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

September 28, 2024

Updated Phase 1 data presented at ESH-iCMLf 26th Annual John Goldman Conference

Reported cumulative MMR rate of 44% (8/18) by 24 weeks, with stable or deepening responses between weeks 12 and 24, which continues to compare favorably to precedent Phase 1 trials of approved BCR::ABL1 TKIs

ELVN-001 remains well-tolerated with no dose reductions reported with 39 patients enrolled and a median treatment duration of 20 weeks at cutoff

BOULDER, Colo., Sept. 28, 2024 (GLOBE NEWSWIRE) -- Enliven Therapeutics, Inc. (Enliven or the Company) (Nasdaq: ELVN), a clinical-stage biopharmaceutical company focused on the discovery and development of small molecule therapeutics, today announced updated, positive data from the Phase 1 clinical trial evaluating ELVN-001 in patients with chronic myeloid leukemia (CML) that has failed, or the patient is intolerant to or not a candidate for, available therapies known to be active for treatment of their CML (NCT05304377) at the European Society of Hematology International Chronic Myeloid Leukemia Foundation (ESH-iCMLf) 26th Annual John Goldman Conference.

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.

"I am happy to present the updated ELVN-001 Phase 1 data today at ESH-iCMLf. ELVN-001 continues to show clinical benefit in heavily pretreated CML patients," said presenting investigator Fabian Lang, M.D., from Goethe University Hospital Frankfurt. "I am encouraged that the initial clinical profile presented in April continues to hold, even as patient numbers and the median duration of exposure increased. We continue to see categorical improvements in molecular response, and the drug remains well-tolerated with an encouraging safety profile. Despite recent advancements in the CML treatment paradigm, there continues to be a need for more efficacious and better tolerated active-site TKIs, especially for patients who have failed treatment with allosteric inhibitors. I remain excited to see the progress of ELVN-001 as the trial continues."

The updated data presented today includes 39 patients across various dose levels, 18 of whom were evaluable for molecular response by 24 weeks. Consistent with the 12-week results the Company presented in April 2024, a cumulative major molecular response (MMR) rate of 44.4% (8/18) was observed by 24 weeks in response-evaluable CML patients. Additionally, ELVN-001 continues to be well-tolerated with no dose reductions and a median treatment duration of 20 weeks.

"We are excited by the continued advancement of the ELVN-001 Phase 1 trial, and we remain confident in ELVN-001's potential to address the limitations of the available active-site TKIs," said Helen Collins, M.D., Chief Medical Officer of Enliven. "With more patients enrolled and longer follow up, we continue to see anti-CML activity in a heavily pre-treated patient population that includes patients previously treated with asciminib. Additionally, ELVN-001's safety profile remains consistent with its high selectivity, even with longer duration and more patients enrolled at higher dose levels. We believe the data demonstrate the potential clinical utility of ELVN-001 for patients across the full spectrum of the CML treatment paradigm."

Patient Demographics

- As of the cutoff date, June 25, 2024, 39 patients have been enrolled in the ongoing Phase 1 clinical trial across five dose levels of ELVN-001, ranging from 10 mg once daily (QD) to 120 mg QD, and the vast majority remain on study with a median treatment duration of 20 weeks.
- Patients enrolled were heavily pretreated:
  - 69.2% of patients had ≥ 3 prior tyrosine kinase inhibitors (TKIs) and 25.6% had ≥ 5 prior TKIs.
  - 53.8% of patients had received prior asciminib.
  - 69.2% of patients had discontinued their last prior TKI due to lack of efficacy.

Updated Efficacy

- Of the enrolled patients, 18 with typical transcripts and without T315I mutations were evaluable for molecular response by 24 weeks.
- ELVN-001 achieved a cumulative MMR rate of 44.4% (8/18) by 24 weeks.
  - Among the 16 patients previously evaluated for efficacy, all 16 had stable or deepening responses between weeks 12 and 24.
  - Among TKI-resistant patients, ELVN-001 achieved a cumulative MMR rate of 41.7% (5/12) by 24 weeks.
  - Among post-asciminib patients, ELVN-001 achieved a cumulative MMR rate of 40.0% (4/10) by 24 weeks.
  - Among patients that were not in MMR at baseline, 23.1% (3/13) achieved MMR by 24 weeks.
- These data continued to compare favorably to precedent Phase 1 cumulative MMRs for approved BCR::ABL1 TKIs, particularly given the more heavily pre-treated patient population in the ELVN-001 clinical trial.

Updated Safety

- ELVN-001 remains well-tolerated, consistent with its selective kinase profile.
- A maximum tolerated dose has not been identified.
- There have been no dose reductions and at ≥ 40 mg, no discontinuations due to treatment-emergent adverse events (TEAE).
- There have been no ≥ Grade 3 non-hematologic treatment-related adverse events (TRAE), no specific non-hematologic TEAE of any grade occurred in >14% of patients, and no TRAE of any grade occurred in >11% of patients.
- Hematologic adverse events observed remain consistent with those observed with the approved BCR::ABL1 TKIs.

"We are very pleased with how the ELVN-001 Phase 1 data is maturing," said Sam Kintz, Co-founder and Chief Executive Officer of Enliven. "We are encouraged to see stable and deepening responses between weeks 12 and 24 and clinical benefit for almost every patient we've enrolled. Most importantly, now with 39 patients enrolled at time of cutoff, we continue to see an impressive safety and tolerability profile, which is especially important given the chronic nature of this disease. We also continue to be encouraged by the Scemblix launch and the 1L data that was presented at ASCO. We believe that Scemblix, an allosteric inhibitor, will soon become an important part of the early-line standard of care in CML, thereby heightening the need for a well-tolerated, active site BCR::ABL1 TKI and creating a great opportunity for ELVN-001."

About the Phase 1 ELVN-001 Trial

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

About ELVN-001

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 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

Enliven is a clinical-stage biopharmaceutical company focused on the discovery and development of small molecule therapeutics 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, plans and expectations and potential opportunities 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 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; the potential for interim, topline, and preliminary data from Enliven's preclinical studies and clinical trials to materially change from the final data; 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.

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