NEWS RELEASE

Shattuck Labs Announces Updated Positive Interim Data from the Phase 1B Dose Expansion Clinical Trial of SL-172154 in Combination with Azacitidine (AZA) in Frontline Higher-Risk Myelodysplastic Syndromes (HR-MDS) and TP53 mutant (TP53m) Acute Myeloid Leukemia (AML) Patients

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– Observed 67% Objective Response Rate (ORR) in frontline HR-MDS patients, primarily with TP53 mutations; initial complete remission (CR)/marrow complete remission (mCR) rate of 58% and median overall survival had not yet been reached –

– Observed 43% ORR in frontline TP53m AML patients, 33% CR/complete remission with incomplete hematologic recovery (CRi) and median overall survival had not yet been reached –

– SL-172154 demonstrated a manageable interim safety profile in combination with AZA –

– Focuses clinical development opportunity in HR-MDS and TP53m AML; these indications may offer the fastest path to potential approval; enrollment underway in randomized, controlled HR-MDS cohort –

– Shattuck to host conference call and webcast today, June 14, 2024 at 7:30 a.m. ET –

AUSTIN, TX & DURHAM, NC, June 14, 2024 (GLOBE NEWSWIRE) -- Shattuck Labs, Inc. (Shattuck) (Nasdaq: STTK), a clinical-stage biotechnology company pioneering the development of bifunctional fusion proteins as a potential new class of biologic medicine for the treatment of patients with cancer and autoimmune disease, today announced updated interim data from the Phase 1B dose expansion clinical trial of SL-172154 in combination with AZA in frontline HR-MDS and TP53m AML patients. These data are to be featured in a poster presentation on June 14, 2024 at 18:00 CEST, during the European Hematology Association (EHA) 2024 Congress.

“We are pleased to present additional data from our Phase 1B dose expansion clinical trial, which further supports our differentiated mechanism of action and underscores SL-172154’s emergence as the leading CD47 inhibitor in hematologic malignancies,” said Taylor Schreiber, M.D., Ph.D., Chief Executive Officer of Shattuck. “This update shows that the rate of complete remission has improved since our last data release in December, with additional patients in both cohorts who continue to improve on therapy. As a result of these encouraging data, and our expectation of rapid enrollment and progress in our ongoing randomized, controlled cohort in HR-MDS, we are focusing our efforts on our opportunity in HR-MDS and TP53m AML. These are indications with high unmet need, limited competition, and potential for accelerated paths to approval.”

Dr. Lini Pandite, MBChB, M.B.A., Chief Medical Officer of Shattuck added, “We are encouraged by the maturing data that continues to underscore the therapeutic potential, and manageable safety profile, of SL-172154 for patients with previously untreated HR-MDS and TP53m AML. Accumulating clinical evidence now shows the pharmacodynamic contribution of CD40 activation in the peripheral blood, and an emerging correlation between clinical remission and CD40 mediated induction of certain cytokines. The TP53m AML and HR-MDS patients we have treated represent a high-risk group with short duration of complete remission and overall survival when treated with azacitidine alone. Median overall survival and duration of remission have not yet been achieved, and we look forward to sharing additional durability data later this year. Enrollment is now underway for our randomized, controlled expansion cohort in frontline HR-MDS patients, and we expect to engage in regulatory discussions later this year regarding the registrational strategy for SL-172154.”

A copy of the EHA poster, titled “Phase 1b Study of SL-172154, a Bi-functional Fusion Protein Targeting CD47 and CD40, in Combination with Azacitidine (AZA) in Previously Untreated Acute Myeloid Leukemia (AML) and Higher-Risk Myelodysplastic Syndromes/Neoplasms (HR- MDS) Patients (pts),” will be made available under posters in the Our Science section of Shattuck’s website.

Phase 1B Trial of SL-172154 in Frontline HR-MDS and TP53m AML
Key takeaways: Additional interim efficacy observed for SL-172154 in combination with AZA in frontline HR-MDS and TP53m AML.

- **HR-MDS**: As of the data cut-off date of April 23, 2024, in 24 treated patients (21 had TP53m, 16 had complex karyotype, and seven had therapy-related MDS), the ORR was 67%.
  - Ten (42%) patients achieved a CR with 3.6 months as the median time to CR.
  - Nine patients are continuing on treatment (five CR, two mCR+HI, one SD+HI, one SD).
  - Three patients proceeded to allogeneic hematopoietic cell transplantation (HCT), all three patients achieved CR prior to HCT.
- **TP53m AML**: As of the data cut-off date of June 4, 2024, in 21 treated patients (all 21 had TP53 mutations or deletion, 19 had a complex karyotype, and 14 had secondary AML) the ORR was 43%.
  - Six (29%) patients achieved a CR. One patient achieved a CRi and two patients achieved a partial remission (PR). The median time to CR was 3.8 months and none of the responders progressed as of the data cutoff.
  - Five responders (three CR, one CRi, one PR) were taken to HCT and seven patients were still undergoing treatment, including two patients in CR. Additional patients may be bridged to transplant in the coming months.
- Preliminary analysis indicates clearance of TP53 mutation in four out of five TP53m HR-MDS patients and two out of four TP53m AML patients who achieved CR and were evaluated as of the data cutoff.
- Median duration of response for OR and CR and overall survival had not yet been reached in either HR-MDS or TP53m AML as of the respective data cutoff dates.

