

Arcturus Therapeutics, Inc.

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RNA in the spotlight

Since the days of Watson, Crick, and Franklin, DNA has hogged the limelight, overshadowing RNA. Recently, however, RNA has claimed center stage as a multi-talented player, dialing gene expression up or down and even altering the genome through gene editing. With precision and power, RNA medicines have the potential to treat and even cure rare genetic diseases, as well as fight viral infections, cancer, and heart disease.

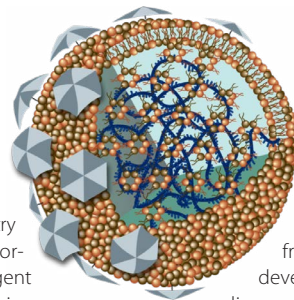
Yet RNA is more vulnerable than DNA to rapid destruction by exonucleases. And in order to exert any effect, an RNA medicine must cross the cell membrane, making a robust delivery system critical. Arcturus Therapeutics has developed unique RNA chemistry and a lipid nanoparticle that overcome these obstacles. These proprietary technologies, UNA (unlocked nucleomonomer agent) and LUNAR (lipid-enabled and unlocked nucleomonomer agent modified RNA), have been shown to deliver single- or double-stranded RNAs to diverse cell types and tissues. With this flexible platform, Arcturus is addressing unmet needs in rare diseases, including cystic fibrosis (CF), metabolic disorders, and hepatitis B.

Figure 1: LUNAR delivery.

Novel nucleoside chemistry

UNA is a novel nucleoside chemistry that lacks ribose but can be incorporated into RNA. UNA is divergent enough from natural RNA that it is unrecognized by either nucleases or immune receptors. The result is a longer, yet transient, residence time for UNA-containing RNAs compared to native RNAs. Single-stranded UNAs also form minimal secondary structure, enabling the formulation and delivery of longer or multiple RNAs.

LUNAR (Fig. 1) is a nanoparticle delivery formulation that incorporates cationic, biodegradable lipids, shortening residence times and reducing the potential for long-term toxicity compared to other lipid particles. LUNAR is also nonimmunogenic, and therefore can be used in repeat dosing and dose-escalation studies that are not feasible with viral delivery systems. LUNAR effectively targets clinically important cells and tissues, including liver hepatocytes and stellate cells, cardiomyocytes, lung cells, and B and T cells.



Highly valued partner

Arcturus has made a strong showing since its founding three years ago, inking major deals with Ultragenyx and Janssen. Ultragenyx paid \$10 million up front to license Arcturus technologies to develop mRNA drugs for rare and ultra-rare diseases. Janssen, in addition to licensing UNA and LUNAR, is collaborating with Arcturus to develop RNA-based drugs for the treatment of HBV. Three additional in-house programs to develop UNA-based mRNA (mUNA) treatments for rare genetic disorders are also under way, targeting CF, ornithine transcarbamylase deficiency, and an unnamed gastrointestinal target.

contact

Neda Safarzadeh
Associate Director, Special Projects
Arcturus Therapeutics, Inc.
San Diego, California, USA
Email: neda@arcturusrx.com