Shattuck Labs Reports Third Quarter 2021 Financial Results and Recent Business Highlights

November 9, 2021

– Announced initial Phase 1 dose-escalation data from SL-172154 in ovarian cancer and SL-279252 in solid tumors at the Society for Immunotherapy of Cancer (SITC) annual meeting; both clinical trials remain ongoing –

– 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 levels of CD47 target occupancy and evidence of dose-dependent CD40-mediated immune activation –

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

– Shattuck and Takeda mutually agree to terminate Collaboration Agreement; Shattuck regains rights to clinical-stage product candidate SL-279252 –

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

AUSTIN, TX and DURHAM, NC, 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 reported financial results for the third quarter ended September 30, 2021, and provided recent business highlights.

“We designed the ARC platform to simultaneously block immune checkpoint targets and activate immune costimulatory receptors in the TNF superfamily. The clinical data presented this week at SITC demonstrate evidence of anti-tumor activity, target receptor binding, and dose-dependent immune activation specific to each of CD40 and OX40,” said Taylor Schreiber, M.D., Ph.D., and Chief Executive Officer of Shattuck. “Both compounds have been well tolerated and are demonstrating predictable dose-response relationships in humans. The doses we have explored to date remain below the recommended Phase 2 doses of benchmark CD47 inhibitors and PD-L1 inhibitors, and we look forward to continuing dose escalation of both SL-172154 and SL-279252 into dose levels that we believe will maximize the pharmacodynamic activity and anti-tumor activity of each compound.”

“We are very encouraged by the initial data from the Phase 1 trial of SL-172154. The data show an excellent safety profile, high CD47 receptor occupancy and clear evidence of CD40 engagement, which collectively differentiate SL-172154 from other CD47 inhibitors,” said Nehal Lakhani, M.D., Ph.D., South Texas Accelerated Research Therapeutics (START) Midwest, Grand Rapids, MI. “We desperately need new therapies for late-stage ovarian cancer patients, particularly in the platinum resistant setting. The combined actions of CD47 inhibition and CD40 activation provided by SL-172154 represents a strategy that has not yet been examined in this disease and may initiate anti-tumor immune responses that could provide lasting benefits in late-stage ovarian cancer.”

“SL-172154 is emerging as a highly differentiated CD47 inhibitor. The clinical data indicate that this compound can safely engage CD40 in a manner that has evaded other CD40-targeted biologics for over twenty years. At the same time, we can compare and contrast the relative potency of CD40 versus OX40 activation, and the clinical data indicate that CD40 targeting provides substantially more immunologic activity than OX40 activation. There are some parallels to these observations in the checkpoint space, where blockade of targets like LAG3, TIM3, and TIGIT has been far more subtle than blockade of CTLA-4 or PD-1,” continued Dr. Schreiber. “The current data suggests that we may be coming close to a recommended Phase 2 dose selection for SL-172154 as monotherapy. We are excited to transition to the combination with liposomal doxorubicin in ovarian cancer, and with azacitidine and venetoclax in AML, and azacitidine in higher-risk MDS and TP53 mutant AML. More importantly, these data help to establish the ARC platform more broadly as a novel class of biologic medicine, which opens opportunities for the rest of our vast pipeline of candidates developed internally at Shattuck.”

Third Quarter 2021 Recent Business Highlights and Other Recent Developments

Agonist Redirected Checkpoint (ARC) Platform Clinical-Stage Pipeline

- **Initial Data from Ongoing SL-172154 (SIRPα-Fc-CD40L) Phase 1 Dose-Escalation Clinical Trial in Platinum Resistant Ovarian Cancer Demonstrate Favorable Safety Profile and High Target Occupancy at the 36th Annual SITC Meeting:** The Phase 1 trial is an open-label, multi-center, dose-escalation study to evaluate the safety, tolerability, pharmacokinetics, anti-tumor activity, and pharmacodynamic effects of SL-172154 administered intravenously in patients with platinum resistant ovarian cancer. Shattuck will continue dose escalation to 10mg/kg.
    - Data reported at SITC was in 14 evaluable patients as of July 6, 2021, across four dose levels on two schedules: schedule 1 (day 1, 8, 15, 29, then every two weeks) at 0.1, 0.3 mg/kg and schedule 2 (weekly) at 0.3, 1.0, 3.0 mg/kg. To date, no dose limiting toxicities have been observed.
    - Preliminary pharmacodynamic parameters for SL-172154 demonstrate on-target, CD40-mediated immune activation. The binding of SL-172154 to CD40+ B cells and monocytes led to rapid activation and margination of these cells post infusion.