Safety Results: As of the data cutoff date of April 23, 2024, SL-172154 showed a manageable safety profile: Infusion-related reactions (IRRs) were the most common SL-172154 treatment-emergent adverse events (TEAEs). There have been no G3 or higher IRRs when patients have been premedicated with dexamethasone. There was no evidence of hemolytic (destructive) anemia.

- **HR-MDS**:
  - Grade 3/4 AEs were reported in ten (42%) patients as related/possibly related to SL-172154: IRR (n=3), febrile neutropenia (n=2), anemia, alkaline phosphate increased, chondrocalcinosis, colitis, cytokine release syndrome, decreased appetite, fatigue, hypertension, left ventricular dysfunction, myocardial infarction (MI), neutropenia, pancytopenia, thrombocytopenia, troponin I increase, each in one patient.
  - There was one death due to AE of sepsis, deemed unrelated to SL-172154, and three treatment discontinuations due to AEs, including MI (n=1), IRR (n=1) and sepsis (n=1).
  - As already reported in the Company's May 2024 EHA abstract, a Grade 4 MI occurred in one patient who first developed sepsis on-study. This patient had a history of coronary artery disease and type II diabetes. The MI occurred eight days after the last dose of SL-172154. Although reported by the investigator as possibly related, Shattuck's assessment is that this event was unlikely related to SL-172154.
- **TP53m AML**:
  - Grade 3/4 AEs were reported in seven patients (33%), as related/possibly related to SL-172154, including neutropenia (n=3), thrombocytopenia (n=2), leukopenia (n=2), ALT increased (n=1), AST increased (n=1), enterococcal bacteremia (n=1), fatigue (n=1), hypoxia (n=1) and pneumonia (n=1).
  - There were three deaths due to AEs deemed unrelated to SL-172154 including sepsis (n=1) and pneumonia (n=2).
  - As already reported in the Company's December 2023 update for the ASH Annual Meeting, a Grade 5 cardiac arrest occurred in one patient with a history of significant cardiovascular disease, prior MI, prior stenting, prior arrhythmia, hypokalemia in the setting of amiodarone, additional adverse risk factors and other comorbidities. Although reported by the investigator as possibly related, Shattuck's assessment is that this event was unlikely related to SL-172154.

Key Takeaways from Phase 1B Trial of SL-172154 in Platinum-Resistant Ovarian Cancer (PROC)
SL-172154 in combination with pegylated liposomal doxorubicin (PLD) or mirvetuximab soravtansine (Elahere)

- Interim efficacy results as of April 23, 2024, showed four of 21 (19%) treated patients in our Phase 1B study of SL-172154 in combination with PLD have achieved partial responses. The Javelin-200 study reported an ORR of 4% with PLD alone. Two additional patients with stable disease showed maximum tumor reductions of 17% and 27% and were continuing on study. The Company is continuing to follow patients for progression free survival and overall survival.
- In our cohort combining SL-172154 with Elahere, the Company has completed enrollment. As of the April 23, 2024 data cutoff, the Company has not observed an ORR benefit beyond Elahere alone, and the Company plans to further follow patients for progression free survival and overall survival.
- Both of these combinations, SL-172154 combined with PLD and SL-172154 combined with Elahere, have shown an acceptable safety profile with IRRs as the most common treatment emergent AE as of the data cutoff.
- The Company is not currently planning to conduct additional clinical development in PROC, in part due to the evolving competitive landscape in this indication. Should progression free survival or overall survival mature favorably in either PROC cohort, we would evaluate further development in PROC at that time. Shattuck will focus all current later-stage clinical development efforts in AML and HR-MDS due to the strength of the emerging efficacy results in those patient

populations, the limited competition, and the potential for these indications to be the fastest path to registration.

Conference Call at 7:30 a.m. ET Today
Shattuck will host a conference call today at 7:30 a.m. ET featuring lead investigator Dr. Naval Daver, MD, (Professor and the Director of the Leukemia Research Alliance Program in the Department of Leukemia and MD Anderson Cancer Center in Houston, TX) to discuss the data from the poster presentation featured at the EHA 2024 Congress, including an interim safety and efficacy update from the frontline expansion cohorts in HR-MDS and TP53m AML. 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 Agonist Redirected Checkpoint (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 platinum-resistant ovarian cancer (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 potential new class of biologic medicine for the treatment of patients with cancer and autoimmune disease. Compounds derived from Shattuck's proprietary 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, statements regarding: future presentations of clinical data; clinical development plans and strategies for SL-172154; timing of anticipated clinical data; future plans for Shattuck's pipeline; and Shattuck's strategies. Words such as "anticipate," "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 the company believes 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 the company 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 Shattuck's filings with the U.S. Securities and Exchange Commission (SEC)), many of which are beyond the company's control and subject to change. Actual results could be materially different. Risks and uncertainties which could cause such outcomes to change include: global macroeconomic conditions and related volatility; expectations regarding the initiation, progress, and expected results of Shattuck's preclinical studies, clinical trials and research and development programs; the potential failure of a clinical trial to provide sufficient results to merit further development; expectations regarding the timing, completion and outcome of the company's 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 Shattuck's Annual Report on Form 10-K for the year ended December 31, 2023 and subsequent disclosure documents filed with the SEC. Shattuck claims the protection of the Safe Harbor contained in the Private Securities Litigation Reform Act of 1995 for forward-looking statements. Shattuck expressly disclaims 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.

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