Arcturus Therapeutics Presents New Clinical Data at 47th Annual European Cystic Fibrosis Conference

June 7, 2024

ARCT-032 is safe and well tolerated with no serious adverse events (SAEs) in 36 study participants, including 4 adults with cystic fibrosis (CF)

Phase 1b interim data includes a CF participant with Class 1 mutations and three participants with *F508del mutations being treated with Trikafta®*

Early trend of improved lung function with an average absolute response of +4.0% (ranging up to +9%) and relative change of +5.8% FEV1 on Day 8, after two doses of ARCT-032

Clinical data is consistent with pre-clinical CF ferret model data

SAN DIEGO--(BUSINESS WIRE)--Jun. 7, 2024-- Arcturus Therapeutics Holdings Inc. (the “Company”, “Arcturus”, Nasdaq: ARCT), a global messenger RNA medicines company focused on the development of infectious disease vaccines and medicines to treat unmet medical needs within liver and respiratory rare diseases, today presented Phase 1 results in healthy volunteers and Phase 1b interim data in people with CF for ARCT-032, an inhaled investigational mRNA therapeutic, at the 47th European Cystic Fibrosis Conference in Glasgow, Scotland.

ARCT-032 administration was generally safe and well tolerated with no serious or severe adverse events in healthy volunteers and the first four dosed participants with CF. The Phase 1b trial showed improvements in FEV1 (Forced Expiratory Volume in 1 second) in the four adults with CF after two inhaled administrations. The absolute change in percent predicted FEV1 averaged +4.0% on Day 8 (5 days after 2nd dose). The relative change in FEV1 averaged +5.8% on Day 8. The observed increases in FEV1 are encouraging and consistent with the previously reported data in the CF ferret model that demonstrated markedly improved mucociliary clearance (MCC) after a single dose of ARCT-032. Of the four participants in Phase 1b to date, one had 2 Class I mutations and the other three had F508del mutations and were being treated with Trikafta®.

Phase 1b Interim ppFEV1* Data

Subject #	Age	Sex	Genotype	On Trikafta®	Baseline ppFEV1	Day 8 ppFEV1
1	24	F	F508	Yes	83%	85%
2	43	M	F508/G85E	Yes	72%	81%
3	27	F	F508	Yes	68%	69%
4	40	F	G542X (Class I)	No	45%	49%

*ppFEV1 = percent predicted Forced Expiratory Volume in 1 second

No bronchospasm or febrile reactions were observed in the CF participants. Dose-related, mild-to-moderate febrile reactions (elevated temperature associated with headache, muscle aches, back pain, or nausea) occurred in some healthy volunteers. Dose-related transient declines in FEV1 observed in healthy volunteers were mitigated by pretreatment with albuterol, a commonly used bronchodilator. No serious adverse events or dose limiting toxicities were observed at any dose level.

“We are pleased to present positive ARCT-032 Phase 1 results and Phase 1b interim data showing that single doses at all dose levels in healthy volunteers and two doses in the first four CF participants were safe and well tolerated with no serious adverse events. It is encouraging to see favorable lung function improvements in all currently dosed CF participants in this early study,” said Dr. Juergen Froehlich, Chief Medical Officer of Arcturus Therapeutics. “We look forward to completing the Phase 1b trial shortly and to evaluate the further potential for lung function improvement of treatment with ARCT-032 in people with CF in a larger, multiple-dose clinical study.”

About Cystic Fibrosis

Cystic fibrosis is a life-shortening disease with a worldwide distribution. Mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene result in a reduction or absence of CFTR protein and/or function in the airways, causing insufficient chloride transport to maintain airway surface homeostasis. CF mucus is more difficult to clear, thus clogging the airways and leading to infection, inflammation, respiratory failure, or other life-threatening complications. Currently approved CFTR modulator therapies are designed to increase function of the CFTR channel to help reduce symptoms yet are ineffective in some people with CF because of their underlying mutations.

About ARCT-032

ARCT-032 has received Orphan Medicinal Product Designation from the European Medicines Agency (EMA) and Orphan Drug Designation from the U.S. Food and Drug Administration (FDA) to treat Cystic Fibrosis. ARCT-032 utilizes Arcturus' LUNAR® lipid-mediated aerosolized platform to deliver CFTR messenger RNA to the lungs. Expression of a functional copy of the CFTR mRNA in the lungs of people with CF has the potential to restore CFTR activity and mitigate the downstream effects that cause progressive lung disease. The ARCT-032 program is supported by preclinical data in rodents, ferrets and primates, as well as demonstrating restoration of CFTR expression and function in human bronchial epithelial cells.

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.

Forward Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact included in this press release, are forward-looking statements, including those regarding strategy, future operations, the expectations for or likelihood of success of any collaborations, the continued clinical development of ARCT-032 including the ability to complete and timing for completion of the CF Phase 1b study, likelihood of success (including safety and efficacy) of ARCT-032, the likelihood that the interim results will be predictive of future clinical results, the likelihood of sharing and timing for sharing interim and final Phase 1b data, the plans to conduct a larger, multiple-dose clinical study and the impact of general business and economic conditions. Arcturus may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in any forward-looking statements such as the foregoing and you should not place undue reliance on such forward-looking statements. These statements are only current predictions or expectations, and are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements, including those discussed under the heading "Risk Factors" in Arcturus' most recent Annual Report on Form 10-K, and in subsequent filings with, or submissions to, the SEC, which are available on the SEC's website at www.sec.gov. Except as otherwise required by law, Arcturus disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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