

# Voice Series

## COVID-19 Special Collection

### Part 2: Interview with Arcturus Therapeutics



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In part 2 of this COVID-19 Special Collection, *BIO Integration* sought insights from Arcturus Therapeutics, a company that is currently producing messenger RNA (mRNA)-based coronavirus 2019 (COVID-19) vaccine using their own unique platform technology, LUNAR®. Herein, we learn first-hand the important issues on COVID-19 vaccine development, COVID-19 mutation and their current breakthrough, and the importance of community vaccination to curb this virus.

**EE:** Why and how did you start working on the vaccine? What are our expectations in the short term?

**Arcturus:** In November 2019, we announced our STARR™ Technology platform that combines self-replicating RNA with LUNAR®. This positioned us to be ready to address the COVID-19 pandemic utilizing the technology created, just for this purpose.

The expectation in the short term with our vaccine is to continue through clinical trials and obtain emergency use authorization (or equivalent) in order to have the vaccine available to the population.

**EE:** What is the new coronavirus variant? How often does this virus mutate? How does the new mutation affect the current epidemic prevention and control? Will it bring a new round of outbreaks?

**Arcturus:** A variant is a virus that contains mutations in its genes. The mutations may change how the virus works. It may change how it infects the host, how quickly it infects the host, the severity of disease it causes in the host, or a combination of the above. Or another case, the mutations may not have any impact at all.

Coronaviruses are generally thought to mutate less than influenza virus. But when there is significant spread of a virus, it creates additional opportunity for a virus to adapt and mutate. A mutation might also change the proteins on the surface of the virus that are recognized by the immune system. This means that someone who may have received a vaccine might have less protection against a variant strain, but this is not always the case. Studies are ongoing in laboratories around the world with the goal of understanding how the blood of people who received these vaccines might respond to these variants. This helps us to understand if newer vaccines need to be developed. The development of these variants reinforces the need to reduce the spread. As fewer individuals become infected, there is less opportunity for a virus to mutate and create new variants. This is why health authorities and vaccine developers are working so hard to provide as many vaccines as possible in order to reduce the spread of the virus.

**EE:** Are current temperature checks and nucleic acid (PCR) tests reliable? Can they effectively prevent and control COVID-19 spread?

**Arcturus:** Surveillance for infection and taking steps to isolate people who are infected is a very important part of the equation of achieving control of COVID-19 spread. Temperature checks are helpful, but it is also true that some people infected with SARS-CoV-2 do not have fever. The PCR test is highly sensitive, but it is challenging and expensive to test a large population frequently. Clever strategies have been adopted globally, applying a blend of both sensitive and less sensitive approaches so that we can immediately identify who might be shedding the SARS-CoV-2 virus. Using the practical solution of limiting exposure to these individuals is very important and has been demonstrated as an effective means of markedly reducing the spread of SARS-CoV-2 in several countries before vaccines were available.

**EE:** What is the progress of COVID-19 vaccine development? Which vaccine is more promising?

**Arcturus:** There has been amazing progress on COVID-19 vaccine development. Presently, there are multiple vaccines approved, and vaccinations are making good progress. We are also seeing a global trend of a decline of SARS-CoV-2 that likely reflects a combination of practical surveillance measures, infection control, and perhaps even a bit from early effectiveness of these vaccines. The data being generated by these vaccines look good across all of the approved vaccines, but these are early days. We will need to continue to watch how all vaccines continue to address the infection and what their safety profiles look like in broader use. The fascinating part of this catalog of vaccines is the different ways in which the vaccines were designed: amazing new technology, like mRNA, is showing success in reducing disease. We will see how they continue to perform—particularly if the coronavirus does not fully go away. Some vaccines may be better suited for repeat vaccination than others.

