NEWS RELEASE

Shattuck Labs Announces Oral Presentation of Preclinical Data at the American Association for Cancer Research (AACR) Annual Meeting 2024

2024-04-09

– Aberrant TRIM7 expression identified as a key driver of immune checkpoint blockade (ICB) acquired resistance; inhibition of TRIM7 with small molecule inhibitors may prevent or reverse acquired resistance to PD-1/L1 blockade –

AUSTIN, TX and DURHAM, NC, April 09, 2024 (GLOBE NEWSWIRE) -- Shattuck Labs, Inc. (Shattuck) (Nasdaq: STTK), a clinical-stage biotechnology company pioneering the development of bifunctional fusion proteins as a new class of biologic medicine for the treatment of patients with cancer and autoimmune disease, today announced preclinical data demonstrating the therapeutic utility of TRIM7 inhibition to prevent or reverse acquired resistance to immune checkpoint therapy. These data were featured in an oral presentation during the AACR Annual Meeting 2024, being held from April 5-10, 2024, in San Diego, California.

“One of the largest areas of unmet medical need in oncology is in the setting of acquired resistance to checkpoint inhibitors, and we expect this to continue to grow because of the broad application of anti-PD1/PD-L1 inhibitors across multiple tumor types. Our efforts in helping to define the underlying biology of acquired resistance were recently revealed with a publication in *Cancer Cell*,” said Taylor Schreiber, M.D., Ph.D., Chief Executive Officer of Shattuck. “I am very pleased to share how our team has leveraged those biological insights to identify a novel target, TRIM7, which appears to be a mediator of the acquired resistant phenotype in mouse and human tumors, and, importantly, this has led to a development compound that reverses PD-1 acquired resistance in pre-clinical studies through specific inhibition of TRIM7. We expect that these efforts will support expansion of our oncology pipeline alongside our lead program, SL-172154.”

Presentation Details
Abstract title: Aberrant TRIM7 Expression Potentiates RACO-1 Mediated Proliferation and Dysregulated Interferon Responsiveness in the Setting of anti-PD-1 Acquired Resistance in Cancer
Location: San Diego Convention Center, San Diego, California
Presenter: Dr. George Fromm, Ph.D., Chief Scientific Officer, Shattuck Labs
Session Category: Experimental and Molecular Therapeutics

Session Title: Drug Discovery 2: New Therapies
Date/Time: Tuesday, April 9, 2024, 4:05 PM - 4:20 PM (PT)
Abstract Presentation Number: 6584

Key Takeaways

- TRIM7 is an E3 ligase which supports tumor cell proliferation downstream of KRAS signaling through ubiquitination and stabilization of RACO-1. TRIM7 also contributes to PD-1 acquired resistance through ubiquitination and degradation of STING and MAVS.
- Shattuck developed a series of small-molecule inhibitors of TRIM7 that specifically disrupt KRAS-mediated tumor cell proliferation, reverse the transcriptional phenotype of PD-1 acquired resistance, and restore sensitivity to anti-PD1 antibodies to PD-1 acquired resistant tumors in pre-clinical models.

Additional meeting information can be found on the AACR website. A copy of the AACR presentation will be available on the Investors section of the Company's website shortly after the event.

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 are designed to 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. 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, statements regarding: the potential benefit of TRIM7 inhibition alone or in combination with KRAS pathway inhibition and/or blockage of PD-L1, clinical development plans and strategies for SL-172154, future plans for Shattuck's pipeline and Shattuck's strategies. Words such as "anticipate," "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 the company 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 the company's control and subject to change. Actual results could be materially different. Risks and uncertainties which could cause such outcomes to change include: global macroeconomic conditions and related volatility; expectations regarding the initiation, progress, and expected results of Shattuck's preclinical studies, clinical trials and research and development programs; expectations regarding the timing, completion and outcome of the company's 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 Shattuck's Annual Report on Form 10-K for the year ended December 31, 2023 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. Shattuck 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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