Arcturus Therapeutics Announces Initiation of Dosing in Phase 2 Multiple Ascending Dose Studies for Cystic Fibrosis (CF) and Ornithine Transcarbamylase (OTC) Deficiency

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First participants initiated Phase 2 dosing for both CF and OTC deficiency in December 2024

Phase 2 interim data for both mRNA therapeutic programs on track for first half of 2025

SAN DIEGO--(BUSINESS WIRE)--Jan. 6, 2025-- Arcturus Therapeutics Holdings Inc. (the “Company”, “Arcturus”, Nasdaq: ARCT), a commercial messenger RNA medicines company focused on the development of infectious disease vaccines and opportunities within liver and respiratory rare diseases, today announced that the first CF and OTC deficiency participants initiated dosing in December 2024, in the Company’s Phase 2 multiple ascending dose studies.

Each participant in the Phase 2 CF study (NCT06747858) is expected to receive daily treatments of ARCT-032 over a period of 28 days.

The first OTC deficient participant receiving 0.5 mg/kg ARCT-810 initiated dosing in December 2024 in the United States. Each participant is expected to receive five intravenous infusions administered over two months. The Company previously announced the completion of the dosing phase (N = 8; 0.3 mg/kg) in a placebo-controlled European study enrolling OTC deficient individuals and expansion of the Phase 2 clinical program of ARCT-810 into the United States with an open-label multiple-dose study (NCT06488313).

“We are very pleased with the recent progress in our Phase 2 studies in people with cystic fibrosis and OTC deficiency. ARCT-032 has the potential to address the significant unmet medical need in the CF community for those who do not qualify for or benefit from available treatment options,” said Dr. Pad Chivukula, Chief Scientific Officer of Arcturus Therapeutics. “ARCT-810 is the only mRNA therapy currently in clinical development intended to enable liver cells to produce OTC enzyme and therefore address the underlying cause of OTC deficiency.”

About Cystic Fibrosis

Cystic fibrosis is a life-shortening disease with a worldwide prevalence. 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 disruption of ion transport necessary to maintain airway surface homeostasis. CF mucus is more difficult to clear, thus clogging the airways and leading to infection, inflammation, and progressive lung damage that may ultimately result in respiratory failure. Standard of care for many CF individuals include CFTR modulators. Nearly 40,000 people in the U.S. and more than 105,000 people worldwide are living with CF. Approximately 15% of individuals with CF do not benefit from CFTR modulator medicines due to absent CFTR protein and/or drug intolerance.

About ARCT-032

ARCT-032 is an inhaled investigational mRNA therapeutic designed to express normal functional CFTR in the lungs of individuals with CF. ARCT-032 has received Orphan Medicinal Product Designation from the European Medicines Agency (EMA) and Orphan Drug Designation along with Rare Pediatric Disease 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. Lung disease is the leading cause of morbidity and mortality in people with CF. 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 the demonstration of restoration of CFTR expression and function ex-vivo in human bronchial epithelial cells.

About Ornithine Transcarbamylase Deficiency

Ornithine transcarbamylase (OTC) deficiency is the most common urea cycle disorder. Urea cycle disorders are a group of inherited metabolic disorders that make it difficult for affected patients to remove toxic waste products as proteins are digested. OTC deficiency is caused by mutations in the OTC gene which leads to a non-functional or deficient OTC enzyme. OTC is a critical liver enzyme which catalyzes an early step in the urea cycle, a metabolic process that converts ammonia to urea. This conversion does not occur properly in patients with OTC deficiency. A deficiency of the OTC enzyme in liver cells can result in high blood ammonia levels and may cause seizures, progressive neurocognitive impairment, coma, and death in untreated patients. OTC deficiency is an inherited X-linked disorder that usually presents early in life, but patients with less severe symptoms may present later in life, as adults. There is currently no cure for OTC deficiency, apart from liver transplant. However, this treatment comes with significant risk of complications such as organ rejection, and transplant recipients must take immunosuppressant drugs for the rest of their lives. The current standard of care for OTC deficiency patients is a well-controlled, but challenging to maintain, low-protein diet and treatment with nitrogen scavenging medications to try to prevent patients from accumulating ammonia. These treatments do not address the underlying cause of disease. In Europe and the U.S., approximately 10,000 people have OTC deficiency.

About ARCT-810

ARCT-810 is an intravenously administered investigational mRNA therapeutic designed to express normal functional OTC enzyme in the liver of individuals with OTC deficiency. ARCT-810 has received Orphan Medicinal Product Designation from the European Medicines Agency (EMA), including an approved pediatric investigation plan (PIP), and Orphan Drug Designation along with Rare Pediatric Disease Designation from the U.S.

Food and Drug Administration (FDA) for the treatment of ornithine transcarbamylase deficiency. OTC is a key enzyme in the urea cycle which converts toxic ammonia into urea. Elevated ammonia can lead to metabolic crises with progressive and irreversible neurocognitive damage. A safe and effective mRNA therapeutic may restore normal functional OTC enzyme in the liver which could eliminate the risk of future metabolic crises. ARCT-810 is based on Arcturus' mRNA design construct and proprietary manufacturing process. ARCT-810 also utilizes Arcturus' extensive and propriety lipid library and employs the Company's LUNAR® delivery platform to deliver OTC mRNA to hepatocytes.

About Arcturus

Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a commercial 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 KOSTAIVE®, the first self-amplifying messenger RNA (sa-mRNA) COVID vaccine 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 (OTC) deficiency and cystic fibrosis (CF), 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 likelihood of success (including safety and efficacy) of ARCT-810 or ARCT-032, the timing for interim data for both studies, the expected treatment regimens and periods in the studies, the potential for ARCT-032 to benefit null patients or other CF patients, the continued clinical development of ARCT-032 and ARCT-810, the likelihood that preclinical or clinical results received to date will be predictive of future clinical results, 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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