Achilles Therapeutics Provides Interim Phase I/IIa Update on Clonal Neoantigen Reactive T Cells in Advanced NSCLC and Melanoma Including First Patients Dosed with Enhanced Host Conditioning

April 4, 2024

– Improved VELOS™ manufacturing process delivering higher cNeT doses –

– Protocols updated to evaluate the benefit of enhanced host conditioning, with further data expected in 2H 2024 –

– First three patients dosed in CHIRON and THETIS with enhanced host chemo-conditioning, along with IL-2 aligned to standard TIL therapy, show improved cNeT persistence and engraftment –

LONDON, April 04, 2024 (GLOBE NEWSWIRE) -- Achilles Therapeutics plc (NASDAQ: ACHL), a clinical-stage biopharmaceutical company developing AI-powered precision T cell therapies targeting clonal neoantigens to treat solid tumors, today announced interim Phase I/IIa data 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. The update includes data from 18 patients across CHIRON (n=12) and THETIS (n=6) dosed since the previous interim update in December 2022, with two CHIRON patients and one THETIS patient having received enhanced chemo-conditioning and IL-2 dosing aligned to standard tumor infiltrating lymphocyte (TIL) therapy (enhanced host conditioning) in a new Cohort C. This new Cohort C will allow the impact of enhanced host conditioning on cNeT engraftment and persistence beyond 28 days to be evaluated.

All trial participants were late-stage, checkpoint refractory patients with progressive disease at the time of lymphodepletion. The observed tolerability profiles remain favorable and similar to standard TIL therapy.

The VELOS™ manufacturing process continued to improve with a median 172 million cNeT dosed across the eighteen patients in the update compared to 18 million cNeT in the December 2022 update, with 10 products over 100 million cNeT and five over one billion cNeT.

“The updated safety, tolerability and translational science data presented today from checkpoint refractory patients continue to be encouraging and reveal important mechanistic learnings about the factors driving durable T cell engraftment and the impact of immune evasion mechanisms at an antigen level. These learnings will inform the development of cNeT and related neoantigen vaccine and TCR-T therapies,” said **Dr Iraj Ali, CEO of Achilles Therapeutics**. “We have made important progress in the optimization of our VELOS manufacturing process with a significant improvement in cNeT doses delivered and are developing our understanding of the relationship between host conditioning and the engraftment of infused cNeT. The next step is to evaluate cNeT persistence and clinical activity in patients with enhanced host conditioning, and we plan to report a meaningful data update in the second half of 2024.”

Dr. Karl Peggs, Chief Medical Officer of Achilles Therapeutics commented, “We have not seen any new objective responses since our last update, which may relate to limited cNeT persistence. With the aim of extending the duration of engraftment and prolonging the early significant peaks of cNeT seen in the blood of these patients, we introduced Cohort C to evaluate enhanced host conditioning in both studies, intensifying lymphodepletion and IL-2 dosing.”

Dr. Sergio Quezada, Chief Scientific Officer of Achilles Therapeutics added, “Emerging translational data from the three patients dosed with the enhanced conditioning show improved cNeT engraftment levels and persistence.”

- **Summary of new patients treated since the previous update**
  - 18 new patients treated since the last update (12 NSCLC in CHIRON, 6 melanoma in THETIS) with a median of two prior lines of therapy
  - Data update includes two CHIRON Cohort C (enhanced host conditioning), one THETIS Cohort C and two THETIS Cohort B patients (checkpoint combination)
  - Median cNeT dose of 172 million in the 18 patients reported since the last update with 10 of 18 patients dosed with over 100 million cNeT, including five products over one billion cNeT
- **Continued favorable tolerability profile for cNeT**
  - Tolerability observations for cNeT compare well with standard TIL therapy
  - Lymphopenia and neutropenia were the most common adverse events, which are principally associated with the conditioning regimen, and no dose limiting high-grade toxicities were observed
- **25% of higher dose (>100M cNeT) patients in CHIRON and THETIS (3 of 12) demonstrated stable disease with some reduction in tumor volume**
  - No new objective responses were observed, which is believed to relate to a lack of cNeT persistence with the previous host-conditioning regimen using lower lymphodepletion and IL-2 compared to standard TIL therapy
  - Early and significant peaks of cNeT, similar to standard TIL therapy, were observed in the blood of patients receiving reduced intensity conditioning, though with a lack of consistent cNeT persistence beyond 28 days

- **Enhanced host conditioning cohort opened in CHIRON and THETIS**
  - Enhanced host conditioning protocol Cohort C has been added to CHIRON and THETIS to evaluate an enhanced regimen of increased lymphodepletion intensity and increased IL-2 dosing on cNeT persistence and hence potentially clinical activity
  - All three patients dosed using the enhanced host conditioning regimen have shown improvement in cNeT engraftment and some tumor reduction in one case
  - TCR tracking shows more durable cNeT engraftment beyond week six in the first patient treated with enhanced host-conditioning regimen
  - A further eight patients are currently under observation with products ready for dosing with a cNeT product
- **VELOS Manufacturing process further enhanced**
  - 172 million median cNeT dose for the last 18 patients in this update compared to a median of 18 million cNeT in the December 2022 update
  - The last 10 products manufactured have delivered a median cNeT dose of 611 million

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.

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. Forward-looking statements in this press release include, but are not limited to, statements regarding the timing of the Company's clinical and translational data updates and the Company's beliefs about recent data updates, and expectations related to the Company's operating expenses and capital expense requirements. 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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