NEWS RELEASE

Shattuck Labs Announces Positive Initial Topline Data from Ongoing Phase 1 A/B Dose Expansion Clinical Trial of SL-172154 with Azacitidine in Frontline Higher-Risk Myelodysplastic Syndromes (HR-MDS) and TP53 mutant (TP53m) Acute Myeloid Leukemia (AML) Patients

2023-12-13

– Observed 79% Objective Response Rate (ORR) in frontline HR-MDS patients, primarily with TP53 mutations; initial complete response (CR)/marrow complete response (mCR) rate of 64% –

– Observed 27% initial CR/complete response with incomplete hematologic recovery (CRi) in frontline TP53m AML patients, and 5/11 evaluable patients achieved stable disease with decreasing blast counts and peripheral blood count improvement, these patients continue on treatment –

– SL-172154 demonstrated an acceptable safety and tolerability profile as a monotherapy and in combination with azacitidine (AZA) –

– Shattuck to host conference call and webcast today, December 13, 2023 at 8:00 a.m. ET –

AUSTIN, TX & DURHAM, NC, Dec. 13, 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 initial topline dose-expansion data from its ongoing Phase 1A/B clinical trial of SL-172154 in combination with AZA in frontline HR-MDS and TP53m AML patients. Initial data from the dose-expansion cohorts build on the complete dose-escalation data featured in a poster presentation on December 11, 2023 at the 65th ASH Annual Meeting.

“Both the frontline HR-MDS and TP53m AML expansion cohorts enrolled quickly after completion of the dose escalation study in the middle of this year, and we are pleased to share initial efficacy data,

which begin to demonstrate the activity of SL-172154 beyond what is expected of AZA alone. In dose escalation, we saw a monotherapy response to SL-172154 in a heavily pre-treated relapsed/refractory (R/R) TP53m AML patient that allowed the patient to receive a stem cell transplant. That patient remains disease free." said Dr. Lini Pandite, MBChB, M.B.A., Chief Medical Officer of Shattuck. "In frontline, the rate of complete responses in both the HR-MDS and TP53m AML cohorts is already encouraging, and when coupled with the observation of peripheral blood count recovery in most patients that have not yet achieved a complete response, and the fact that many of these patients are very early in their course of treatment and have not yet reached the median time at which a complete response is expected for azacitidine, suggests that the complete response rate may continue to improve in the coming months. As a result, we have amended both studies to increase the sample size and look forward to providing another update by mid-year 2024."

Phase 1B Trial of SL-172154 in Frontline TP53m AML and HR-MDS
Key takeaways: Early efficacy observed for SL-172154 in combination with AZA in previously untreated HR-MDS and TP53m AML:

- **HR-MDS**: In 14 evaluable patients with previously untreated HR-MDS (13 of whom had TP53m or deletion), five patients achieved a CR. Four patients achieved a mCR (3 with hematologic improvement in at least one lineage), and two patients achieved stable disease (both with hematologic improvement in at least one lineage).
- **TP53m AML**: In 11 evaluable patients with previously untreated TP53m AML, two patients achieved a CR. Another patient achieved a CRi and was taken to allogeneic hematopoietic cell transplantation (allo-HCT). Seven additional subjects with stable disease had blast reductions, five of which had recovery of platelets or neutrophils and remain on study and their response may improve. One subject died during the first cycle.
- **Safety**: Preliminary data suggest that SL-172154 has an acceptable safety and tolerability profile in combination with azacitidine.
- **Data Overview:** As of the data cut-off date of December 1, 2023, 14 frontline patients enrolled in the TP53m AML cohort, and 22 frontline patients enrolled in the HR-MDS cohort. Initial enrollment was completed in the fourth quarter of 2023 and Shattuck has elected to expand the cohorts with additional data expected mid-year 2024.
- **Preliminary signs of anti-tumor activity:** Early signals of activity, in the form of rapid blast count reductions, were observed in 100% of frontline TP53m AML patients treated with SL-172154 in combination with AZA who received an on-treatment bone marrow biopsy. Most patients in the HR-MDS cohort showed blast count reductions with hematologic improvement early in the treatment course.
- **SL-172154 had an acceptable safety and tolerability profile:** Infusion-related reactions (IRRs) were the most common SL-172154 related treatment-emergent adverse events (TEAEs).
    - In the TP53m AML and HR-MDS cohorts, IRRs were reported in seven patients (50%) and seven patients (32%) respectively.
    - Grade 3 or 4 AEs related to SL-172154 were reported in two patients (14%) in TP53m AML and four patient (18%) in HR-MDS, including IRR (2), increased AST (1), increased ALT (1), fatigue (1), hypoxia (1), pneumonia (1), chondrocalcinosis (1), and febrile neutropenia (1). There were no reports of destructive anemia.
    - In the TP35m AML expansion cohort, there was one Grade 5 AE of cardiac arrest reported in one patient with history of coronary artery disease, recent arrhythmia, and hypokalemia in the setting of amiodarone use. In the HR-MDS cohort, there were no Grade 5 AEs related to SL-172154 reported.

Phase 1A Trial of SL-172154 in R/R AML and HR-MDS and Frontline TP53m HR-MDS
A copy of the ASH presentation, titled "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)," is

accessible under posters in the "Our Science" section of Shattuck's website.

Key takeaways: Anti-tumor responses were observed as monotherapy and in combination with AZA. SL-172154 alone and in combination with AZA had an acceptable safety profile, consistent with the safety profile of the individual agents (see SL-172154 safety above). No destructive anemia was observed.

- **Data Overview**: As of the data cut-off date of September 15, 2023, 32 adult patients with R/R AML and HR-MDS 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. An additional five subjects with frontline TP53m HR-MDS received SL-172154 with AZA.
- **Preliminary signs of anti-tumor 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.
    - SL-172154 monotherapy activity (Morphologic Leukemia-Free State) was observed in a heavily pretreated R/R AML patient and subsequently proceeded to allo-HCT.
        - Patient achieved MLFS (blast reduction from 19% to <5%) after one cycle of SL-172154.
    - Anti-tumor activity was also observed in combination with AZA in previously untreated TP53m HR-MDS patients. Out of four evaluable previously untreated TP53m HR-MDS patients, there was one CR and one mCR. One patient with mCR and one patient with SD proceeded to allo-HCT. The patient in a CR remains in a CR long term.

Conference Call at 8:00 a.m. ET Today
Shattuck will host a conference call today at 8:00 a.m. ET featuring key opinion leader Dr. Naval Daver, MD, (Professor, Director Leukemia Research Alliance Program, Department of Leukemia, The University of Texas MD Anderson Cancer Center, Houston, TX) to present the initial data from the frontline expansion cohorts in HR-MDS and TP53m AML. Additionally, a review of data from the poster presentation featured at the 65th ASH Annual Meeting will be discussed. To listen to the live webcast, please visit the Investor Relations page of the Shattuck Labs website here. Participants may register for the call here. While not required, interested participants are encouraged to join 10 minutes prior to the start of the event.

A replay of the webcast will be available following the conclusion of the live call and will be accessible on the Company's website.

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 clinical benefit of SL-172154 in frontline HR-MDS and TP53m AML patients, the safety and tolerability profile of SL-172154, and the anticipated timing of additional data from our clinical trials. 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.