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

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): April 11, 2024

Enliven Therapeutics, Inc.

(Exact name of registrant as specified in its charter)

Delaware	**001-39247**	**81-1523849**
(State or other jurisdiction of incorporation)	(Commission File Number)	(IRS Employer Identification No.)
6200 Lookout Road **Boulder, Colorado** (Address of principal executive offices)		**80301** (Zip Code)

Registrant's telephone number, including area code: 720 647-8519

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions (see General Instruction A.2. below):

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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	ELVN	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§ 230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§ 240.12b-2 of this chapter).

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. ☐

Item 8.01 Other Events.

On April 11, 2024, Enliven Therapeutics, Inc. (the "Company") issued a press release announcing initial proof of concept data from the Phase 1 clinical trial evaluating ELVN-001 in patients with chronic myeloid leukemia who are relapsed, refractory, or intolerant to available tyrosine kinase inhibitors.

A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated herein by reference.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

Exhibit Number	Exhibit Description
99.1	Press release dated April 11, 2024
104	Cover Page Interactive Data File (embedded within the Inline XBRL document)

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Enliven Therapeutics, Inc.

Date: April 11, 2024

By: /s/ Samuel Kintz
Name: Samuel Kintz
Title: President and Chief Executive Officer

Exhibit 99.1

Enliven Therapeutics Announces Positive Proof of Concept Data from Phase 1 Clinical Trial of ELVN-001 in Chronic Myeloid Leukemia

Achieved initial cumulative MMR rate of 44% (7/16) by 12 weeks in response-evaluable patients, which compares favorably to precedent Phase 1 trials of approved BCR::ABL1 TKIs

Achieved initial cumulative MMR rate of 44% (4/9) by 12 weeks in response-evaluable patients who were previously treated with asciminib

ELVN-001 was well tolerated with no ≥ Grade 3 treatment-related non-hematologic toxicities reported

Company to host virtual event with Key Opinion Leaders at 8:00 AM ET Today

BOULDER, Colo., April 11, 2024 (GLOBE NEWSWIRE) — Enliven Therapeutics, Inc. (Enliven or the Company) (Nasdaq: ELVN), a clinical-stage precision oncology company focused on the discovery and development of next-generation small molecule kinase inhibitors, today announced positive proof of concept data from the Phase 1 clinical trial evaluating ELVN-001 in patients with chronic myeloid leukemia (CML) who are relapsed, refractory, or intolerant to available tyrosine kinase inhibitors (TKIs) (NCT05304377).

ELVN-001 is a potent, highly selective, potentially best-in-class small molecule kinase inhibitor designed to specifically target the BCR-ABL gene fusion, the oncogenic driver for patients with CML.

“Significant advancements have been made over the past few decades for patients with CML, and the approved TKIs provide important treatment options for patients with CML. However, there are limitations with the available therapies, including intolerance or resistance, that result in inadequate target coverage, the loss of molecular response and disease progression in many patients,” said presenting investigator Fabian Lang, M.D., from Goethe University Hospital. “Similar to our experience with previous successful Phase 1 trials in CML, ELVN-001 looks promising. The preliminary data support that ELVN-001 is a potent and highly selective BCR::ABL1 inhibitor that has activity in heavily pre-treated patients, including post-asciminib patients.”

“We are excited to present the first look at the safety and clinical activity of ELVN-001, which we believe supports the potential for ELVN-001 to address the limitations of the available active-site TKIs,” said Helen Collins, M.D., Chief Medical Officer of Enliven. “Across a wide dose range, ELVN-001 demonstrated activity in a heavily pre-treated patient population that includes post-asciminib patients, with a preliminary safety profile consistent with its highly selective design. Not only did all evaluable patients have improved or stable BCR::ABL1 transcript levels, but, importantly, 89% of all patients enrolled remain on study. We believe the initial data demonstrate the potential clinical utility of ELVN-001 for all types of patients, including those that are earlier in the treatment paradigm.”

Patient Demographics

- As of the cutoff date, March 18, 2024, 27 patients had enrolled in the ongoing Phase 1 clinical trial across five dose levels of ELVN-001, ranging from 10mg once daily (QD) to 120mg QD. Of the enrolled patients, 16 were evaluable for molecular response by 12 weeks.
- Patients enrolled were heavily pretreated:
    - 70% of patients had $\geq$ 3 prior TKIs.
    - 70% of patients had received prior ponatinib and/or prior asciminib.
    - 67% of patients had discontinued their last prior TKI due to lack of efficacy.

Preliminary Efficacy

- ELVN-001 achieved a cumulative major molecular response (MMR) rate of 44% (7/16) by 12 weeks and demonstrated responses in patients with prior exposure to asciminib and/or who were TKI-resistant:
    - Among post-asciminib patients, ELVN-001 achieved a cumulative MMR rate of 44% (4/9) by 12 weeks.
    - Among TKI-resistant patients, ELVN-001 achieved a cumulative MMR rate of 40% (4/10) by 12 weeks.
- Among response-evaluable patients, all had improved or stable BCR::ABL1 transcript levels by 12 weeks.
- These data compare favorably to precedent Phase 1 cumulative MMR rates for approved BCR::ABL1 TKIs, particularly given the shorter time frame for response assessment and a more heavily pre-treated patient population.

Preliminary Safety

- ELVN-001 has been well tolerated, consistent with its selective kinase profile.
- A maximum tolerated dose has not been identified, and there have been no dose reductions.
- No $\geq$ Grade 3 non-hematologic treatment-related adverse events (TRAE) and no specific non-hematologic TRAE of any grade occurred in >11% of patients.
- Hematologic adverse events observed are consistent with the approved BCR::ABL1 TKIs.