- High target occupancy was observed on CD47+ leukocytes at the doses studied, with preferential binding to leukocytes as compared to red blood cells.
- Cyclical increases in certain innate and adaptive serum cytokines were consistent with CD40 receptor engagement and activation following dosing. There were no notable increases in IL-6 or TNFα, or evidence of bell-shaped dose responses.
- SL-172154 has been well tolerated at doses which achieve near-complete target occupancy for both CD40 and CD47, with evidence of on-target pharmacodynamic activity which has not yet plateaued, warranting further dose escalation.

- **Combination Study of SL-172154 with Liposomal Doxorubicin Expected to Begin First Half of 2022:** A Phase 1B clinical trial of SL-172154 in combination with liposomal doxorubicin to evaluate safety, tolerability, pharmacokinetics, anti-tumor activity, and pharmacodynamics is planned to begin enrolling in the first half of 2022. Shattuck continues to evaluate additional combination agents for SL-172154 for the treatment of patients with ovarian cancer.
- **Open IND for SL-172154 in AML and HR-MDS:** Shattuck submitted an investigational new drug application to the U.S. Food and Drug Administration for a Phase 1A/B clinical trial for SL-172154 in patients with acute myeloid leukemia, or AML and, higher-risk myelodysplastic syndromes, or HR-MDS, in September. The IND is now open, and the trial will evaluate safety, tolerability, pharmacokinetics, anti-tumor activity, and pharmacodynamic effects of SL-172154, as both monotherapy and in combination. In AML, Shattuck plans to evaluate SL-172154 in combination with both azacitidine and venetoclax. In both HR-MDS and TP53 mutant AML, Shattuck plans to evaluate SL-172154 in combination with azacitidine. Initial data from the trial are expected in the second half of 2022.
- **Continued Enrollment of SL-172154 Phase 1 Clinical Trial in Squamous Cell Carcinoma of the Head and Neck or Skin:** Shattuck continues to enroll patients in a Phase 1 clinical trial for SL-172154, in patients with squamous cell carcinoma of the head and neck or skin. The Phase 1 trial is evaluating the safety, tolerability, pharmacokinetics, anti-tumor activity, and pharmacodynamic effects of SL-172154, administered intratumorally as monotherapy. Initial dose-escalation data from the trial are expected in the first half of 2022.
- **Initial Data from Ongoing SL-279252 (PD1-Fc-OX40L) Phase 1 Dose-Escalation Clinical Trial in Advanced Solid Tumors Demonstrate Evidence of Anti-Tumor Activity at the 36th Annual SITC Meeting:** The ongoing Phase 1 trial is an open-label, multi-center, dose-escalation, and dose-expansion study to evaluate the safety, tolerability, pharmacokinetics, anti-tumor activity, and pharmacodynamic effects of SL-279252 as monotherapy in patients with advanced solid tumors. Today, Shattuck reported continued enrollment at the next dose level, 12 mg/kg.

    - Data reported at SITC as of June 11, 2021, was in 43 patients, dosed intravenously, with 30 patients treated on schedule 1 (day 1, 8, 15, 29, then every 2 weeks) from dose level 0.0001-6 mg/kg, and 13 patients treated on schedule 2 (weekly) from dose level 0.3-3 mg/kg. SL-279252 was well-tolerated in heavily pretreated subjects with refractory solid tumors with no maximum tolerated dose reached. A total of 16 patients were treated at doses of 1 mg/kg or higher on schedule 1.
    - Best response was one confirmed partial response (iPR) (ocular melanoma, four prior systemic regimens, including PD-1 and CTLA-4 inhibitors) in a patient who remained on treatment for more than one year, and stable disease (iSD) in 12 patients (including 1 unconfirmed iPR). iSD for > 24 weeks occurred in 5/12 patients.
    - 58% of patients had received PD-1/L1 therapy, and of available tumor biopsies most tumors lacked PD-L1 expression as measured by TPS.
    - SL-279252 exhibited high OX40 target engagement and OX40-dependent PD effects.
    - Shattuck is currently enrolling patients with known PD-L1 positive tumors at dose levels of 12 mg/kg, to fully characterize PK, PD, and anti-tumor activity.

Corporate Updates

- **Shattuck and Takeda Mutually Agree to Termination of Collaboration Agreement:** In November 2021, Shattuck and Takeda mutually agreed to termination of the Collaboration Agreement for SL-279252 and SL-115154, originally executed in 2017. Shattuck is no longer required to satisfy any remaining performance obligations, the Company will not make any payments to or receive any future milestone or royalty payments from Takeda, and all options to license and rights of first negotiation held by Takeda under the Collaboration Agreement were terminated.
- **Changes to Shattuck's Board:** In October 2021, Shattuck announced changes to its board of directors.

