NEWS RELEASE

Shattuck Labs Announces Phase 1 Results for SL-325

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- *Potentially best-in-mechanism immunogenicity profile, with only 3.7% of participants developing antidrug antibodies*
- *Complete blockade of TL1A binding to DR3 for over 3 months expected at doses of 1 mg/kg and higher*
- *Well tolerated with a favorable safety profile consistent with the TL1A inhibitor class*
- *No evidence of DR3 agonism*
- *RECEPTIVE-CD1 Phase 2b clinical trial in patients with Crohn's disease expected to initiate in the third quarter of 2026*
- *Lead bispecific product candidate, SL-846 (DR3xIL-23R), currently being evaluated in IND-enabling toxicology studies; Phase 1 initiation expected in the first half of 2027*

AUSTIN, TX and DURHAM, NC, June 08, 2026 (GLOBE NEWSWIRE) -- Shattuck Labs, Inc. (Shattuck or the Company) (NASDAQ: STTK), a clinical-stage biotechnology company pioneering the development of potential first-in-class monoclonal and bispecific DR3 blocking antibodies for the treatment of patients with inflammatory and immune-mediated diseases, today announced data from its Phase 1 clinical trial of SL-325, Shattuck's lead DR3 blocking antibody candidate.

"SL-325 is now the first antibody that blocks the receptor for TL1A, known as DR3, to generate human clinical data. The profile of SL-325 is highly encouraging, including a potentially best-in-mechanism immunogenicity profile, saturation of DR3 at low doses of SL-325, and durable inhibition of TL1A binding for months after a single dose." said Taylor Schreiber, M.D., Ph.D., Chief Executive Officer of Shattuck. "These data indicate that blocking DR3 with SL-325, or with our DR3 by IL-23 receptor blocking bispecific antibody candidate, SL-846, may substantially improve upon the efficacy shown to date with the TL1A inhibitor class, providing an opportunity to maximize potential efficacy for TL1A blockade in IBD and beyond."

Key Phase 1 Findings

The Phase 1 trial is a first-in-human, randomized, placebo-controlled trial evaluating the safety, tolerability, pharmacokinetics ("PK"), receptor occupancy ("RO"), pharmacodynamics ("PD"), and immunogenicity of SL-325 in healthy volunteers. The study enrolled 72 participants, across six single-ascending dose cohorts, with doses ranging from 0.1 mg/kg to 30.0 mg/kg, and three multiple-ascending dose cohorts, with doses ranging from 1 mg/kg to 10 mg/kg.

- **Immunogenicity:** Antidrug antibodies ("ADA") to SL-325 were detected in 3.7% [2/54] of participants who received SL-325.
    - In these two participants, ADA were low titer (≤16), and no impact to PK or receptor occupancy was observed.
    - The ADA assay used to detect ADA to SL-325 has a sensitivity of 5.0 ng/ml and drug tolerance of up to SL-325 concentrations of 160.0 µg/ml in the serum. For each participant in this Phase 1 trial, samples were analyzed over a time course, ensuring that samples from each participant fell within the dynamic range of the assay across the full dose range, and thus limiting the possibility of false negative results.
    - Published and emerging data suggest that ADA to anti-TL1A antibodies impact efficacy. SL-325's potentially best-in-mechanism immunogenicity profile is expected to lead to improved efficacy at both the induction and maintenance timepoints compared to anti-TL1A antibodies.
- **Pharmacokinetics and Receptor Occupancy:**
    - Complete DR3 occupancy, as measured by blockade of TL1A binding, was observed at doses of 0.1 mg/kg and higher in all participants.
    - Complete inhibition of TL1A binding was durable for more than 10 weeks, and extended PK modeling suggests that complete inhibition of TL1A binding may be sustained for greater than 3 months at doses of greater than1 mg/kg of SL-325.
    - The PK profile of SL-325 demonstrated proportional increases in Cmax and AUClast across all dose levels.
    - Repeated dosing demonstrated an accumulation ratio of 1.64-1.75.
    - A subcutaneous formulation of SL-325 has been developed. These Phase 1 results indicate the potential for quarterly dosing at a volume compatible with an autoinjector pen.
- **Pharmacodynamics:** Clinical data now corroborate our previous preclinical findings that SL-325 is a pure DR3 blocking antibody.
    - No evidence of DR3 agonism was observed.
    - No evidence of SL-325 mediated lymphocyte proliferation or changes in serum cytokines was observed in any participant at any dose level.
    - No increases in serum levels of TL1A from baseline were observed.
- **Safety:** SL-325 was well tolerated at all dose levels and upon repeat dosing, with a favorable safety profile consistent with the TL1A inhibitor class.
    - There were no serious treatment-emergent adverse events ("TEAEs") or serious adverse events.
    - All treatment-related adverse events ("TRAEs") were Grade 1. TRAEs were observed in 12 participants.

