NEWS RELEASE

Shattuck Labs to Present Topline Data from Phase 1 A/B Clinical Trial of SL-172154 in Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML) and Higher-Risk Myelodysplastic Syndromes (HR-MDS) Patients at the American Society of Hematology (ASH) 2023 Annual Meeting

2023-11-02

– SL-172154 as monotherapy and in combination with azacitidine demonstrates anti-leukemic activity and an acceptable safety and tolerability profile –

AUSTIN, Texas and DURHAM, N.C., Nov. 02, 2023 (GLOBE NEWSWIRE) -- Shattuck Labs, Inc. (Shattuck) (NASDAQ: STTK), a clinical-stage biotechnology company pioneering the development of bi-functional fusion proteins as a new class of biologic medicine for the treatment of patients with cancer and autoimmune disease, today announced the presentation of topline data from the dose escalation portion of its Phase 1 A/B clinical trial of SL-172154 as monotherapy and in combination with azacitidine (AZA) in primarily R/R AML and HR-MDS patients. These data will be featured in a poster presentation at the 65th ASH Annual Meeting, which is being held both virtually and in San Diego, CA from December 9-12, 2023.

“Response rates are historically low for heavily pretreated relapsed/refractory AML and HR-MDS patients. We were particularly pleased to observe initial anti-leukemic activity, unique pharmacodynamic activity, and an acceptable safety and tolerability profile for SL-172154 as monotherapy and in combination with azacitidine. We are excited to continue development of our unique bifunctional protein SL-172154, as we seek to improve the lives of patients with hematologic malignancies.” said Dr. Lini Pandite, MBChB, M.B.A., Chief Medical Officer of Shattuck. “The observation of a monotherapy response, dose-dependent increases in serum cytokines, and accumulation of mature myeloid cells in bone marrow support a potential contribution of CD40 stimulation in these heme malignancies. Notably, preliminary data shows anti-leukemic effects detected in previously untreated TP53m-MDS and R/R AML patients. We look forward to sharing additional data from the frontline expansion cohorts later this year. Overall, we are encouraged by the growing body of data

that further validates the unique mechanism of action of SL-172154 and its therapeutic potential to address the unmet needs for patients with AML and HR-MDS."

The full abstract (#4278) is accessible on the ASH Congress portal, and additional details are provided below.

- Title: Safety, Pharmacodynamic, and Anti-Tumor Activity of SL-172154 as Monotherapy and in Combination with Azacitidine (AZA) in Relapsed/Refractory (R/R) Acute Myeloid Leukemia (AML) and Higher-Risk Myelodysplastic Syndromes/Neoplasms (HR-MDS) Patients (pts)
- Session Title: Acute Myeloid Leukemias: Investigational Therapies, Excluding Transplantation and Cellular Immunotherapies: Poster III
- Presenter: Dr. Naval Daver
- Format: Poster Presentation
- Session Date: Monday, December 11, 2023
- Time: 6:00 PM - 8:00 PM PT

Key Takeaways: SL-172154 monotherapy response was observed in a heavily pretreated patient with R/R AML after just a single cycle of treatment, as well as early efficacy signals for SL-172154 in combination with AZA in previously untreated HR-MDS with TP53 mutant patients. SL-172154 was tolerable at 3mg/kg as a monotherapy and in combination with AZA.

- **Data Overview**: As of the abstract data cut-off date of May 25, 2023, 37 adult patients with R/R AML and HR-MDS had received SL-172154 as monotherapy or in combination with AZA in the parallel staggered dose-escalation portion of a Phase 1A/B clinical trial. Patients had a median of two prior lines of therapy.
- **Preliminary signs of anti-leukemic activity**: Monotherapy response in a R/R AML patient and early signals of anti-leukemic activity (in the form of blast count reductions) in patients with R/R AML who received SL-172154 in combination with AZA were observed in a dose-dependent manner. Early signals of activity with SL-172154 in combination with AZA in frontline patients with TP53 mutant HR-MDS were observed.
    - SL-172154 monotherapy response (Morphologic Leukemia-Free State) (n=1 at 6 mg/kg) was observed in a heavily pretreated R/R AML patient who subsequently proceeded to allogeneic hematopoietic cell transplantation (allo-HCT).
    - Anti-leukemic activity, in the form of blast count reductions, was observed in R/R AML patients in combination with AZA (n=2 at 1 mg/kg, n=5 at 3 mg/kg) and one patient subsequently proceeded to allo-HCT.
    - Out of four evaluable previously untreated HR-MDS with TP53m patients, there was one confirmed complete response (3 mg/kg), one marrow complete response (1 mg/kg), and two stable diseases (n=1 at 1 mg/kg, n=1 at 6 mg/kg). Two patients subsequently proceeded to allo-HCT.
- **SL-172154 had an acceptable safety profile as monotherapy and in combination with AZA.**
    - Infusion-related reactions (IRRs) were the most common SL-172154-related treatment-emergent AEs (TEAEs) and were reported in 13 patients (68%) as monotherapy and 8 patients (44%) in combination with AZA.
    - Other TEAEs observed were increased AST (aspartate aminotransferase) (4; 21%), ALT (alanine aminotransferase) (3; 16%) and nausea (3; 17%) in monotherapy cohorts, and nausea (3; 17%) in combination cohorts. All events of increased AST/ALT were transient.
    - SL-172154 in combination with AZA had an acceptable safety profile with one dose-limiting toxicity event at 6mg/kg of SL-172154. The dose of 3 mg/kg is being evaluated in the dose expansion.
- **CD47 and CD40 target engagement and CD40-dependent pharmacodynamic effects observed at the 3 mg/kg dose.**

