Achilles Therapeutics Announces Research Collaboration with Arcturus Therapeutics to Explore Second-Generation Personalized mRNA Cancer Vaccines

May 22, 2024

Combines Achilles' best-in-class AI-driven, tumor-targeting technology with Arcturus' world-leading self-amplifying mRNA platform

Combined technologies have the potential to generate potent and durable T cell responses in pre-clinical IND-enabling studies

LONDON, May 22, 2024 (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 a research collaboration with Arcturus Therapeutics Holdings Inc. (NASDAQ: ARCT), an mRNA medicines company, to evaluate best-in-class, self-amplifying mRNA (sa-mRNA) personalized cancer vaccines (PCVs) targeting clonal neoantigens. The research collaboration will combine Achilles' best-in-class AI-driven, tumor-targeting technology with Arcturus' world-leading sa-mRNA platform.

"This collaboration combines the unique capability of PELEUS to select targets with the highest immunogenic potential expressed by all tumour cells, together with the proven, world-class STARR vaccine platform. With this combination we aim to deliver more potent and durable responses that could positively impact the outcomes for patients," said Dr Iraj Ali, CEO of Achilles Therapeutics. "While we advance our TIL-based, clonal neoantigen reactive T cells (cNeT) programs in the ongoing CHIRON and THETIS Phase 2 trials, this collaboration allows us to leverage our neoantigen expertise in a new modality that could benefit a different group of earlier-stage patients."

The collaboration has the potential to generate IND-enabling data which demonstrate the ability of PELEUS to select multiple, highly immunogenic clonal neoantigens that can be expressed with the Arcturus STARR$^®$ platform to generate potent and durable T cell responses. Any subsequent clinical development will be jointly agreed by the parties.

About Cancer Vaccines
Tumor cells will typically express hundreds of mutations, called neoantigens, as potential targets for immunotherapy, however only a very small proportion of these are able to induce T cell responses that can lead to tumor control. Cancer vaccines aim to boost the activity of the T cells that can recognize these rare neoantigens. However, vaccine platforms are limited by the number of neoantigens they can target (typically 20-30) and it is therefore critical to select the most potent neoantigens that can activate the T cells in order to maximize the potential of delivering clinical efficacy. Achilles' PELEUS™ platform uses proprietary AI-technology to select the most immunogenic clonal neoantigens with the lowest immune evasion potential that are present on all of a patient's cancer cells.

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 PELEUS
PELEUS is a proprietary, AI-powered bioinformatics platform built and validated through exclusive access to TRACERx knowhow and genomics data. PELEUS uses sophisticated Bayesian statistical algorithms to distinguish which mutations, or neoantigens, in a patient's tumor are clonal or subclonal by analyzing DNA sequencing information from multiple tumor regions. Clonal neoantigens are protein markers that are present on all of an individual's cancer cells but are absent from healthy tissue, making them ideal cancer targets. The information from PELEUS provides the foundation for Achilles' VELOS manufacturing process to produce clonal neoantigen-reactive T cells, or cNeT.

About TRACERx
TRACERx (TRAcking Cancer Evolution through therapy (Rx)), led by Professor Charles Swanton at UCL, is one of the largest tumor evolution studies to generate deep sequencing multi-region and multi-time point genetic data from over 3,200 tumor samples from nearly 800 lung cancer patients. TRACERx has transformed the understanding of tumor evolution and has convincingly shown that tumors originate from a single cell that evolves in a Darwinian manner and the early (clonal) mutations are preserved in all subsequent primary and metastatic tumor cells. The study, which has generated numerous publications, uncovered important mechanisms of cancer evolution and immune evasion by analyzing genetic signatures in lung tumors and tracking how they evolve over time from diagnosis through to relapse. These findings provide the ability to identify a novel class of tumor markers called clonal neoantigens that are present on all tumor cells yet absent from healthy tissue, making them ideal cancer targets. TRACERx represents the largest investment in lung cancer research by Cancer Research UK and Achilles has exclusive commercial rights to the TRACERx study data for development of neoantigen-targeting cell therapies and vaccines.

About Arcturus Therapeutics
Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a global mRNA medicines and vaccines company with enabling technologies: (i) LUNAR® lipid-mediated delivery, (ii) STARR® mRNA Technology (sa-mRNA) and (iii) mRNA drug substance along with drug product manufacturing expertise. Arcturus developed the first self-amplifying messenger RNA (sa-mRNA) COVID vaccine (Kostaive®) in the world to be approved. Arcturus has an ongoing global collaboration for innovative mRNA vaccines with CSL Seqirus, and a joint venture

in Japan, ARCALIS, focused on the manufacture of mRNA vaccines and therapeutics. Arcturus' pipeline includes RNA therapeutic candidates to potentially treat ornithine transcarbamylase deficiency and cystic fibrosis, along with its partnered mRNA vaccine programs for SARS-CoV-2 (COVID-19) and influenza. Arcturus' versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines including messenger RNA, small interfering RNA, circular RNA, antisense RNA, self-amplifying RNA, DNA, and gene editing therapeutics. Arcturus' technologies are covered by its extensive patent portfolio (over 400 patents and patent applications in the U.S., Europe, Japan, China, and other countries). For more information, visit www.ArcturusRx.com. In addition, please connect with us on Twitter and LinkedIn.

About STARR®

The STARR Technology platform combines self-replicating RNA with LUNAR®, a leading nanoparticle delivery system, into a single solution to produce proteins inside the human body. The versatility of the STARR Technology enables it upon delivery into the cell to generate a protective immune response or drive therapeutic protein expression to potentially prevent against or treat a variety of diseases. The self-replicating RNA-based prophylactic vaccine triggers rapid and prolonged antigen expression within host cells resulting in protective immunity against infectious pathogens. This combination of the LUNAR and STARR technologies are expected to deliver prolonged antigen expression and stronger immune responses compared to conventional mRNA-based vaccines.

Arcturus' state-of-the-art STARR platform combines self-amplifying mRNA (sa-mRNA) with LUNAR, a leading nanoparticle delivery system. The sa-mRNA technology triggers rapid and prolonged antigen expression, promoting protective immunity against infectious pathogens at lower doses compared to first-generation mRNA vaccines. Distinct from standard mRNA vaccines, sa-mRNA vaccines instruct the target cell to make more mRNA resulting in prolonged antigen expression and stronger immune responses.

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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