Instil Bio Announces Poster Presentations at the 2021 Society for Immunotherapy of Cancer (SITC) Annual Meeting

November 15, 2021

DALLAS, Nov. 15, 2021 (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 poster presentations demonstrating pre-clinical data of the CoStimulatory Antigen Receptor (CoStAR) platform at the 36th Annual Meeting of the Society for Immunotherapy of Cancer (SITC 2021), held from November 10-14, 2021. Instil also presented a Trials-in-Progress poster detailing DELTA-1, the ongoing Phase 2 study of ITIL-168 in advanced melanoma.

Pre-clinical data of the anti-FOLR1 CoStAR construct utilized in ITIL-306, Instil's first genetically-engineered CoStAR-TIL product candidate, was shown in Poster 198. The results demonstrated that CoStAR broadly enhances effector function of T cells including cytolytic activity, cytokine secretion and proliferation of T cells. CoStAR did not stimulate T cells on its own, but only increased T-cell function in the presence of signals activating both the tumor-reactive TCR and the CoStAR molecule. Additionally, data were presented that showed CoStAR was transduced at high efficiency (greater than 40%) into primary ovarian cancer TILs and effector function of CoStAR-TIL was increased over untransduced TILs when cocultured with autologous tumor cells.

The proprietary CoStAR platform utilizes intracellular CD28 and CD40 domains to deliver novel synergistic costimulatory activity to T cells. Poster 199 showcased enhanced activity of T cells engineered with dual CD28/CD40-containing CoStARs, with greater proliferation, enhanced effector function, and a superior cytokine secretion profile compared to a CD28-only CoStAR. Importantly, CoStAR-expressing T cells proliferated exponentially after exposure to tumor antigen, even in the absence of exogenous interleukin (IL)-2, a key required growth factor for T cells *in vitro*.

"These data further support our excitement for the CoStAR platform, which addresses a major challenge for solid tumor cell therapy: the lack of effective costimulation within the tumor microenvironment," said Mark Dudley, Ph.D., Head of Research at Instil. "The optimized intracellular signaling domains of our CoStAR platform include CD28 and CD40, which demonstrate superior performance over CoStARs containing only CD28."

"With the encouraging preclinical data presented at SITC, we are optimistic that CoStAR may be able to enhance the activity of TILs in patients with cancer and may eliminate the need for high doses of post-infusion IL-2, which is a frequent cause of toxicity in unmodified TIL therapy," said Zachary Roberts, M.D. Ph.D., Chief Medical Officer of Instil Bio. "We continue to look forward to the upcoming Phase 1 first-in-human study of ITIL-306 which we expect to initiate in the first half of 2022."

The company also presented a trial-in-progress poster for DELTA-1, the ongoing Phase 2 study of ITIL-168 in advanced melanoma (Poster 544).

Details of the poster presentations are as follows:

Title: **Costimulatory antigen receptor (CoStAR): a novel platform that enhances the activity of TILs**
Authors: Sukumaran S, et al.
Poster/Abstract Number: 198 / DOI: 10.1136/jitc-2021-SITC2021.198

Title: **Potent T cell costimulation mediated by a novel costimulatory antigen receptor (CoStAR) with dual CD28/CD40 signaling domains to improve adoptive cell therapies**
Authors: Sykorova M, et al.
Poster/Abstract Number: 199 / DOI: 10.1136/jitc-2021-SITC2021.199

Title: **A global, multicenter phase 2 study of ITIL-168, an unrestricted autologous TIL cell therapy, in adult patients with advanced cutaneous melanoma**
Authors: Gastman B, et al.
Poster/Abstract Number: 544 / DOI: 10.1136/jitc-2021-SITC2021.544

The posters are available on the publications section of the Instil Bio website: www.instilbio.com/publications.

