NEWS RELEASE

Shattuck Labs to Present Complete Dose-Escalation Data from Phase 1A Monotherapy Clinical Trial of SL-172154 in Platinum-Resistant Ovarian Cancer (PROC) at the American Society of Clinical Oncology (ASCO) 2023 Annual Meeting

2023-05-25

- SL-172154 demonstrated favorable safety and tolerability profile across doses, with maximal CD47 and CD40 target engagement and CD40-dependent pharmacodynamic effects observed at the 3 mg/kg dose –

AUSTIN, TX and DURHAM, NC, May 25, 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 complete dose-escalation data from the Phase 1A monotherapy clinical trial of SL-172154 in PROC. These data will be featured in a poster presentation at the ASCO Annual Meeting, being held both virtually and in Chicago, IL from June 2-6, 2023.

“We are excited to present data at ASCO that we believe positions SL-172154 as a differentiated CD47 inhibitor and further underscores its therapeutic potential in heavily pretreated PROC patients,” said Dr. Lini Pandite, MBChB, M.B.A., Chief Medical Officer of Shattuck. “We believe SL-172154, a dual CD47 inhibitor and CD40 agonist, has a differentiated safety and pharmacodynamic profile and its hexameric structure enables CD40 activation in a fundamentally different manner than prior CD40 agonist therapies studied in humans. Preliminary analysis of pre- and on-treatment tumor biopsies further validates its mechanism of action.”

Dr. Pandite continued, “In the Phase 1A dose-escalation trial, SL-172154 had maximal CD47 and CD40 target engagement and CD40-dependent pharmacodynamic effects observed at the 3 mg/kg dose. SL-172154 had a favorable safety and tolerability profile across doses. Based on these encouraging data, we believe we have selected the optimal dose with maximal pharmacodynamic activity, which further supports our SL-172154 dose-expansion strategy in combination trials for patients with PROC. Our ongoing clinical trial of SL-172154 in combination with liposomal doxorubicin remains on track, and we

expect to share initial data midyear. Additionally, we expect to share initial data from our clinical trial of SL-172154 in combination with mirvetuximab soravtansine in the second half of 2023."

The full abstract (#5544) is accessible on the ASCO Congress portal, and additional details are provided below.

- Title: Phase 1 dose escalation study of SL-172154 (SIRPα-Fc-CD40L) in platinum-resistant ovarian cancer
- Presenter: Nehal J. Lakhani, M.D., Ph.D., START Midwest
- Format: Poster #239
- Session Title: Gynecologic Cancer
- Session Date and Time: Monday, June 5 at 1:15 p.m. CT

Key Takeaways:

- SL-172154 was generally well tolerated in heavily pretreated PROC patients.
  - While a maximum tolerated dose was not reached, one dose-limiting toxicity was reported of Grade 3 ALT at 10 mg/kg requiring dose interruption for resolution.
  - There were no fatal adverse events (AEs) and no AEs that led to drug discontinuation.
  - Infusion related reactions (IRR) were the most common drug related AE and were readily manageable. The frequency of IRR events increased with dose and slowing the rate of infusion was utilized for mitigation.
- Best response per RECIST 1.1 was stable disease in 6 (22%) patients.
- Maximal CD47 and CD40 target engagement and CD40-dependent PD effects were observed with ≥ 3 mg/kg of SL-172154.
  - SL-172154 exhibited greater than dose proportional pharmacokinetics at or above 3 mg/kg, potentially due to target saturation.
  - Dose-dependent target engagement of CD47 and CD40 on CD4 T cells and B cells, respectively, approached 100% by the 3 mg/kg dose level.
  - Significant dose-dependent increases in IL-12, along with post-dose increases in multiple other serum cytokines, including CXCL-8, CXCL-10, IL-10, CCL2, CCL20, and CCL22, concurrent with rapid dose-dependent egress of CD40+ B cells and monocytes from the peripheral blood, were maximal at ≥ 3 mg/kg.

About the Phase 1A Dose Escalation Clinical Trial
As of the data cut-off of January 3, 2023, the first-in-human, open-label, multi-center, dose-escalation clinical trial evaluated SL-172154 as monotherapy in 27 patients with advanced platinum-resistant ovarian, fallopian tube and primary peritoneal cancers. SL-172154 was administered intravenously across 5 dose levels (0.1, 0.3, 1.0, 3.0, and 10.0 mg/kg). Dose escalation followed a modified toxicity probability interval 2 design. Objectives included evaluation of safety, dose-limiting toxicity, recommended Phase 2 dose, pharmacokinetic and pharmacodynamic parameters, and antitumor activity.

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 with SL-172154 are ongoing, including trials for patients with PROC (NCT05483933) and 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 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. Additionally, the company is advancing a proprietary Gamma Delta T Cell Engager, GADLEN™, platform, which is designed to bridge gamma delta T cells to cell-based antigens for the treatment of patients with cancer and autoimmune disease. 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, therapeutic potential, efficacy and clinical benefits of SL-172154, the safety, pharmacodynamic and tolerability profile of SL-172154, the optimal dosing of SL-172154, SL-172154 as a potentially differentiated CD47 inhibitor, the anticipated timing of the results from our clinical trials, 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.

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