NEWS RELEASE

Shattuck Labs Announces Positive Data from the Preclinical GLP Toxicology Study of SL-325 at the 20th Congress of European Crohn's and Colitis Organization (ECCO) in Inflammatory Bowel Diseases 2025

2025-02-20

– SL-325 is a high-affinity DR3 blocking antibody being developed for the treatment of inflammatory bowel disease (IBD); No evidence of toxicity or residual agonism observed in non-human primate toxicology study –

– SL-325 receptor occupancy (RO) and pharmacokinetic (PK) profile observed suggestive of extended dosing intervals; IND filing expected in the third quarter of 2025 –

AUSTIN, TX & DURHAM, NC, Feb. 20, 2025 (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 inflammatory and immune-related diseases, today announced positive preclinical data from an IND-enabling GLP toxicology study of SL-325 in non-human primates (NHP). These data were featured in a digital oral presentation on February 20, 2025, during the 20th Congress of ECCO in Inflammatory Bowel Diseases 2025 in Berlin, Germany.

"Clinical data has continued to demonstrate that inhibition of the TL1A/DR3 signaling axis provides monotherapy complete remission rates that match or exceed those observed with IL-23 or α4β7 blocking antibodies. While DR3 blocking antibodies are technically more challenging to develop than TL1A blocking antibodies, the constitutive expression pattern and greater abundance of DR3 in IBD patients as compared to TL1A, suggests DR3 blockade may more completely neutralize the axis than TL1A blockade," said Taylor Schreiber, M.D., Ph.D., Chief Executive Officer of Shattuck. "The preclinical data shared today at ECCO from our NHP toxicology studies showed that SL-325 was very well tolerated, achieved full and durable DR3 receptor occupancy at low doses, and confirmed the absence of DR3 agonism at any dose level. Population PK modeling indicates that extended dosing intervals are likely in humans. We are excited for SL-325 to enter Phase 1 clinical trials later this year."

A copy of the ECCO digital oral presentation, titled “Pre-Clinical Development of SL-325, a High Affinity DR3 Blocking Antibody, for Durable Blockade of the DR3/TL1A Axis in Inflammatory Bowel Disease,” will be made available under the Events and Presentations section of Shattuck’s website.

Key Takeaways from Preclinical Testing of SL-325 in Non-Human Primates:

- Safety, PK, pharmacodynamics, and immunogenicity of SL-325 were evaluated in a GLP toxicology study in cynomolgus macaques over a 4-week dosing period followed by a 4-week recovery period to support a Phase 1 single ascending and multi-ascending dose trial in healthy volunteer subjects.
  - Naïve cynomolgus macaques received three doses of intravenous SL-325 (vehicle, 1 mg/kg, 10 mg/kg or 100 mg/kg dose groups), each given two weeks apart, and no evidence of toxicity or organ dysfunction was observed.
  - No-observed-adverse effect level is the top dose of 100 mg/kg.
  - No infusion-related reactions were observed in any groups.
  - No significant SL-325-related variations were noted in any clinical pathology parameter in any group, nor in the gross pathology or histopathology analysis.
- Full and durable DR3 RO was observed in peripheral blood lymphocytes at each of the three doses.
- Peripheral blood flow cytometry confirmed that there was no evidence of CD4 or CD8 T cells activation or Treg proliferation in any treated animal during the course of the study.
- Results from this preclinical study indicate that SL-325 is a high-affinity DR3 blocking antibody with no evidence of toxicity or residual agonism in cynomolgus macaques, and with an RO/PK profile suggestive of extended dosing intervals that will be studied in an upcoming Phase 1 clinical trial.
  - Projected dose and schedule in human subjects are 1 mg/kg at Q2W induction through Q4W maintenance and 3 mg/kg Q2W induction through Q8W maintenance.

About SL-325
SL-325 is a potential 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 has completed a GLP toxicology study in non-human primates, with an IND filing expected in the third quarter of 2025.

About Shattuck Labs, Inc.
Shattuck Labs, Inc. (Nasdaq: STTK) is a biotechnology company specializing in the development of potential treatments for autoimmune/inflammatory diseases. The Company is developing a potentially first-in-class antibody for the treatment of inflammatory bowel disease (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 potential 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, our expectations regarding: plans for our preclinical studies, clinical trials and research and development programs, particularly with respect to SL-325; the anticipated timing of any regulatory filings for SL-325; the anticipated timing of our preclinical studies and Phase 1 clinical trial for SL-325; the clinical benefit, safety and tolerability of SL-325; and the anticipated trial design for our Phase 1 clinical trial of SL-325. 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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