Shattuck Labs Announces Preliminary Clinical Data from Ongoing Phase 1 Clinical Trials of ARC Fusion Proteins SL-172154 and SL-279252

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– SL-279252 (PD1-Fc-OX40L) demonstrates anti-tumor activity and evidence of dose-dependent immune activation in heavily pretreated, checkpoint experienced patients –

– SL-172154 (SIRPα-Fc-CD40L) demonstrates high CD47 target occupancy and CD40 target engagement and evidence of dose-dependent immune activation in heavily pretreated platinum resistant ovarian cancer patients –

– Open IND for clinical trial of SL-172154 in acute myeloid leukemia (AML) and higher-risk myelodysplastic syndromes (HR-MDS) –

– SL-172154 and SL-279252 data to be presented at the Society for Immunotherapy of Cancer (SITC) 36th annual meeting –

– Shattuck Labs to host conference call and webcast on November 12th at 8:00 a.m. ET –

AUSTIN, Texas and DURHAM, N.C., Nov. 09, 2021 (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 with three ongoing Phase 1 clinical trials, today announced the first clinical data from its Agonist Redirected Checkpoint (ARC) platform compounds, SL-172154 and SL-279252, in patients with advanced cancer.

For SL-172154 (SIRPα-Fc-CD40L), initial monotherapy Phase 1 dose-escalation data show favorable safety and tolerability for a CD40 agonist, high levels of CD47 target occupancy and CD40 target engagement, and escalating pharmacodynamic activity in heavily pretreated, platinum resistant ovarian cancer patients. For SL-279252 (PD1-Fc-OX40L), anti-tumor activity has been observed in heavily pretreated patients, including one confirmed partial response (PR), and a second unconfirmed PR, both in patients with PD-1/L1 inhibitor pretreated non-cutaneous melanoma. Both SL-172154 and SL-279252 have been well tolerated, and a recommended Phase 2 dose has not yet been identified. These data will be presented at the Society for Immunotherapy of Cancer's 36th annual meeting being held Wednesday, November 10, 2021, to Sunday, November 14, 2021. Additional data from both programs will be presented at the meeting and on an investor call on November 12, 2021.

"We are incredibly pleased to provide our first clinical update for our ARC fusion proteins, SL-172154 and SL-279252, which are both in Phase 1 dose-escalation trials," said Lini Pandite, MBChB, M.B.A., Chief Medical Officer of Shattuck. "The preliminary anti-tumor activity in the first-in-human dose escalation of SL-279252 in a heavily pretreated, PD-L1 unselected patient population, is highly encouraging. In addition, the tolerable safety profile, near-complete target occupancy of CD47 and target engagement of CD40, and compelling pharmacodynamic effects observed give us confidence that SL-172154 has now emerged as a differentiated CD47 inhibitor. Our observations of target occupancy and safety data to date suggests that we will not be limited in continuing dose escalation to identify a recommended Phase 2 dose with maximal pharmacodynamic activity. We are also pleased to report that the Investigational New Drug application is now open to expand clinical development of SL-172154 into studies in AML and HR-MDS."

SL-172154 Clinical Update

As of the data cut-off of July 6, 2021, 14 heavily pretreated, platinum resistant ovarian cancer patients with a median of five prior therapies were treated with intravenous administration of SL-172154 across four dose levels on two schedules: Schedule 1 (day 1, 8, 15, 29, Q2 weeks) at 0.1, 0.3 mg/kg and Schedule 2 (weekly) at 0.3, 1.0, 3.0 mg/kg.

SL-172154 has been well tolerated at all dose levels, with no dose-limiting toxicities reported. Low grade infusion-related reactions occurred in 53% of subjects, however all subjects have completed dosing. A maximum tolerated dose (MTD) has not been reached and dose escalation continues to 10 mg/kg.

The serum concentration of SL-172154 has increased through 3 mg/kg, as target engagement on both CD47 and CD40 has approached nearly 100%. The terminal elimination phase has not yet been characterized, likely due to target-mediated drug disposition. Significant dose-dependent increases in IL-12, along with post-dose increases in multiple other serum cytokines, including CCL2, CCL3, CCL4, and CCL22, and concurrent with rapid margination of CD40+ B cells and monocytes from the peripheral blood have been observed. Initial analysis of pre- and on-treatment tumor biopsies suggests that intravenous infusion of SL-172154 induces increases in multiple immune populations within the tumor microenvironment.