    - Dr. Carrie Brownstein was appointed to the board and serves as a member of the Nominating and Corporate Governance Committee. Dr. Brownstein brings over 15 years of clinical research and development experience

having held clinical leadership roles at Roche, Regeneron, Celgene and Cellectis and as a practicing pediatric hematologist oncologist.

- Dr. George Golumbeski was appointed chairman of the Board. Dr. Golumbeski has served on Shattuck's Board as an independent director since 2018. Dr. Golumbeski replaces Josiah Hornblower as chairman of the board. Mr. Hornblower resigned from the board in October 2021.

Third Quarter 2021 Financial Results

- **Cash Position:** As of September 30, 2021, cash and cash equivalents and short-term investments were $290.2 million, as compared to $335.4 million as of December 31, 2020.
- **Research and Development (R&D) Expenses:** R&D expenses for the third quarter ended September 30, 2021, were $15.1 million, as compared to $11.8 million for the third quarter ended September 30, 2020. The increase was primarily driven by increases in clinical development, personnel-related costs, and laboratory capabilities.
- **General and Administrative (G&A) Expenses:** G&A expenses for the third quarter ended September 30, 2021, were $4.3 million, as compared to $2.5 million for the third quarter ended September 30, 2020. The increase was primarily driven by an increase in personnel related costs to support the operational expansion and costs associated with being a public company.
- **Net Loss:** Net loss was $17.4 million for the third quarter ended September 30, 2021, or $0.41 per basic and diluted share, as compared to a net loss of $11.8 million for the third quarter ended September 30, 2020, or $1.54 per basic and diluted share.

2021 Financial Guidance

Shattuck believes its cash and cash equivalents and short-term investments will be sufficient to fund its operations into the second half of 2024, which is beyond results from its Phase 1 clinical trials of SL-172154 and SL-279252. The reduction in cash runway guidance from our last issued guidance is primarily attributable to increased clinical activities for SL-172154 and ongoing process development and manufacturing to support our ongoing and future clinical trials, including the development of a manufacturing process suitable for registrational trials. This cash runway guidance is based on the Company's current operational plans and excludes any additional funding that may be received or business development or additional clinical development activities that may be undertaken.

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 immune checkpoint 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. 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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PART I - FINANCIAL INFORMATION

Item 1. Financial Statements

SHATTUCK LABS, INC.

BALANCE SHEETS

(In thousands)

	September 30, 2021 (unaudited)	December 31, 2020
Assets		
Current assets:		
Cash and cash equivalents	$ 85,094	$ 157,898
Short-term investments	205,121	177,551
Prepaid expenses and other current assets	11,429	10,190
Total current assets	301,644	345,639
Property and equipment, net	8,651	3,000
Other assets	273	349
Total assets	$ 310,568	$ 348,988
Liabilities and Stockholders' Equity		
Current liabilities:		
Accounts payable	$ 3,251	$ 1,754
Accrued expenses	13,783	7,352
Deferred revenue	2,801	7,728
Total current liabilities	19,835	16,834
Deferred revenue, net of current portion	27,277	21,306
Deferred rent	2,290	987
Total liabilities	49,402	39,127
Stockholders' equity:		
Common stock	5	5
Additional paid-in capital	387,902	382,012
Accumulated other comprehensive loss	(1,827)	(63)
Accumulated deficit	(124,914)	(72,093)
Total stockholders' equity	261,166	309,861
Total liabilities and stockholders' equity	$ 310,568	$ 348,988

SHATTUCK LABS, INC.

STATEMENTS OF OPERATIONS AND COMPREHENSIVE LOSS

(Unaudited)

(In thousands, except share and per share amounts)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Collaboration revenue - related party	$ 1,900	$ 2,435	$ (61)	$ 8,592
Operating expenses:				
Research and development	15,137	11,804	40,356	27,696
General and administrative	4,343	2,470	14,098	5,816

Expense from operations	19,480	14,274	54,454	33,512
Loss from operations	(17,580)	(11,839)	(54,515)	(24,920)
Other income (expense):				
Interest income	251	86	1,947	474
Other	(81)	(76)	(253)	(145)
Total other income	170	10	1,694	329
Net loss	$ (17,410)	$ (11,829)	$ (52,821)	$ (24,591)
Unrealized loss on short-term investments	(207)	(28)	(1,764)	(64)
Comprehensive loss	$ (17,617)	$ (11,857)	$ (54,585)	$ (24,655)
Net loss per share – basic and diluted	$ (0.41)	$ (1.54)	$ (1.26)	$ (3.21)
Weighted-average shares outstanding – basic and diluted	42,155,981	7,700,371	41,946,852	7,656,077

Source: Shattuck Labs, Inc.