Achilles Therapeutics Presents Data at the Society for Immunotherapy of Cancer (SITC) Annual Meeting Demonstrating the Ability to Detect, Quantify and Track Patient-specific cNeT and Significant Increase in cNeT Dose from VELOS™ Process 2 Manufacturing

November 12, 2021

- Conference call and webcast scheduled for today at 8:30am ET / 1:30pm UK -

LONDON, Nov. 12, 2021 (GLOBE NEWSWIRE) -- Achilles Therapeutics plc (NASDAQ: ACHL), a clinical-stage biopharmaceutical company developing precision T cell therapies to treat solid tumors, today presented two posters at the Society for Immunotherapy of Cancer (SITC) Annual Meeting demonstrating the ability to detect, quantify, and track patient-specific clonal neoantigen-reactive T cells (cNeT) and generate increased cNeT doses from VELOS™ Process 2 manufacturing. cNeT target clonal neoantigens, which are unique targets expressed on every cancer cell within a patient but not on healthy tissue.

Samra Turajlic, MD, PhD, Chief Investigator for Achilles' Phase I/IIa THETIS trial for metastatic malignant melanoma at the Royal Marsden NHS Foundation Trust in London, UK, presented Poster 543, entitled '*Sensitive quantification and tracking of the active components of a clonal neoantigen T cell (cNeT) therapy: From manufacture to peripheral circulation'* which shows Achilles' ability to detect, quantify and track patient-specific cNeT pre- and post-infusion in the ongoing PI/IIa CHIRON and THETIS clinical trials for non-small cell lung cancer (NSCLC) and metastatic malignant melanoma, respectively. Joseph Robinson, PhD, Senior Scientist, Process Development at Achilles Therapeutics, presented Poster 193, '*The Achilles VELOS™ Process 2 boosts the dose of highly functional clonal neoantigen-reactive T cells for precision personalized cell therapies*' highlighting data from a proof-of-concept study showing an 18-fold increase in median cNeT generated from VELOS™ Process 2 compared to Process 1.

"The data we presented today continue to illustrate the differentiated profile of our cNeT product and overall platform that builds on standard TIL therapy by leveraging clonal neoantigen targeting to deliver a more precise and potent product," said **Dr Iraj Ali, Chief Executive Officer of Achilles**. "The ability to reliably detect and quantify our active component is a key differentiator of our world-class technology that is unique in the field and which we believe will be critical for the successful development of TIL-based therapies."

Engraftment Kinetics, Quantification and Tracking of cNeT in CHIRON and THETIS

Data presented from the first eight patients dosed across the first-in-human PI/IIa CHIRON and THETIS trials confirm the ability of Achilles' VELOS manufacturing process to generate fit, polyclonal cNeT that can target multiple cancer neoantigens present on all tumor cells. Achilles' platform can detect, quantify and track the patient-specific cNeT during manufacturing and post patient administration, allowing for extensive product characterization and immune-monitoring.

At the data cut-off for this presentation, five patients with melanoma (THETIS) and three patients with NSCLC (CHIRON) had received their cNeT infusion. The median age of the cohort was 57 years and patients had received a median of 2.5 lines of prior therapy. 88% (7 of 8) of the cNeT products dosed targeted multiple clonal neoantigens present on all tumor cells. In these seven products, the number of individual reactivities ranged from two to twenty-eight and cNeT were detected in the blood of 71% (5 of 7) of the patients following infusion at time points up to six weeks post dosing. Best response in the eight dosed patients was stable disease in 63% (5 of 8) in this initial, low-dose cohort generated using VELOS Process 1. The tolerability profile was generally similar to that of standard TIL products that have not been enriched for cNeT reactivity, with none of the higher-grade adverse events more commonly associated with the use of higher doses of interleukin-2 (IL-2). There were no suspected unexpected serious adverse reactions reported since the previous update on the first six patients earlier in 2021. Overall, in the cohort there were three events of cytokine release syndrome and one ICANS event deemed to be possibly related to cNeT treatment. A previously disclosed case of encephalopathy was subsequently deemed unlikely related to cNeT treatment following an Independent Data Safety Monitoring Committee review.