Anti-tumor activity of CD47 inhibitors is dependent upon the presence of a pro-phagocytic "eat me" signal, which can be provided by tumor-targeted antibodies with FcγR binding function, chemotherapy, or radiation. Based on our current understanding of the combined profile of SL-172154, we plan to begin a combination study with liposomal doxorubicin in patients with platinum resistant ovarian cancer in the first half of 2022. In addition, an IND is now open to study SL-172154 as monotherapy and in combination with azacitidine in HR-MDS and TP53 mutant AML patients, as well as in combination with azacitidine and venetoclax in patients with AML. The combined data from these trials will inform Shattuck's global development strategy to progress SL-172154 to become the leading CD47- and CD40-targeted cancer immunotherapy.

SL-279252 Clinical Update

As of the data cut-off of June 11, 2021, 43 patients were enrolled and dosed intravenously with SL-279252 (median age 64 years; 56% male; median of 3 [range of 0-5] prior systemic therapies for metastatic disease). 30 patients were treated on Schedule 1 (day 1, 8, 15, 29, then every two weeks) from dose level 0.0001-6 mg/kg, and 13 patients were treated on Schedule 2 (weekly) from dose level 0.3-3 mg/kg. 58% of patients were previously treated with one or more PD-1/L1 inhibitors. Both PD-L1 and OX40 expression were low in available pre-treatment tumor biopsies. SL-279252 has

been well tolerated, with no treatment-related dose-limiting toxicities reported to date. An MTD has not been reached.

Serum concentrations of SL-279252 have increased with dose, and the PK profile suggests that OX40 and PD-L1 binding approached saturating concentrations at the 6 mg/kg dose level. A preliminary half-life of ~23 hours has been observed. As a point of reference, the approved dose of PD-L1 blocking antibodies is approximately 10-15 mg/kg. Dose-dependent increases in post-treatment margination of OX40+CD4+ T cells was noted through 6 mg/kg and accompanied by a trend toward increasing numbers of CD8+ memory T cells in the peripheral blood. Post-treatment biopsies suggest that treatment with SL-279252 was associated with large increases in CD8+ cytolytic T cells in the tumors of some patients.

A confirmed PR was observed in a patient with metastatic ocular melanoma who had received five prior lines of therapy, including a PD-1 inhibitor. An unconfirmed PR was observed in a patient with mucocutaneous melanoma who had received therapy with anti-CTLA-4 and anti-PD-1 inhibitors. Stable disease was observed in an additional 12 patients, including six patients who experienced stable disease for greater than 24 weeks.

Dose escalation is ongoing using Schedule 1, at 12 mg/kg.

Shattuck Webcast Investor Meeting

Shattuck will host a conference call and webcast at 8:00 a.m. ET on Friday, November 12, 2021, to discuss the clinical data from SL-172154 and SL-279252 and to provide a general corporate update. Participants are invited to listen by dialing (833) 614-1555 (domestic) or (516) 575-8754 (international) five minutes prior to the start of the call and providing the passcode 4068596. 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 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 cancers. Two Phase 1 clinical trials are ongoing, the first for patients with advanced and platinum resistant ovarian cancer (NCT04406623) and the second for patients with advanced squamous cell carcinoma of the head, neck or skin (NCT04502888).

About SL-279252

SL-279252 (PD1-Fc-OX40L) is an investigational ARC® fusion protein designed to simultaneously inhibit the PD-1/PD-L1 checkpoint interaction and activate the OX40 costimulatory receptor to bolster an anti-tumor immune response receptor in patients with advanced solid tumors. A Phase 1 trial in patients with solid tumors and lymphoma is ongoing (NCT03894618).

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, with three ongoing Phase 1 clinical trials. Compounds derived from Shattuck's proprietary Agonist Redirected Checkpoint, ARC®, platform simultaneously inhibit checkpoint molecules and activate costimulatory molecules within a single therapeutic. The company's SL-172154 (SIRPα-Fc-CD40L) program, which is designed to block the CD47/SIRPα checkpoint interaction and simultaneously agonize the CD40 pathway, is being evaluated in two Phase 1 trials. A second product candidate, SL-279252 (PD1-Fc-OX40L), is being evaluated in a Phase 1 trial in solid tumors or lymphomas. Additionally, the company is advancing a proprietary Gamma Delta T Cell Engager, GADLEN™, platform, which is designed to bridge gamma delta T cells to tumor antigens for the treatment of patients with cancer. 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 safety, efficacy and clinical benefit of our product candidates, the potential for our proprietary ARC technology, our expectations regarding plans for our clinical trials, the association of preclinical data with potential clinical benefit, the timing of anticipated milestones, plans and objectives of management for future operations and future results of anticipated product development efforts, and the timing of expected announcements. 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 the Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the U.S. Securities and Exchange Commission ("SEC") and other subsequent documents we file with the SEC, many of which are beyond our control and subject to change. Actual results could be materially different. 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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