Instil Bio Announces IND Clearance of First CoStAR-TIL program, ITIL-306, Designed to Enhance Activity in the Tumor Microenvironment

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- *FDA granted IND clearance for ITIL-306, Instil's first genetically-engineered CoStAR-TIL therapy for the treatment of NSCLC, RCC, and ovarian cancer*
- *Instil to present in vivo data with CoStAR T cells demonstrating enhanced expansion, persistence, and tumor control at the 2022 ASCO Annual Meeting*
- *ITIL-306 Phase 1 clinical study will enroll first patient with NSCLC and feature a regimen free of post-infusion IL-2*

DALLAS, May 27, 2022 (GLOBE NEWSWIRE) -- Instil Bio, Inc. ("Instil") (Nasdaq: TIL), a clinical-stage biopharmaceutical company focused on developing tumor infiltrating lymphocyte, or TIL, therapies for the treatment of patients with cancer, today announced IND clearance by the U.S. Food and Drug Administration ("FDA") of ITIL-306, Instil's first genetically-engineered Costimulatory Antigen Receptor TIL (CoStAR-TIL) therapy, as well as the presentation of supporting *in vivo* CoStAR data at the 2022 ASCO Annual Meeting.

"TILs have shown the ability to achieve complete responses in patients with solid tumors that are refractory to approved therapies, making these cells both a meaningful therapy for patients and a platform for innovation and next-generation therapies," said Bronson Crouch, Chief Executive Officer of Instil Bio. "CoStAR is designed to leverage the diversity and tumor-specificity of native TILs while enhancing their anti-tumor activity to improve the efficacy of TILs."

"TIL therapy can be limited by T cell exhaustion, which can be caused by chronic antigen stimulation in the absence of costimulation, conditions often found in the immunosuppressive tumor microenvironment," said Mark Dudley, PhD, Chief Scientific Officer of Instil Bio. "CoStAR is designed to address this challenge by providing synthetic costimulation in the tumor microenvironment to increase proliferative potential and improve the effector function of T cells, which may boost the efficacy of TILs."

ITIL-306 is an autologous TIL cell therapy engineered with a novel and proprietary Costimulatory Antigen Receptor (CoStAR) that is activated by folate receptor alpha (FRα) to provide robust costimulatory signals. CoStAR builds on the key advantages of native TILs, including their polyclonal anti-tumor reactivity, to enhance the cytokine release, cytolytic activity, and proliferation of TILs in the tumor microenvironment. The design of Instil's first-in-human Phase 1 study of ITIL-306 will enroll patients with non-small cell lung cancer (NSCLC), ovarian cancer, and renal cell carcinoma (RCC) and will start with a dose of one billion CoStAR-transduced TILs. Manufacturing for ITIL-306 will occur at Instil's Tarzana, California manufacturing facility.

"CoStAR was designed to enhance the clinical activity of TILs and expand the reach of TIL therapy into solid tumor indications which have presented challenges for immunotherapy," said Zachary Roberts, MD, PhD, Chief Medical Officer of Instil Bio. "Based on extensive preclinical data supporting a novel mechanism of action lending markedly improved function, proliferation and persistence of CoStAR-expressing cells, we have designed the initial ITIL-306 clinical regimen to feature a significantly reduced dose of lymphodepleting chemotherapy and no post-infusion IL-2, a mainstay of unmodified TIL regimens. We believe these features of the study design are a first for the TIL field and were selected to improve patient safety while maximizing CoStAR's clinical potential."

The poster presentation at the 2022 ASCO Annual Meeting will outline findings from studies evaluating anti-FOLR1 CoStAR T cells *in vitro* as well as a mouse solid tumor model *in vivo*. The poster presentation highlights results demonstrating enhanced T cell function and tumor control by CoStAR-modified T cells. Importantly, improved tumor control in a mouse solid tumor model occurred without exogenous IL-2 administration, supporting a clinical CoStAR-TIL regimen free of high-dose IL-2. CoStAR T cells showed limited upregulation of PD-1 after target exposure and demonstrated improved persistence *in vivo*.

Details of the poster presentation are as follows:

Title: Antitumor activity of T cells expressing a novel anti-folate receptor alpha (FOLR1) costimulatory antigen receptor (CoStAR) in a human xenograft murine solid tumor model and implications for in-human studies
Session Type: Poster Session
Session Title: Developmental Therapeutics—Immunotherapy
Poster: 190
Date & Time: Sunday June 5, 2022, 9:00 AM EDT
Abstract Number: 2535

Additional information about the presentation and the ASCO Annual Meeting is available on the ASCO website.

About Instil Bio

Instil Bio, Inc. (Nasdaq: TIL) is a clinical-stage biopharmaceutical company focused on developing tumor infiltrating lymphocyte, or TIL, therapies for

the treatment of patients with cancer. Instil has assembled an accomplished management team with a successful track record in the development, manufacture, and commercialization of cell therapies. Using Instil's proprietary, optimized, and scalable manufacturing processes at its in-house manufacturing facilities, Instil is advancing its lead TIL product candidate, ITIL-168, for the treatment of advanced melanoma and other solid tumors as well as ITIL-306, a next-generation, genetically-engineered TIL therapy using the CoStAR platform for multiple solid tumors. For more information visit www.instilbio.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. Words such as "anticipates," "expects," "future," "intends," "may," "target," and "will," or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning or implying the therapeutic potential of our product candidates, including ITIL-306; our research, development and regulatory plans for our product candidates; the design and timing of our ongoing and potential future clinical trials and studies and the availability of data therefrom, including our expectations concerning the enrollment and initiation of a Phase 1 study of ITIL-306; the potential for ITIL-306 to provide synthetic costimulation in the tumor microenvironment to increase proliferative potential and improve the effector function of T cells; our expectations concerning the manufacturing of ITIL-306; the potential for us to make submissions concerning, and for our product candidates to receive, regulatory approval from the FDA or equivalent foreign regulatory agencies and whether, if approved, these product candidates will be successfully distributed and marketed; and other statements that are not historical fact. Forward-looking statements are based on management's current expectations and are subject to various risks and uncertainties that could cause actual results to differ materially and adversely from those expressed or implied by such forward-looking statements, including risks and uncertainties associated with the costly and time-consuming cell therapy product development process and the uncertainty of clinical success, including risks related to failure or delays in successfully initiating, enrolling, reporting data from or completing clinical studies, as well as the risks that results obtained in pre-clinical studies or clinical trials to date may not be indicative of results obtained in ongoing or future trials and that Instil's product candidates may otherwise not be effective treatments in their planned indications; the ongoing COVID-19 pandemic, which could materially and adversely affect Instil's business and operations, including Instil's ability to timely initiate, enroll and complete its ongoing and future clinical trials; the time-consuming and uncertain regulatory approval process; additional regulatory risks associated with developing our product candidates for use in combination with other therapies or third-party product candidates; risks inherent in the manufacturing and testing of cell therapy products; the sufficiency of Instil's cash resources, and other risks and uncertainties affecting Instil and its development programs, including those discussed in the section titled "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2021 available on the SEC's website at www.sec.gov, and in our Quarterly Report on Form 10-Q for the quarter ended March 31, 2022 to be filed with the SEC. Additional information will be made available in other filings that we make from time to time with the SEC. Such risks may be amplified by the impacts of the COVID-19 pandemic. Accordingly, these forward-looking statements do not constitute guarantees of future performance, and you are cautioned not to place undue reliance on these forward-looking statements. These forward-looking statements speak only as of the date hereof, and we disclaim any obligation to update these statements except as may be required by law.

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