"The encouraging data from this low-dose cohort are important as they show how the Achilles platform can answer potency questions, gives a first look at mechanism of action in a TIL product, and adds confidence to now move to higher cell doses," said **Dr Samra Turajlic, THETIS Chief Investigator, Royal Marsden NHS Foundation Trust, London, UK**. "I look forward to exploring higher median doses from VELOS Process 2 manufacturing that should more predictably be in the anticipated therapeutic range, based on work done with other cell therapies. As we move to higher cNeT doses I expect improved cellular engraftment, both in terms of peak expansion and durability, and hope to see greater evidence of anti-tumor activity."

The median cNeT dose in patients in this low-dose, Process 1 cohort was 14.2 million cNeT, which is in line with previous updates. VELOS Process 1 manufacturing generated doses between 0.1 million and 287 million cNeT. cNeT reactivity, defined as the percentage of clonal neoantigen-reactive cells in the final dosed products, ranged from 5% to 77%. As the dataset expands and matures, these metrics of detection and expansion will be correlated with product, clinical and genomic characteristics to determine variables associated with peripheral cNeT dynamics and clinical response.

VELOS™ Process 2 Manufacturing

Achilles' VELOS Process 2 manufacturing generated an 18-fold increase in cNeT compared to Process 1 in this proof-of-concept study. The increased cNeT contained multiple polyclonal reactivities and key phenotypic features associated with high cell fitness and reduced cell exhaustion. VELOS

Process 2 improves upon Process 1 by introducing additional culture media supplementation and an expansion-boosting stimulation cocktail during the co-culture period, without adding any time to the overall manufacturing process. Complementary GMP scale manufacturing data from Process 2 will be presented at the ESMO Immuno-Oncology Congress taking place December 8-11, 2021. This GMP scale manufacturing is identical to the process for Achilles' clinical studies and formed the basis of the Company's regulatory submissions to move the ongoing clinical studies to Process 2.

"We are thrilled to see that our Process 2 generated such a robust increase in cells while maintaining a highly functional phenotype and we look forward to treating patients with higher doses manufactured using VELOS Process 2," said **Dr Sergio Quezada, Chief Scientific Officer of Achilles**. "Based on our experience with other cell therapies, we are confident that Process 2 will deliver doses able to elicit detectable clinical activity."

Achilles' proprietary potency assay enabled the quantification of the proportion of tumor reactive cNeT within the expanded TIL population. Both processes generated CD4+ and CD8+ cells able to recognize clonal neoantigens. Process 2 delivered a polyclonal product with a median of five neoantigen reactivities (range 3 to 18) detected per patient. The immunophenotype of cNeT generated by Process 1 and 2 was largely similar, with the majority of the cells bearing an effector memory phenotype. Cells generated from both processes are also functionally similar as determined by their ability to secrete INF-γ, IL-2 and TNF-α in response to polyclonal stimulus.

Poster presentations are available in the Events & Presentations section of the Company website.

Webcast and Conference Call Details
The company will host a live webcast and conference call today, Friday, November 12, 2021 at 8:30am ET / 1:30pm UK to review the SITC presentations and provide a corporate update. A slide presentation to accompany today's webcast and conference call will be available on the webcast and in the Events & Presentations section of the Company's website. The live webcast can be accessed in the Events & Presentations section of the Company's website. The conference call dial-in for investors and analysts are (833) 732-1204 (toll free within the USA), 0800 0288438 (toll free within the United Kingdom) or (720) 405-2169 (outside the USA) with the access code 4795875.

About Achilles Therapeutics
Achilles is a clinical-stage biopharmaceutical company developing 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 unresectable locally advanced and metastatic 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.

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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