**EE:** What is significantly different in your vaccine compared with others?

**Arcturus:** Our vaccine represents an exciting new chapter for the mRNA vaccines under development. Our vaccine differs from the Moderna and Pfizer/BioNTech vaccines by being a “self-amplifying” mRNA. In other words, there is a mechanism in the vaccine that allows for greater amount of protein to be produced by our cells with each dose. These proteins and how the cells use them to attract the immune system is a key part of how our immune systems work. Thus, with this “self-amplifying” element, there is the possibility to achieve a targeted response with a lower dose and even the possibility with a single dose. We are working to confirm this in our trials right now.

**EE:** How do we view and interpret the safety and efficacy of COVID-19 vaccine?

**Arcturus:** From the publicly disclosed data that each sponsor shares in relation to the safety profile, the efficacy data are generally excellent, and the safety profile of these vaccines appears to be similar to other licensed vaccines. For example, the vaccine efficacy for COVID-19 appears to be initially better than for influenza vaccines, and this is really encouraging. Of course, each vaccine has a risk of side effects, including rare side effects, but overall, the nature of side effects with vaccination appears to be mostly mild or moderate and lasts a day or two in people who have received them.

**EE:** Is there sufficient data from clinical trials to demonstrate that vaccines are safe and effective?

**Arcturus:** With the size of these trials, we have a very solid grasp on the type and nature of common side effects and even less common side effects that occur with vaccination. However, these trials have limitations in terms of the many different types of people who will ultimately be vaccinated. Thus, what is impossible to predict are the rare side effects. This is where the major health authorities have really taken

this matter seriously and have put measures in place to continue to monitor safety as people are vaccinated. They are already reviewing and publishing analyses on these data. This provides an additional comfort that there is ongoing surveillance and the ability to intervene in the event that something unexpected is seen.

**EE:** What is the point of universal vaccination?

**Arcturus:** Vaccination has three key benefits: reduction of the risk of contracting the disease, possible reduction of the risk of spread of the disease, and reduction of the opportunities for the virus to replicate and mutate.

**EE:** Do weak people also need to be vaccinated? How safe is it for this segment of the population?

**Arcturus:** Certainly, people with underlying medical conditions or weakened immune systems are often the population that is prone to the more severe complications of any infectious disease. We continue to work toward developing vaccines that might help to improve their individual responses to a vaccine. But often, because of the underlying medical condition, the response to the vaccine is less predictable. This is why it is important for others to be vaccinated. By reducing the spread from healthier individuals, there is an added layer of protection that we can offer for these higher-risk individuals.

## About Arcturus Therapeutics

Founded in 2013 and based in San Diego, CA, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a clinical-stage mRNA medicines and vaccines company with enabling technologies such as (i) LUNAR<sup>®</sup> lipid-mediated delivery, (ii) STARR<sup>™</sup> mRNA Technology, and (iii) mRNA drug substance along with drug product manufacturing expertise. Arcturus’ diverse pipeline of RNA therapeutic and vaccine candidates includes mRNA vaccine programs for SARS-CoV-2 (COVID-19) and influenza and other programs as well as potential treatment for ornithine transcarbamylase deficiency and cystic fibrosis along with partnered programs including glycogen storage disease type 3, hepatitis B virus, and non-alcoholic steatohepatitis. Arcturus’ versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines including mRNA, small interfering RNA, replicon RNA, antisense RNA, microRNA, DNA, and gene editing therapeutics. Arcturus’ technologies are covered by its extensive patent portfolio (209 patents and patent applications, issued in the United States, Europe, Japan, China, and other countries). Arcturus’ commitment to the development of novel RNA therapeutics has led to collaborations with Janssen Pharmaceuticals, Inc., part of the Janssen Pharmaceutical Companies of Johnson & Johnson, Ultragenyx Pharmaceutical, Inc., Takeda Pharmaceutical Company Limited, CureVac AG, Synthetic Genomics Inc., Duke-NUS Medical School, and the Cystic Fibrosis Foundation. For more information, visit [www.ArcturusRx.com](http://www.ArcturusRx.com). In addition, please connect with us on Twitter (@ArcturusRx) and LinkedIn (Arcturus Therapeutics).