NEWS RELEASE

Shattuck Labs Provides Company Update and Announces SL-325, a First-In-Class Death Receptor 3 (DR3) Antagonist Targeting the TL1A/DR3 Signaling Pathway

2024-10-01

– Interim clinical data for SL-172154 in combination with azacitidine in TP53 mutant (TP53m) acute myeloid leukemia (AML) and higher-risk myelodysplastic syndromes (HR-MDS) showed only modest improvement in median overall survival compared to azacitidine monotherapy benchmarks; further development of SL-172154 discontinued –

– Prioritization to focus on SL-325, a first-in-class antagonist antibody to DR3, the receptor for TL1A, intended for clinical development in inflammatory bowel disease (IBD); IND filing expected in Q3 2025 –

– SL-172154 associated restructuring expected to extend cash runway into 2027 –

– Company to host investor call today at 8:00 AM Eastern Time (ET) –

AUSTIN, TX and DURHAM, NC, Oct. 01, 2024 (GLOBE NEWSWIRE) -- Shattuck Labs, Inc. (Shattuck) (Nasdaq: STTK), a biotechnology company pioneering the development of novel therapeutics targeting tumor necrosis factor (TNF) superfamily receptors for the treatment of patients with cancer and chronic immune-related diseases, today announced a strategic pipeline prioritization to include the discontinuation of its clinical program, SL-172154. The Company will turn its focus to SL-325, its DR3 antagonist antibody, and plans initial clinical development in patients with IBD, where TL1A/DR3 blocking antibodies have demonstrated compelling monotherapy efficacy.

“We are disappointed that the promising complete remission rates we previously shared from our Phase 1 clinical trial did not translate to clinically meaningful improvements in median overall survival for TP53m AML and HR-MDS patients treated with SL-172154 in combination with azacitidine. We thank our clinical team and investigators for conducting an excellent clinical study, yet we must accept this result as it stands and move on to other opportunities with a higher probability of success,” said Taylor Schreiber, M.D., Ph.D., Chief Executive Officer of Shattuck.

Dr. Schreiber continued, “We are announcing a strategic shift to focus on SL-325, a DR3 antagonist antibody designed to achieve a more complete blockade of the clinically validated TL1A/DR3 signaling pathway. We believe SL-325 could be a first-in-class DR3 receptor blocking antibody, and that this approach will prove more potent than blocking TL1A, for many of the same reasons that blocking PD-1 has proven more potent than blocking PD-L1. This strategic shift in our clinical development plans and subsequent realignment of our organization with an approximate 40% reduction in workforce will allow us to use our resources most efficiently to position Shattuck for long-term success. I would like to express my gratitude to the patients who participated in our clinical trials to date as well as to the Shattuck team members who were impacted by this realignment.”

Top-line Phase 1B SL-172154 Clinical Trial Results

HR-MDS

- **Interim Overall Survival (OS)** analysis was completed on September 3, 2024.
- **Overall Survival:** Current median OS of 15.6 months. The median survival for patients with TP53m HR-MDS is currently 10.6 months and will not improve beyond 13.1 months with subsequent data cuts.
- **Benchmark Data:** Benchmark median OS of approximately 9–12 months for TP53m HR-MDS patients treated with azacitidine alone.
- **Safety and Tolerability:** No deaths have occurred in patients (n=3) without TP53m. SL-172154 showed a manageable safety profile with Infusion-Related Reactions (IRRs) as the most common SL-172154 treatment-emergent adverse events (TEAEs).

TP53m AML

- **Interim OS** analysis was completed on September 3, 2024.
- **Overall Survival:** Current median OS is 10.5 months and will not improve beyond 11.7 months with subsequent data cuts.
- **Benchmark Data:** Benchmark median OS of approximately 5-8 months for TP53m AML patients treated with azacitidine alone.
- **Safety and Tolerability:** SL-172154 showed a manageable safety profile with IRRs as the most common SL-172154 treatment-emergent adverse events TEAEs.

