Arcturus Therapeutics Receives Orphan Drug Designation from the U.S. FDA for ARCT-810, for Treatment of Ornithine Transcarbamylase (OTC) Deficiency

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SAN DIEGO, June 27, 2019 (GLOBE NEWSWIRE) -- Arcturus Therapeutics Holdings Inc. (NASDAQ: ARCT), a leading RNA medicines company focused on the development and commercialization of therapeutics towards rare, liver and respiratory diseases with significant unmet medical need, today announced the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation for the Company's lead product candidate ARCT-810 to treat ornithine transcarbamylase deficiency (OTCD). OTCD is the most common urea cycle disorder. Urea cycle disorders are a group of inherited metabolic disorders that make it difficult for afflicted patients to remove toxic waste products, as proteins are digested. ARCT-810 utilizes Arcturus' LUNAR® lipid-mediated delivery platform to safely and effectively deliver OTC messenger RNA to liver cells.

The FDA grants Orphan Drug Designation to novel drugs that seek to treat a rare disease or condition and provides 7 years of market exclusivity if approved, plus significant development incentives, including tax credits related to clinical trial expenses, an exemption from the FDA-user fee, and FDA assistance in clinical trial design.

“Orphan Drug Designation is a very important regulatory milestone in our development plan for ARCT-810,” said Joseph Payne, President and Chief Executive Officer of Arcturus Therapeutics. "We are working diligently to address the significant unmet medical need in people afflicted by OTC deficiency and this designation furthers our mission to develop a mRNA therapeutic product utilizing our LUNAR technology.”

“OTC deficiency is a life-threatening genetic disease. Current treatment options involve life-long restriction of protein intake, nitrogen scavenger therapy as well as liver transplant for those patients that are suitable,” said Pad Chivukula, Ph.D., Chief Scientific Officer of Arcturus. “Our therapeutic approach, based on our LUNAR platform, is designed to enable OTC-deficient patients to naturally produce healthy functional OTC enzymes in their own liver cells. By intervening directly in the underlying disease process, ARCT-810 has the potential to be a transformative messenger RNA therapy for these patients.”

About ARCT-810
ARCT-810, Arcturus’ first development candidate, represents a novel approach to treat ornithine transcarbamylase deficiency (OTCD). ARCT-810 is based on Arcturus mRNA design construct and proprietary manufacturing process. ARCT-810 also utilizes Arcturus’ propriety lipid library and employs the Company's LUNAR® delivery platform to safely and effectively deliver OTC mRNA to hepatocytes. ARCT-810 is an mRNA replacement therapy designed to enable OTC-deficient patients to naturally produce healthy functional OTC enzyme in their own liver cells. Arcturus plans to submit an Investigational New Drug (IND) application to the FDA in the first quarter of 2020. ARCT-810 is advancing toward the clinic on the strength of preclinical proof-of-concept data, demonstrating that LUNAR technology can deliver mRNA to liver cells and results in expression of functional OTC protein in animal models. Replacing the deficient OTC protein restores the urea cycle pathway, resulting in reduced plasma ammonia and urinary orotate concentrations.

About Ornithine Transcarbamylase Deficiency (OTCD)
OTC deficiency is caused by mutations in the OTC gene which leads to a non-functional or deficient OTC enzyme. OTCD is the most common urea cycle disorder. Urea cycle disorders are a group of inherited metabolic disorders that make it difficult for afflicted patients to remove toxic waste products as proteins are digested. OTC deficiency is a life-threatening genetic disease. OTC is a critical enzyme in the urea cycle, which takes place in liver cells, and 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. This can cause severe symptoms including vomiting, headaches, coma and death. 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 patients is a low-protein diet and ammonia scavengers to try and prevent patients from accumulating ammonia. These treatments do not address the underlying cause of disease.

About Arcturus Therapeutics Holdings Inc.
Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (NASDAQ: ARCT) is an RNA medicines company with enabling technologies – LUNAR® lipid-mediated delivery and Unlocked Nucleomonomer Analog (UNA) chemistry – and mRNA drug substance along with drug product manufacturing. Arcturus’ diverse pipeline of RNA therapeutics includes programs to potentially treat Ornithine Transcarbamylase (OTC) Deficiency, Cystic Fibrosis, Glycogen Storage Disease Type 3, Hepatitis B, and non-alcoholic steatohepatitis (NASH). Arcturus’ versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines including messenger RNA, small interfering RNA, replicon RNA, antisense RNA, microRNA, DNA, and gene editing therapeutics. Arcturus technologies are covered by its extensive patent portfolio (167 patents and patent applications, issued in the U.S., Europe, Japan, China and other countries). Arcturus’ commitment to the development of novel RNA therapeutics has led to partnerships with Janssen Pharmaceuticals, Inc., part of the Janssen Pharmaceutical Companies of Johnson & Johnson, Ultragenyx Pharmaceutical, Inc., Takeda Pharmaceutical Company Limited, Synthetic Genomics Inc. and the Cystic Fibrosis Foundation. For more information, visit www.Arcturusrx.com.

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 regarding

strategy, future operations, collaborations, future financial position, prospects, plans and objectives of management, the likelihood of success of the Company's technology or potential development of any products, the status of the preclinical development program for any of the clinical development programs of Arcturus, the status of IND-enabling studies and early clinical development related to any of the clinical development programs of Arcturus, the benefits to patients or the Company of the FDA's grant of orphan drug designation, expectations of market exclusivity concerning clinical development programs, drug substances or drug products of the Company, the sufficiency of any drug substances or drug products of the Company to meet the Company's current clinical goals or expectations, the date that an IND may be filed with the FDA, the potential market or success for the clinical development programs of Arcturus, current standards of care, and the Company's future cash and financial position are forward-looking statements. 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. Actual results and performance could differ materially from those projected in any forward-looking statements as a result of many factors, including without limitation, an inability to develop and market product candidates, inability to generate positive verifiable data, unexpected clinical results, unforeseen expenses and general market conditions that may prevent such achievement or performance. Such statements are based on management's current expectations and involve risks and uncertainties, including those discussed under the heading "Risk Factors" in Arcturus' Annual Report on Form 10-K for the fiscal year ended December 31, 2018, filed with the SEC on March 18, 2019 and in subsequent filings with, or submissions to, the SEC. 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.

Contact
Neda Safarzadeh
Arcturus Therapeutics
(858) 900-2682
IR@ArcturusRx.com

Arcturus Investor Contacts
Michael Wood
LifeSci Advisors LLC
(646) 597-6983
mwood@lifesciadvisors.com

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