About CoStAR

CoStAR (Co-Stimulatory Antigen Receptor) is a novel platform technology used to create a new class of genetically engineered TIL therapies. These modified TILs rely on their native, patient-specific T cell receptors, or TCRs, for detection of tumor-specific antigens, with significantly enhanced effector function when the CoStAR molecule is simultaneously bound to its target in the tumor microenvironment. Submission of the IND for ITIL-306, Instil's lead CoStAR-TIL product candidate which binds FOLR1 (Folate Receptor Alpha), is anticipated for the first half of 2022.

About ITIL-168

ITIL-168 is an investigational, autologous cell therapy made from tumor infiltrating lymphocytes, or TILs. Made from each patient's digested and cryopreserved tumor, ITIL-168 is a TIL cell therapy manufactured to offer an unrestricted T cell receptor (TCR) repertoire. Instil's proprietary, optimized, and scalable manufacturing process has been designed to capture and preserve the maximum diversity of each patient's TILs. By collecting the patient's tumor and immediately processing and then cryopreserving it, our process offers significant scheduling flexibility for patients and physicians at the time of both tumor resection and TIL treatment. In addition to DELTA-1, Instil plans to investigate ITIL-168 in additional solid tumor indications in Phase 1 clinical trials beginning in 2022.

About DELTA-1

DELTA-1 is a global, multicenter Phase 2 clinical trial of ITIL-168 in adult patients with advanced melanoma. Using an open-label, single-arm design, the main study cohort will evaluate the efficacy and safety of ITIL-168, when administered after a 5-day course of lymphodepleting chemotherapy and followed by up to 8 doses of high-dose interleukin-2 (IL-2), in patients whose cancer has progressed following a PD-1 inhibitor and, if positive for a BRAF-activating mutation, a BRAF inhibitor. Approximately 80 subjects are planned for enrollment and treatment in Cohort 1. Cohort 2 is anticipated to enroll approximately 25 subjects and is designed to evaluate the efficacy and safety of the regimen in patients who required discontinuation of PD-1 inhibitor(s) due to unacceptable toxicity, regardless of best overall disease response. Cohort 3 is also anticipated to enroll approximately 25 subjects and will evaluate efficacy and safety in patients whose best ongoing response to PD-1 inhibitor(s) is stable disease. Patients in Cohorts 2 and 3 whose cancer expresses a BRAF-activating mutation will be required to have experienced disease progression following BRAF inhibitor therapy. The primary endpoint of DELTA-1 is the objective response rate (ORR) according to RECIST v1.1 as assessed by independent central review. Secondary endpoints include disease control rate, duration of response, progression-free survival, overall survival, and safety.

About Instil Bio

Instil Bio, Inc. (Nasdaq: TIL) is a clinical-stage biopharmaceutical company focused on developing TIL therapies for the treatment of patients with cancer and as an innovation platform for next generation therapies. The Company has assembled an accomplished management team with a successful track record in the development, manufacture, and commercialization of cell therapies. Using the Company'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 for multiple solid tumors. For more information visit www.instilbio.com and LinkedIn.

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," "believes," "expects," "intends," "projects," and "future" or similar expressions are intended to identify forward-looking statements. Forward-looking statements include statements concerning or implying the potential of our product candidates to positively impact quality of life and alter the course of disease in the patients we seek to treat, our research, development and regulatory plans for our product candidates, the timing of our ongoing and potential future clinical trials and the availability of data therefrom, the potential for our product candidates to receive regulatory approval from the FDA or equivalent foreign regulatory agencies, whether, if approved, these product candidates will be successfully distributed and marketed, our plans to expand clinical manufacturing capabilities, and the potential benefits of orphan drug designation to ITIL-168, the adequacy of our cash resources, 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. 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. Risks regarding our business are described in detail in our Securities and Exchange Commission ("SEC") filings, including in our prospectus dated March 18, 2021, as filed with the SEC on March 22, 2021, pursuant to Rule 424(b) under the Securities Act of 1933, as amended, and the section titled "Risk Factors" in our Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 available on the SEC's website at www.sec.gov. 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. 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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