Arcturus Therapeutics Provides Updates for Ornithine Transcarbamylase (OTC) Deficiency and Cystic Fibrosis (CF) Programs

July 1, 2024

ARCT-810 Phase 2 study completed enrollment at 0.3 mg/kg dose level in Europe with data expected later this year

ARCT-810 to expand Phase 2 clinical program in the U.S. to enroll patients with more severe disease

ARCT-032 IND for Phase 2 multiple ascending dose study to be submitted in the next 60 days

SAN DIEGO--(BUSINESS WIRE)--Jul. 1, 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 is providing mid-year updates for ARCT-810, an investigational mRNA therapeutic to treat ornithine transcarbamylase (OTC) deficiency, and ARCT-032, an investigational inhaled mRNA therapeutic to treat cystic fibrosis (CF).

“CFTR replacement using mRNA therapeutics is an area of significant medical interest, as it may benefit null patients and potentially many other CF patients,” said Dr. Juergen Froehlich, Chief Medical Officer of Arcturus Therapeutics. “The safety profile of ARCT-032 observed in Phase 1 and after two administrations in Phase 1b for patients dosed to date, including the trend of lung function improvement in the Class I participant, is encouraging. These data are supportive of expanding our clinical program to the U.S. and other regions with a Phase 2 multiple ascending dose protocol, and I look forward to a successful conduct and outcome of this planned study. We are also excited to have started patient screening for the expansion of our ARCT-810 clinical program in the U.S. to more severely affected OTC deficiency patients.”

ARCT-810 (OTC Deficiency) Update

The double blind ARCT-810 Phase 2 study in the EU and UK has completed enrollment of eight (8) subjects, including adolescents and adults, at the 0.3 mg/kg dose level. The participants in this group are randomized 3:1 and receive 6 doses of ARCT-810 or placebo administered every 14 days. Treatment and follow-up are ongoing with the safety and complete set of biomarker data expected later this year.

ARCT-810 is expanding the Company’s clinical program in the U.S. by enrolling patients with more severe disease. Patient screening has been initiated and the Company expects the Phase 2 clinical program to be completed in the United States. More details pertaining to the U.S. trial expansion and interim data will be provided later this year.

ARCT-032 (CF) Update

The Company plans to submit an IND application in the next 60 days for an ARCT-032 Phase 2 multiple ascending dose study designed to identify a safe and effective dose in Class I (null) and other CF participants who do not benefit from CFTR modulators. This study is supported by safety and tolerability data collected in healthy volunteers (N = 32) and the ongoing two-administration Phase 1b study. No serious adverse events (SAEs) have been observed in any clinical trial participants to date. No febrile reactions have been observed within the target dose range of the planned Phase 2 study. The Phase 1b study is ongoing with the seventh and final participant scheduled to be dosed soon. Of the seven total CF participants in Phase 1b, six are receiving CFTR modulator treatment while one subject has Class I mutations and therefore does not benefit from modulator therapy. The Class I CF subject had low lung function at baseline (ppFEV1 below 50%) and showed an improvement of 4% in ppFEV1 on Day 8, after receiving two well-tolerated administrations, with no febrile reactions.

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 enzyme in the urea cycle, which takes place in liver cells, and together with the other enzymes in the urea cycle converts ammonia to urea. This conversion does not occur properly in patients with OTC deficiency and ammonia accumulates in their blood, acting as a neurotoxin and liver toxin. A lack of the OTC enzyme in liver cells can results in high blood ammonia levels and cause seizures, coma, and death in untreated patients. OTC deficiency is an inherited disease that can cause developmental problems, seizures and death in newborn babies. It is an X-linked disorder, so is more common in males. 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. Current standard of care for OTC deficiency patients is a well-controlled, but challenging to maintain, low-protein diet and treatment with ammonia scavengers to try and 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 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 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. 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 dysfunctional or 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 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 likelihood of success (including safety and efficacy) of ARCT-810 or ARCT-032, the likelihood that the trend of lung function changes in the Class I participant for ARCT-032 will continue or provide meaningful efficacy, the expected timing for the safety and biomarker data for ARCT-810, the planned expansion of the ARCT-810 clinical program and the Company's ability and decision to enroll and conduct such expansion, the continued clinical development of ARCT-810, the potential for CFTR replacement to benefit null patients or other CF patients, the continued clinical development of ARCT-032 including the likelihood of and timing for submission of an IND for and plans to conduct a Phase 2 study, the likelihood that clinical results received to date (including data in the ARCT-032 Phase 1b study) will be predictive of future clinical results or sufficient to further advance the CF program, the likelihood of and timing for expanding the CF clinical program 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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