RECEPTIVE-CD1 Phase 2b Trial of SL-325 in Crohn's Disease

The RECEPTIVE-CD1 clinical trial is designed as a randomized, double-blind, placebo-controlled Phase 2b clinical trial to evaluate the safety and efficacy of two dose levels of SL-325 as monotherapy versus placebo in moderate-to-severe Crohn's disease. SL-325 will be administered intravenously, and the trial will include a 12-week induction period, followed by a 40-week maintenance period, for a total of 52 weeks of treatment for each patient enrolled.

- RECEPTIVE-CD1 is expected to enroll approximately 174 patients, randomized 1:1:1, with patients receiving either low dose SL-325, high dose SL-325, or placebo. RECEPTIVE-CD1 will enroll patients at clinical sites in the United States, Canada, and Europe.
- RECEPTIVE-CD1 is expected to enroll patients with moderate-to-severe Crohn's disease, as defined with a Crohn's Disease Activity Index ("CDAI") score of between 220 and 450.
- The primary endpoint is expected to be endoscopic response at Week 12, and the key secondary endpoint will be clinical remission at Week 12.
- Patients randomized to the placebo arm will be eligible to receive SL-325 after the 12-week induction period.
- The primary endpoint, endoscopic response at 12 weeks, is expected to be disclosed in the first half of 2028.

SL-846: A Dual DR3 and IL-23 Receptor Blocking Antibody

SL-846 is Shattuck's lead bispecific product candidate and is designed to simultaneously bind to DR3 and to IL-23 receptor, blocking the interaction with TL1A and IL-23, respectively, while avoiding the risk of immune complex formation and resulting ADA challenges of the TL1A-based bispecifics.

- SL-846 is an Fc-silenced, half-life extended, IgG1 bispecific antibody.
- Preclinical data demonstrated that SL-846 was equipotent, or more potent, than sequence equivalents of risankizumab and icotrokinra controls in multiple *in vitro* and cell-based potency assays.
- SL-846 is currently being evaluated in an ongoing IND-enabling GLP toxicology study in non-human primates. Safety and immunogenicity data are expected in the second half of 2026.
- Shattuck expects to submit an IND for SL-846 in the first half of 2027.

About SL-325

SL-325 is a potentially first-in-class Death Receptor 3 (DR3) blocking antibody designed to achieve a complete and durable blockade of the clinically validated DR3/TL1A pathway. Shattuck's preclinical studies demonstrate high affinity binding and superior activity over TL1A antibodies, and offer a data-driven rationale for targeting the TNF receptor, DR3, versus its ligand, TL1A. SL-325 is a fully Fc-silenced, fully human immunoglobulin G monoclonal antibody with a favorable safety profile, potentially best-in-mechanism immunogenicity profile, no evidence of residual DR3 agonism capable of providing durable blockade of TL1A binding to DR3 at low doses in a recently completed Phase 1 clinical trial. SL-325 is expected to be evaluated in a Phase 2b clinical trial in Crohn's Disease patients initiating in the third quarter of 2026.

About SL-846

SL-846 is a potentially first-in-class Death Receptor 3 (DR3) by IL-23 receptor (IL-23R) blocking bispecific antibody designed to achieve complete and durable blockade of the clinically validated DR3/TL1A and IL-23/IL-23R pathways. Shattuck's preclinical studies demonstrate high affinity binding to both DR3 and IL-23R, with equivalent or superior *in vitro* potency in comparison to benchmark IL-23 controls (sequence equivalents of risankizumab and icotrokinra) in a variety of preclinical assays. SL-846 is an Fc-silenced, half-life extended, fully human immunoglobulin G bispecific antibody currently being evaluated for safety, tolerability, immunogenicity, and pharmacodynamics in an IND-enabling GLP toxicology study in non-human primates.

About Shattuck Labs, Inc.

Shattuck Labs, Inc. is a clinical-stage biotechnology company pioneering the development of potentially first-in-class monoclonal and bispecific DR3 blocking antibodies for the treatment of patients with inflammatory and immune-mediated diseases. Shattuck's expertise in protein engineering and the development of novel TNF receptor therapeutics come together in its lead program, SL-325, a potentially first-in-class DR3 antagonist antibody designed to achieve a more complete blockade of the clinically validated DR3/TL1A pathway. The Company 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, Shattuck's expectations regarding: plans for its preclinical studies, clinical trials and research and development programs, particularly with respect to SL-325; the anticipated timing of release of data from the Company's ongoing Phase 1 clinical trial of SL-325; the anticipated timing of initiation of a Phase 2 clinical trial of SL-325 in patients with Crohn's disease; the clinical benefit, safety and tolerability of SL-325; anticipated development of additional preclinical pipeline candidates; the timing of nomination, release of preclinical data and development timelines of a lead bispecific antibody candidate; and expectations regarding the time period over which the Company's capital resources will be sufficient to fund its 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 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 it 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 its 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 the Company's preclinical studies, clinical trials and research and development programs; expectations regarding the timing, completion and outcome of the Company's preclinical studies and 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, including the time period over which current capital resources are expected to the fund the Company's operations; and other risks and uncertainties identified in Shattuck's Annual Report on Form 10-K for the year ended December 31, 2025, 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. The Company 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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