Pharmacokinetics (PK) & Target Coverage

- ELVN-001's PK profile supports once daily dosing with flexible administration requirements (no significant food effect and minimal risk of drug-drug interactions).
- Importantly, given the strong correlation between target coverage and 1L efficacy for the approved BCR::ABL1 TKIs,
    - ELVN-001, at doses equal to or greater than 40mg QD, achieved superior target coverage compared to 2nd Generation, active-site TKIs.
    - ELVN-001, at 80mg QD, achieved similar target coverage compared to asciminib.

"We are thrilled with ELVN-001's initial Phase 1 data in heavily pre-treated patients with CML," said Sam Kintz, Co-founder and Chief Executive Officer of Enliven. "We believe that with the data presented today, ELVN-001 has initially addressed each key area of our target product profile. Given our expectation that asciminib [Scemblix] will soon become an important standard of care in the early-line CML setting, we hope to initially position ELVN-001 as the best-in-class active-site BCR::ABL1 TKI. We believe that ELVN-001's initial cumulative MMR rate, including in post-asciminib patients, and its tolerability profile are supportive of this positioning. These data are supported by ELVN-001's pharmacokinetic data, which showed superior target

coverage at doses equal to or greater than 40mg QD compared to 1st and 2nd Generation TKIs. Finally, and most importantly, we recognize that this achievement is made possible by the patients, caregivers, and investigators who are participating in the ELVN-001 trial, and we offer them our sincere gratitude."

Company Event with Investigators and Key Opinion Leaders (KOLs)

Enliven is hosting a company event with KOLs today at 8:00 AM ET. The event will feature leading CML investigators and hematology care experts, Michael Mauro, M.D., from Memorial Sloan Kettering Cancer Center, and Fabian Lang, M.D., from Goethe University Hospital, along with the management of Enliven Therapeutics. The discussion will cover details of ELVN-001's Phase 1 initial proof of concept data, the evolving treatment paradigm in CML, and how ELVN-001 could fit into the CML landscape.

The event will be webcast live and can be accessed by visiting the investor relations section of the Company's website at https://ir.enliventherapeutics.com. To participate in the live event, please register using this link. An archived webcast will be available following the event.

About the Phase 1 ELVN-001 Trial

The Phase 1 clinical trial of ELVN-001 is a dose escalation trial designed to evaluate the safety and tolerability, and determine the recommended dose for further clinical evaluation of, ELVN-001 in patients with CML with and without T315I mutations who are relapsed, refractory or intolerant to TKIs. The primary endpoint of the study is safety. Secondary endpoints include pharmacokinetics, MMR by central qPCR, duration of MMR, BCR::ABL1 transcript levels and complete hematologic response.

About ELVN-001

ELVN-001 is a potent, highly selective, small molecule kinase inhibitor designed to specifically target the BCR-ABL gene fusion, the oncogenic driver for patients with chronic myeloid leukemia. As a highly selective active site inhibitor, ELVN-001 has a mechanism of action that is complementary to allosteric BCR::ABL1 inhibitors, which may play an increasingly important role in the standard of care. ELVN-001 was also designed to have activity against the T315I mutation, the most common BCR::ABL1 mutation, which confers resistance to nearly all approved TKIs as well as activity against mutations known to confer resistance to allosteric BCR::ABL1 inhibitors.

About Enliven Therapeutics

Enliven Therapeutics is a clinical-stage biopharmaceutical company focused on the discovery and development of small molecule inhibitors to help people with cancer not only live longer, but live better. Enliven aims to address existing and emerging unmet needs with a precision oncology approach that improves survival and enhances overall well-being. Enliven's discovery process combines deep insights in clinically validated biological targets and differentiated chemistry to design potentially first-in-class or best-in-class therapies. Enliven is based in Boulder, Colorado.

Forward-Looking Statements

This press release contains forward-looking statements (including within the meaning of Section 21E of the Securities Exchange Act of 1934, as amended, and Section 27A of the Securities Act of 1933, as amended) concerning Enliven and other matters. These statements may discuss goals, intentions and

expectations as to future plans, trends, events, results of operations or financial condition, or otherwise, based on current beliefs of the management of Enliven, as well as assumptions made by, and information currently available to, management of Enliven. Forward-looking statements generally include statements that are predictive in nature and depend upon or refer to future events or conditions, and include words such as “may,” “will,” “should,” “would,” “expect,” “anticipate,” “plan,” “likely,” “believe,” “estimate,” “project,” “intend,” and other similar expressions or the negative or plural of these words, or other similar expressions that are predictions or indicate future events or prospects, although not all forward-looking statements contain these words. Statements that are not historical facts are forward-looking statements. Forward-looking statements in this press release include, but are not limited to, statements regarding the potential of, and plans and expectations regarding ELVN-001; statements by Enliven’s Chief Medical Officer, Enliven’s Chief Executive Officer and Dr. Lang. Forward-looking statements are based on current beliefs and assumptions that are subject to risks and uncertainties and are not guarantees of future performance. Actual results could differ materially from those contained in any forward-looking statement as a result of various risks and uncertainties, including, without limitation: the limited operating history of Enliven; the ability to advance product candidates through preclinical and clinical development; the ability to obtain regulatory approval for, and ultimately commercialize, product candidates; the potential for clinical trials of ELVN-001 to differ from preclinical, initial, interim, preliminary or expected results; 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), which may be found in the section titled “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. Except as required by applicable law, Enliven undertakes no obligation to revise or update any forward-looking statement, or to make any other forward-looking statements, whether as a result of new information, future events or otherwise.

Head-to-Head Comparisons

The Company has not performed any head-to-head trials for ELVN-001. As a result, the data referenced in this press release is 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.

Contact:

Investors

ir@enliventherapeutics.com

Media

media@enliventherapeutics.com