- SL-172154 induced elevations in serum IL-12p40, IP-10, IL-8, IL-10, MIP3α, and MCP1 with greater response at 3 mg/kg compared to 1 mg/kg and similar response between 3 mg/kg and 6 mg/kg.
- In bone marrow, abundant staining of SL-172154 was observed, along with a dose-dependent increase in phagocytic cells within mature myeloid immune cell compartments. Reduction in leukemic blasts was associated with an increase in mature myeloid and phagocytic cell phenotypes.

About SL-172154
SL-172154 (SIRPα-Fc-CD40L) is an investigational ARC® fusion protein designed to simultaneously inhibit the CD47/SIRPα checkpoint interaction and activate the CD40 costimulatory receptor to bolster an anti-tumor immune response in patients with advanced cancer. Multiple Phase 1 clinical trials are ongoing for patients with PROC (NCT04406623, NCT05483933) and patients with AML and HR-MDS (NCT05275439).

About Shattuck Labs, Inc.
Shattuck Labs, Inc. (NASDAQ: STTK) is a clinical-stage biotechnology company pioneering the development of bi-functional fusion proteins as a new class of biologic medicine for the treatment of patients with cancer and autoimmune disease. Compounds derived from Shattuck's proprietary Agonist Redirected Checkpoint, ("ARC®"), platform are designed to simultaneously inhibit checkpoint molecules and activate costimulatory molecules with a single therapeutic. The company's lead SL-172154 (SIRPα-Fc-CD40L) program, which is designed to block the CD47 immune checkpoint and simultaneously agonize the CD40 pathway, is being evaluated in multiple Phase 1 trials. Shattuck has offices in both Austin, Texas and Durham, North Carolina. For more information, please visit: www.ShattuckLabs.com.

Forward-Looking Statements
Certain statements in this press release may constitute "forward-looking statements" within the meaning of the federal securities laws, including, but not limited to, the therapeutic potential, efficacy and clinical benefits of SL-172154, the safety, pharmacodynamic and tolerability profile of SL-172154, the anticipated timing of the results from our expansion cohorts, and potential clinical benefit of our product candidates. Words such as "may," "might," "will," "objective," "intend," "should," "could," "can," "would," "expect," "believe," "design," "estimate," "predict," "potential," "develop," "plan" or the negative of these terms, and similar expressions, or statements regarding intent, belief, or current expectations, are forward-looking statements. While we believe these forward-looking statements are reasonable, undue reliance should not be placed on any such forward-looking statements, which are based on information available to us on the date of this release. These forward-looking statements are based upon current estimates and assumptions and are subject to various risks and uncertainties (including, without limitation, those set forth in our filings with the U.S. Securities and Exchange Commission (the "SEC")), many of which are beyond our control and subject to change. Actual results could be materially different. Risks and uncertainties include: global macroeconomic conditions and related volatility, expectations regarding the initiation, progress, and expected results of our preclinical studies, clinical trials and research and development programs; expectations regarding the timing, completion and outcome of our clinical trials; the unpredictable relationship between preclinical study results and clinical study results; the timing or likelihood of regulatory filings and approvals; liquidity and capital resources; and other risks and uncertainties identified in our Annual Report on Form 10-K for the year ended December 31, 2022, and subsequent disclosure documents filed with the SEC. We claim the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. We expressly disclaim any obligation to update or alter any statements whether as a result of new information, future events or otherwise, except as required by law.

The Company intends to use the investor relations portion of its website as a means of disclosing material non-public information and for complying with disclosure obligations under Regulation FD.

Investor & Media Contact:
Conor Richardson
Vice President of Investor Relations
Shattuck Labs, Inc.
InvestorRelations@shattucklabs.com

Source: Shattuck Labs, Inc.