Arcturus Therapeutics Holdings Inc.
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# Arcturus—a clinical-stage mRNA therapeutics and vaccines company

**With its unique mRNA therapeutics platform, Arcturus Therapeutics is a leading clinical-stage mRNA medicines company focused on the development of infectious disease vaccines and significant opportunities within liver and respiratory rare diseases.**

Arcturus Therapeutics, based in San Diego, has proprietary enabling technologies: (i) LUNAR lipid-mediated delivery, (ii) self-transcribing and replicating mRNA (STARR) technology, and (iii) innovative manufacturing of mRNA drug substance and the LUNAR-formulated drug product.

Arcturus' lead clinical stage product candidates include a first-in-class, self-amplifying mRNA vaccine for COVID-19 and an mRNA replacement therapy for ornithine transcarbamylase (OTC) deficiency (Fig. 1). Preclinical programs include wholly owned mRNA therapeutics for cystic fibrosis and influenza, along with partnered programs in glycogen storage disease type 3, hepatitis B, and non-alcoholic steatohepatitis.

Arcturus' versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines including mRNA, siRNA, replicon RNA, asRNA, DNA, and gene editing therapeutics. Arcturus' technologies are covered by a portfolio of 209 patents and patent applications, issued in the US, Europe, Japan, China and other regions. Arcturus' development partners include Janssen Pharmaceuticals, Ultragenyx, Takeda, CureVac, Synthetic Genomics, Duke-National University of Singapore (NUS) Medical School, and the Cystic Fibrosis Foundation.

## STARR-based COVID-19 vaccine

Arcturus' COVID-19 vaccine candidate, ARCT-021, developed in conjunction with Duke–NUS Medical School, elicits an immune response to the SARS-CoV-2 virus spike protein. ARCT-021 is a single shot, lyophilized, non-viral vector vaccine that potentially provides extended variant coverage and can be used for periodic re-dosing (Fig. 2). Due to its up to 40-fold smaller dose requirement, ARCT-021 requires less manufacturing capacity than other currently authorized mRNA vaccines for emergency use.

| Product name | Indication | Stage |
|---|---|---|
| **Vaccines** | | |
| LUNAR-COV19 (ARCT-021) | COVID-19 | Clinical |
| LUNAR-FLU | Influenza | Preclinical |
| **Hepatic** | | |
| LUNAR-OTC (ARCT-810) | Ornithine transcarbamylase deficiency | Clinical |
| **Respiratory** | | |
| LUNAR-CF (ARCT-032) | Cystic fibrosis | Preclinical |

**Fig. 1 | Arcturus' pipeline of mRNA-based therapeutics.** Arcturus has developed a diverse pipeline of mRNA-based therapeutics to address infectious disease vaccines and opportunities within liver and respiratory rare diseases.

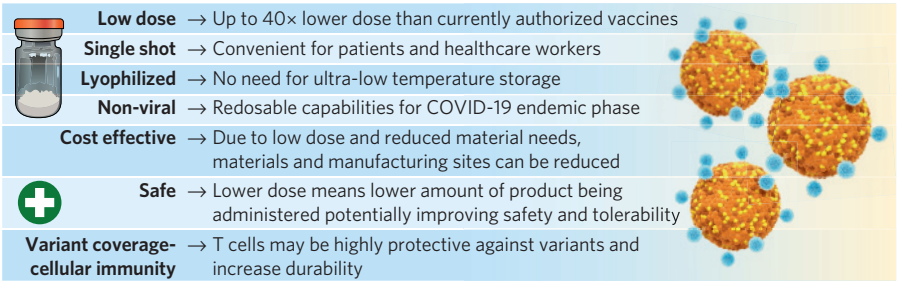


**Fig. 2 | Arcturus' COVID-19 vaccine candidate.**

A key challenge for RNA-based therapeutics is handling the drug product from its manufacture until it is delivered into patients. While other mRNA vaccines are distributed as frozen liquids, ARCT-021 is a lyophilized vaccine that preserves therapeutic efficacy while not requiring an ultra-cold (i.e. less than -70°C) supply chain.

The platform is highly scalable, and with a library of more than 250 proprietary lipids, Arcturus can customize the LUNAR particles for specific indications and targets. Following endocytosis, the acidic environment in the endosomes triggers the LUNAR particles to release their cargo into the cytoplasm.

STARR directs the cellular protein production machinery to either generate a protective immune response or to produce therapeutic proteins of interest. Compared to other non-self-replicating mRNA-based therapeutic platforms, the sustained protein expression provided by the STARR mRNA brings reduced dosing requirements and improved results. STARR mRNA is delivered with Arcturus'LUNAR delivery system. By combining these two technologies, Arcturus is developing a vaccine product that addresses both the pandemic and the endemic phases.

## Clinical stage mRNA therapeutics for rare diseases

Arcturus' platform has great potential for helping treat rare diseases, including metabolic diseases. The company's ARCT-810 program addresses OTC deficiency, a rare genetic disease that can lead to life threatening accumulation of ammonia in the blood. ARCT-810 uses the LUNAR platform to deliver mRNA into liver cells to produce functioning OTC with disease-modifying effects. ARCT-810 has received orphan drug designation from the US Food and Drug Administration. In a phase 1 study, ARCT-810 demonstrated favorable safety, tolerability and PK profiles. Arcturus has now initiated a phase 1b study with ARCT-810 and is planning a phase 2 multiple-dose study in the second half of 2021.

"Our key proprietary technology generates a one-dose, lyophilized drug product that addresses the major hurdles in RNA therapeutics development, namely the effective and safe delivery of RNA molecules to disease-relevant target tissues," said Joseph Payne, President and CEO of Arcturus. "We believe the versatility of our platform to target multiple tissues, its compatibility with various nucleic acid therapeutics, and our expertise in developing scalable manufacturing processes puts us in a position to deliver the next generation of nucleic acid medicines."

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