Corporate Updates

- **Shattuck to discontinue SL-172154 program and pivot to pipeline compound:** Approval of SL-172154 in TP53m AML and HR-MDS would require meaningful improvement in OS in large-scale, randomized studies. The Company saw only modest improvements in OS in its Phase 1 trial and historically some erosion in efficacy would be expected in larger, randomized trials. Given Shattuck’s current resources, the lack of a definitive OS benefit to date, and that no CD47 inhibitor has shown a significant efficacy signal in any indication to date, the Company has chosen to reallocate its resources to drive SL-325 through Phase 1 clinical development.
- **Shattuck and Ono Pharmaceutical Co., Ltd. mutually agree to termination of license agreement:** On September 30, 2024, Shattuck and Ono Pharmaceutical Co., Ltd. (Ono) mutually agreed to terminate the Collaboration and License Agreement dated February 13, 2024 (Collaboration Agreement). Under the Collaboration Agreement, Ono and Shattuck were collaborating on preclinical development of certain compounds. Following the mutual termination, Shattuck is no longer required to satisfy any remaining performance obligations and

will not receive any future research activity reimbursements or upfront, milestone, or royalty payments from Ono.

- **Shattuck's lead candidate, SL-325, is a potentially first-in-class DR3 antagonist antibody**: SL-325 is a DR3 blocking antibody for the treatment of IBD and other inflammatory autoimmune diseases. In preclinical studies, SL-325 demonstrates high affinity binding, superior efficacy over TL1A antibodies, and offers a data-driven rationalization for targeting the TNF receptor, DR3, versus its ligand, TL1A. Shattuck expects to file an IND for SL-325 in the third quarter of 2025.

Financial Guidance Update

As of June 30, 2024, cash and cash equivalents and investments were $105.3 million.

Shattuck has implemented a restructuring plan to prioritize the development of the Company's DR3 program. The plan is intended to optimize the Company's cost structure by aligning the size and structure of its workforce with the Company's current goals and strategy, following the discontinuation of SL-172154. Approximately 40% of Shattuck's workforce will be impacted by the changes. The Company expects to complete the reduction in force in the fourth quarter of 2024.

Given the changes to Shattuck's operations and cost structure, the Company believes its cash and cash equivalents and investments will be sufficient to fund its planned operations into 2027, beyond results from its planned Phase 1 clinical trial of SL-325. This cash runway guidance is based on the Company's current operational plans and excludes any additional capital that may be received, proceeds from potential business development transactions, and/or additional costs associated with additional development activities that may be undertaken.

Shattuck Labs Investor Call and Webcast

Shattuck will host a conference call and webcast at 8:00 a.m. ET on Tuesday, October 1, 2024, to discuss clinical data from SL-172154 and outline a strategic pipeline prioritization to focus on SL-325, a first-in-class DR3 antagonist targeting the TL1A/DR3 signaling pathway. Participants are invited to listen by dialing (800) 715-9871 (domestic) or +1 (646) 307-1963 (international) five minutes prior to the start of the call and providing the passcode 6989140. A live webcast presentation will be available here or on the company's website at www.ShattuckLabs.com under Events & Presentations. A replay of the webcast will be archived on the company's website following the presentation.

About Shattuck Labs, Inc.

Shattuck Labs, Inc. (Nasdaq: STTK) is a biotechnology company specializing in the development of potential treatments for autoimmune/inflammatory diseases and cancer. Shattuck is developing a potentially first-in-class antibody for the treatment of IBD and other inflammatory autoimmune diseases. Shattuck's expertise in protein engineering and the development of novel TNF receptor agonist and antagonist therapeutics come together in its lead program, SL-325, a first-in-class DR3 antagonist antibody designed to achieve a more complete blockade of the clinically validated TL1A/DR3 pathway. 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, our expectations regarding: plans for our preclinical studies, clinical trials and research and development programs, particularly with

respect to SL-325; plans for the realignment of our strategic pipeline and discontinuation of clinical development of SL-172154; the anticipated timing of any regulatory filings for SL-325; the anticipated timing of our preclinical studies and clinical trials for SL-325; the clinical benefit, safety and tolerability of SL-325; the effects of the proposed restructuring and reduction in force on the Company's results of operations and financial condition; and expectations regarding the time period over which our capital resources will be sufficient to fund our anticipated operations. 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 (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; our expectations regarding the overall benefit of the strategic prioritization of our pipeline; liquidity and capital resources; and other risks and uncertainties identified in our Annual Report on Form 10-K for the year ended December 31, 2023, 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.

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