



Acuitas Therapeutics – Backgrounder

Founded in February 2009, Vancouver-based Acuitas Therapeutics is a private biotechnology company that specializes in the development of delivery systems for nucleic acid therapeutics based on lipid nanoparticles (LNP). The company partners with pharmaceutical companies, biotechnology organizations and academic institutes to advance nucleic acid therapeutics to the clinical trial phase and to the marketplace. The team works with partners to develop new therapies to address unmet clinical needs based on the internationally recognized capabilities in delivery technology developed by Acuitas Therapeutics.

Acuitas Therapeutics is known globally as a leader in the field of lipid nanotechnology. The team, led by founder Dr. Thomas Madden, is made up of highly experienced researchers, scientists, project managers and administrative professionals – all of whom are focused on excellence in their respective roles and as a company.

About mRNA COVID-19 Vaccines

Currently, Acuitas Therapeutics is supporting several international partners in the development of mRNA COVID-19 vaccines. These partnerships include BioNTech (which is partnering with Pfizer), CureVac and Imperial College London. Through these partnerships, the Acuitas delivery technology is being utilized to develop effective messenger RNA vaccines for COVID-19.

BioNTech began Phase I/II clinical trials on April 23, 2020 and CureVac and Imperial College London began Phase I/II clinical trials in June 2020. BioNTech recently released data from their clinical studies (<https://bit.ly/3gfzmP9>).

These COVID-19 vaccines use messenger RNA (mRNA) technology that codes for a protein made by the virus. The vaccines work by allowing the human immune system to recognize this protein so that the immune system can prevent the virus from infecting our cells and causing disease. A major advantage of mRNA vaccines is that they can be developed much more rapidly in response to a new virus compared to conventional vaccines.

About Acuitas Therapeutics' Technology

Acuitas Therapeutics specializes in the development of lipid nanoparticle delivery systems for molecular therapeutics. In lay terms, they work with partners to develop drugs that use new technologies based on biological processes or compounds. These new technologies include messenger RNA (mRNA) technology.

All living organisms, including humans and viruses, make proteins. Proteins are the workhorses that carry out all of the tasks needed by that organism. The “blueprints” for these proteins are in our genes (DNA), but this information needs to be converted into a message that tells the body to make a particular protein. This message is called mRNA. Scientists can make a synthetic mRNA that provides the body with the information to make any protein. There are many clinical uses for these new proteins. They can be antibodies to fight an infection or disease, including cancer; gene editing proteins to correct a genetic disorder; or viral proteins that result in a protective immune response (mRNA vaccines).

The Acuitas Therapeutics technology allows the mRNA to work. When a synthetic mRNA is used as a vaccine (or a drug), there are two challenges: The mRNA is fragile and if injected into the body, it would break down quickly. It is also a very large biological molecule. This means that it



cannot get into our cells without help – and it needs to get into the cells in our body to work. The technology developed by Acuitas Therapeutics provides tiny delivery vehicles (lipid nanoparticles) that protect the mRNA after it is injected. Then, the lipid nanoparticles carry the mRNA into the cells, allowing it to do its important job.

Imagine that you want to buy an exceptionally fragile glass ornament online and you would like to have it delivered to your home. If you used the equivalent of the Acuitas Therapeutics delivery technology, the ornament would be packed inside a carrier to shield it. No matter how bumpy or rough the journey was, the Acuitas Therapeutics delivery technology would make sure that the ornament was protected. The carrier would find your house, open the front door by itself, let itself in, unwrap your glass ornament, and leave it in the front hallway for you to pick up.

Acuitas Therapeutics scientists have synthesized over 500 novel cationic lipids and evaluated these novel compounds in LNP. This evaluation characterizes the potency and safety of the LNP carriers for delivery of nucleic acid payloads including siRNA, mRNA and DNA.

The team has undertaken the biophysical characterization of such novel LNP systems and has conducted correlation analyses to determine which structural and biophysical properties of the cationic lipids are critical for activity. The rational design and screening approach has resulted in the identification of LNP compositions with a greatly improved potency and therapeutic index. The team has also established the mechanism by which LNP carriers are taken up by cells.

Importantly, Acuitas LNP systems are clinically validated. An Acuitas LNP is used by Alnylam Pharmaceuticals for Onpattro™. Onpattro™ was approved in 2018 in the U.S. and Europe for the treatment of transthyretin amyloidosis, a rare condition characterized by an abnormal buildup of a protein called amyloid in the body's organs and tissues. Onpattro™ is the first in a new class of drugs, called RNAi therapeutics, to receive regulatory approval.

Acuitas Therapeutics' discovery and development programs are ongoing, with the mandate to build upon their leadership position in LNP technology.

For more information on other work being done by Acuitas, please see their expertise and capabilities information on their website (<https://bit.ly/3eVJMTZ>).