to a fetus and to use effective contraception.

References: Scemblix (asciminib) USPI.

Scemblix (asciminib) USPI: Adverse Reactions (≥ 10%) in Patients with CML in ASCEMBL

Table 3: Adverse Reactions (≥ 10%) in Patients with Ph+ CML in CP, Previously Treated with Two or More TKIs Who Received SCEMBLIX in ASCEMBL

	SCEMBLIX N = 156		Bosutinib N = 76	
Adverse Reaction	**All Grades %**	**Grade 3 or 4 %**	**All Grades %**	**Grade 3 or 4 %**
Infections and infestations				
Upper respiratory tract infection[a]	26	0.6	12	1.3
Musculoskeletal and connective tissue disorders				
Musculoskeletal pain[b]	22	2.6	16	1.3
Arthralgia	12	0	3.9	0
Nervous system disorders				
Headache	19	1.9	15	0
General disorders and administration-site conditions				
Fatigue[c]	17	0.6	11	1.3
Skin and subcutaneous tissue disorders				
Rash[d]	17	0.6	30	8
Vascular disorders				
Hypertension[e]	13	6	5	3.9
Gastrointestinal disorders				
Diarrhea[f]	12	0	71	11
Nausea	12	0.6	46	0
Abdominal pain[g]	10	0	24	2.6

Table 3 Abbreviations & Footnotes:
Ph+ CML in CP, Philadelphia chromosome-positive chronic myeloid leukemia (Ph+ CML) in chronic phase (CP); TKIs, tyrosine kinase inhibitors.
[a]Upper respiratory tract infection includes: nasopharyngitis, upper respiratory tract infection, rhinitis, pharyngitis, respiratory tract infection, and pharyngotonsillitis.
[b]Musculoskeletal pain includes: pain in extremity, back pain, myalgia, non-cardiac chest pain, neck pain, bone pain, spinal pain, arthritis, and musculoskeletal pain.
[c]Fatigue includes: fatigue and asthenia.
[d]Rash includes: rash, rash maculopapular, dermatitis acneiform, rash pustular, eczema, dermatitis, skin exfoliation, dermatitis exfoliative generalised, rash morbilliform, drug eruption, erythema multiforme, and rash erythematous.
[e]Hypertension includes: hypertension and hypertensive crisis.
[f]Diarrhea includes: diarrhea and colitis.
[g]Abdominal pain includes: abdominal pain, abdominal pain upper, abdominal discomfort, abdominal pain lower, abdominal tenderness, and epigastric discomfort.

References: Scemblix (asciminib) USPI.

Asciminib and Bosutinib: Adverse Events Over Time in ASCEMBL

Figure 8: Adverse events over time – (Study ABL011A2301) (Safety Set)

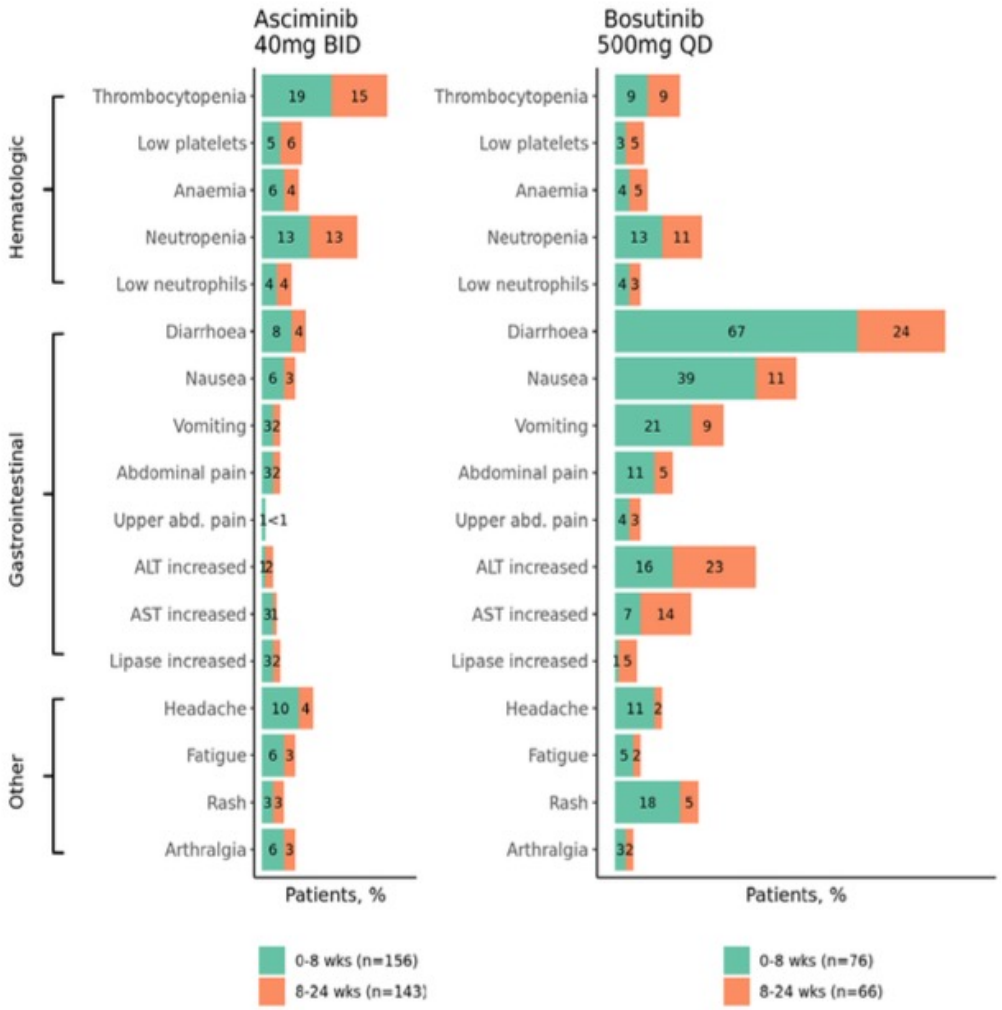


Figure 8. Adverse events over time: proportion of patients with on-treatment AEs occurring during the first 8 weeks of treatment, and newly occurring between weeks 8-24 of treatment. Denominators are the number of patients on treatment at the beginning of the indicated time interval. A patient with multiple occurrences of an AE with the same preferred term within the same time interval is counted only once in that time interval.

Study ABL001A2301 (ASCEMBL) Safety Set: asciminib (N=156), bosutinib (N=76).

References: Scemblix (asciminib) NDA/BLA Multi-disciplinary Review and Evaluation {NDA 215358}. Source: Novartis ABL001A Summary of Clinical Safety-Figure 2-1.