Achilles Therapeutics Presents Encouraging Phase I/IIa Update on Clonal Neoantigen Reactive T Cells in Advanced NSCLC and Melanoma at ESMO IO Congress 2022

December 6, 2022

- Early proof-of-concept data support durable clinical benefit including confirmed partial response and stable disease in heavily pre-treated patients with advanced NSCLC -

- Safety and tolerability profile potentially expands opportunity to include patients ineligible for high dose lymphodepletion or high dose IL-2 -

- Mechanism of action informed by translational science platform's capability to correlate cNeT with anti-tumor activity -

- Additional monotherapy data and initial anti-PD-1 combination data expected in 2023 -

- Conference call and webcast today at 8:00am ET / 1:00pm UK -

LONDON, Dec. 06, 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 presented an encouraging interim Phase I/IIa update on the use of clonal neoantigen reactive T cells (cNeT) from the CHIRON study in advanced unresectable or metastatic non-small cell lung cancer (NSCLC) and the THETIS study in recurrent or metastatic malignant melanoma at the ESMO Immuno-Oncology Congress 2022 (ESMO IO).

"The early safety, tolerability, and durable clinical benefit in heavily pre-treated patients presented today are encouraging and illustrate the promising therapeutic potential of cNeT monotherapy. Further, the strength of our translational science platform was shown by our ability to track key elements of activity that correlated to cNeT presence," said **Dr Iraj Ali, CEO of Achilles Therapeutics**. "We look forward to providing further updates in 2023, including additional monotherapy data from CHIRON and THETIS, and initial THETIS combination data evaluating cNeT with a PD-1 checkpoint inhibitor."

"The partial response and stable disease observed with low doses of cNeT in this difficult to treat patient population are encouraging, and coupled with the well-tolerated safety profile, highlight a favorable therapeutic window to further dose escalate and help drive deeper, more durable responses," added **Dr. Karl Peggs, Chief Medical Officer of Achilles Therapeutics**. "We believe this is the first time a response in lung cancer has been demonstrated using a cell therapy with a low dose conditioning and IL-2 regimen, which importantly, could expand eligibility of this therapy to include patients with comorbidities or reduced fitness that may not be candidates for traditional TIL therapy."

Dr. Sergio Quezada, Chief Scientific Officer of Achilles Therapeutics added, "In addition to the durable clinical benefit, our translational science platform begins to deliver key mechanistic insights for our cNeT therapy that are not possible with a standard TIL product, including assessment of phenotypic markers as well as proliferative and cytolytic capacity of the tumor reactive cNeT component. By virtue of knowing the cNeT targets and being able to characterize and track specific cNeT in the product and in the blood of patients, we can monitor cNeT dose, markers of function and exhaustion, engraftment, activation, and other features related to the patient, product, and performance *in vivo*."

- **Early, encouraging proof-of-concept data support the potential of cNeT monotherapy to deliver durable clinical benefit**
  - 14 patients treated (8 NSCLC in CHIRON, 6 melanoma in THETIS) with median of two prior lines of therapy
  - Two additional patients dosed since ESMO IO cut-off: one in CHIRON and one in THETIS Cohort B (checkpoint combination)
- **Confirmed partial response and stable disease achieved with low doses of cNeT and reduced dose lymphodepletion and IL-2 in NSCLC**
  - 1 partial response (PR, 56% tumor reduction maintained at week 36) and 6 patients with stable disease (SD) with overall durable clinical benefit at 12 weeks in 71% of evaluable patients (5/7) with advanced NSCLC
  - cNeT driven anti-tumor activity in the partial responder is supported by T cell engraftment and cytokine profiles
  - Stable disease in 50% of evaluable patients (3/6) with melanoma
  - cNeT product characterization supports a polyfunctional active component
- **Encouraging early safety and tolerability profile for cNeT**
  - 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
  - Reduced dose lymphodepletion and IL-2 may expand patient eligibility criteria to include those with greater co-morbidities
- **Robust translational science platform correlates cNeT to activity**

- cNeT display an activated and functional phenotype including markers associated with tissue migration and a transcriptional profile supporting proliferation and cytotoxic function
- Effective lymphodepletion and subsequent immune reconstitution were observed in all patients despite lower doses of lymphodepleting agents
- Functional activity of cNeT supported by the observation of peak expansion of cytokine-secreting cNeT 21 days post infusion, coinciding with a peak in IL-6, with detection of cNeT beyond 12 weeks by TCR analysis

- **Manufacturing process evolution continues to increase cNeT doses**
  - 78 million median cNeT dose of first Process 2 products (n=3, CHIRON), with median 17% reactivity
  - 47 million median cNeT dose across patient products since last update vs. 14 million in the first eight patients reported at SITC 2021

Webcast and Conference Call Details
The company will host a live webcast and conference call today, 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 and a slide presentation will be made available 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.

Investors:
Achilles Therapeutics
Lee M. Stern, VP, IR & External Communications
l.stern@achillestx.com

LifeSci Advisors
John Mullaly
jmullaly@lifesciadvisors.com

Media:
Consilium Strategic Communications
Mary-Jane Elliott, Sukaina Virji, Melissa Gardiner
+44 (0) 203 709 5000
achillestx@consilium-comms.com