Achilles Therapeutics to Present Early Proof of Concept of Safety and Clinical Activity of Clonal Neoantigen Reactive T Cells at the ESMO Immuno-Oncology Annual Congress 2022

November 30, 2022

- Durable partial response (PR) and stable disease (SD) achieved in heavily pre-treated non-small cell lung cancer (NSCLC) patients dosed with cNeT monotherapy -

- Updated interim Phase I/II results show encouraging safety and tolerability profile with potential for deep and durable responses in NSCLC with cNeT and reduced-dose lymphodepletion and IL-2 -

- Company to host a conference call and webcast on December 6, 2022 at 8:00am ET / 1:00pm UK -

LONDON, Nov. 30, 2022 (GLOBE NEWSWIRE) -- Achilles Therapeutics plc (NASDAQ: ACHL), a clinical-stage biopharmaceutical company developing AI-powered precision T cell therapies to treat solid tumors, today announced that an abstract highlighting updated interim results from the ongoing Phase I/IIa CHIRON and THETIS clinical trials evaluating clonal neoantigen-reactive T cells (cNeT) has been accepted for a poster presentation at the ESMO Immuno-Oncology Annual Congress (ESMO IO) taking place in Geneva, Switzerland from December 7-9, 2022. cNeT are the active component of the final, precision T cell product which target tumors through recognition of a patient's clonal neoantigens present on all tumor cells.

"We are encouraged by the partial response and stable disease we have seen thus far with our cNeT monotherapy in heavily pre-treated patients with advanced NSCLC. We believe this supports the potential for deep and durable clinical responses that can ultimately help extend overall survival," said **Dr Karl Peggs, Chief Medical Officer of Achilles Therapeutics.** "The encouraging safety and tolerability profile, coupled with reduced dose lymphodepletion and IL-2 continues to support expanded application to a broader patient population. We look forward to sharing additional updated safety, activity, and translational science details at ESMO IO."

Data on 14 heavily pre-treated patients (eight patients from CHIRON with advanced NSCLC and six patients from THETIS with recurrent melanoma) that received cNeT as monotherapy and had completed at least one post-treatment scan six weeks following dosing by the abstract cut-off date will be presented. Safety and tolerability observations of cNeT compare favorably to standard tumor infiltrating lymphocytes (TIL) due to less IL-2 related toxicity. Lymphopenia and neutropenia were the most common adverse events, which are principally associated with the conditioning regimen, and no dose limiting high-grade toxicities associated with IL-2 were reported.

The best clinical response was a partial response (ongoing at week 33) in a NSCLC patient that showed an investigator-reported 57% total tumor reduction at week 24. Translational science analysis shows that peak expansion of cytokine-secreting cNeT at day 21 was coincident with signs of systemic immune activation including increased serum IL-6. Stable disease was observed in five NSCLC patients through week 12, with two patients remaining stable beyond weeks 15 and 26. Further characterization of cNeT using single cell RNA and TCR-seq suggests that cNeT products are polyclonal, with reactive T cell clusters bearing signatures of T cell proliferation, cytokine secretion, and tissue migration.

Abstract Details
Title: Early Proof of Concept of Safety and Clinical Activity of Clonal Neoantigen Reactive Cells (cNeT)
Authors: M. Forster, *et al*
Session Date and Time: December 7, 2022 from 10:00am CET (Poster Exhibition, Foyer ABC)
Abstract ID: 179P

An e-poster will be available online on December 6, 2022 at 12:00pm CET (6:00am ET / 11:00am UK) in the meeting program for conference attendees and in the Events & Presentations section of the Company website at https://ir.achillestx.com/events-and-presentations.

Webcast and Conference Call Details
The company will host a live webcast and conference call on Tuesday, December 6, 2022 at 8:00am ET / 1:00pm UK to review the interim update presented at ESMO IO. The live conference call will be webcast in listen-only mode in the Events & Presentations section of the Company website at https://ir.achillestx.com/events-and-presentations. For listeners who wish to participate in the question-and-answer session via telephone, please pre-register here.

About Achilles Therapeutics
Achilles is a clinical-stage biopharmaceutical company developing AI-Powered precision T cell therapies targeting clonal neoantigens: protein markers unique to the individual that are expressed on the surface of every cancer cell. The Company has two ongoing Phase I/IIa trials, the CHIRON trial in patients with advanced non-small cell lung cancer (NSCLC) and the THETIS trial in patients with recurrent or metastatic melanoma. Achilles uses DNA sequencing data from each patient, together with its proprietary PELEUS™ bioinformatics platform, to identify clonal neoantigens specific to that patient, and then develop precision T cell-based product candidates specifically targeting those clonal neoantigens.

About the CHIRON and THETIS Clinical Trials
CHIRON is an open-label, multi-center Phase I/IIa clinical trial evaluating the safety, tolerability, and clinical activity of cNeT therapy as a single dose in adult patients with advanced metastatic NSCLC. THETIS is an open-label, multi-center Phase I/IIa clinical trial evaluating the safety, tolerability, and clinical efficacy of cNeT therapy as a single dose in patients with recurrent or metastatic malignant melanoma as monotherapy and in combination with

a PD-1 inhibitor.

Forward-Looking Statements
This press release contains express or implied forward-looking statements that are based on our management's belief and assumptions and on information currently available to our management. Although we believe that the expectations reflected in these forward-looking statements are reasonable, these statements relate to future events or our future operational or financial performance, and involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance, or achievements to be materially different from any future results, performance or achievements expressed or implied by these forward-looking statements. The forward-looking statements in this press release represent our views as of the date of this press release. We anticipate that subsequent events and developments will cause our views to change. However, while we may elect to update these forward-looking statements at some point in the future, we have no current intention of doing so except to the extent required by applicable law. You should therefore not rely on these forward-looking statements as representing our views as of any date subsequent to the date of this press release.

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