November 17th, 2025

Acuitas Therapeutics Unveils Next-Generation Lipid Nanoparticle Advancements at the 2025 mRNA Health Conference

- *Key presentation unveiled Acuitas' Next-Generation LNP Advancements, which is designed to enhance potency and safety, expand delivery beyond the liver, and enable broader therapeutic impact*
- *Additional presentations showcased broadened therapeutic applications of ALC-315™, and improved performance enabled by novel LNP formulations*

Vancouver, B.C. – Acuitas Therapeutics, a global leader in lipid nanoparticle (LNP) delivery systems for the acceleration of partners' clinical development, recently presented its Next-Generation LNP advancements, a suite of novel and enhanced technologies that expand the range of diseases treatable with mRNA-LNP medicines, at the 13th International mRNA Health Conference in Berlin. Also at the conference, the company highlighted additional preclinical data on its LNP formulations' applicability in cancer vaccines, potency, and safety.

"Commercial validation of our technology has provided both an important milestone of success and the impetus for continued advancement," said Dr. Thomas Madden, CEO of Acuitas Therapeutics. "Our research, presented at the mRNA Health Conference, is focused on two key goals: expanding the application of our technology into new therapeutic areas and enhancing the potency and safety of the platform itself, with novel LNP formulations and various improvement strategies. Underpinning both is our commitment to improving the translatability of preclinical data, which is essential for accelerating the journey of mRNA and personalized therapies from the laboratory bench to the clinic."

Next-Generation LNP for mRNA-based Therapeutics

At the conference, Acuitas' Chief Scientific Officer, Dr. Ying Tam, showcased the company's Next-Generation LNP advancements, a comprehensive approach that uses multiple technologies and strategies to improve all aspects of LNP utility and applicability – from potency, safety, extrahepatic targeting, to manufacturing.

The advancements were featured in an oral presentation titled "Next-Generation Lipid Nanoparticles for Clinical Development of mRNA-based Therapeutics." The presentation detailed

Acuitas' efforts in advancing mRNA-LNP beyond current clinical standards and broadening the range of diseases these therapies can treat. Key highlights of the presentation include:

- Novel LNP candidates engineered for significantly improved potency, as high as a four-fold increase for some cases, in gene editing and vaccine applications.
- Optimized lipid structures reduced liver exposure, leading to increased tolerability, lowered liver enzymes, while preserving therapeutic activity in mice.
- DARPin-conjugated LNP candidates that achieved highly targeted delivery to immune cells (T-lymphocytes), with a long-circulating format further enhancing uptake efficiency and expression levels.
- Mucous penetrant mRNA-LNP candidates capable of extrahepatic delivery to airway epithelial cells in cystic fibrosis lung models, enabling effective gene editing compared to control LNP.
- An alternative LNP manufacturing approach, called pre-formed vesicles (PFV), with equivalent potency to standard benchmark manufacturing methods, offered significant improvements in cost, storage, distribution, and flexibility of LNP manufacturing, especially for personalized mRNA-LNP therapies.

Additional Posters Presented

In addition to its lead presentation, Acuitas also showcased three posters that elucidated the mechanics of LNP delivery and assessed its existing slate of lipids, as well as explored novel options for future formulations.

Applying Clinically Approved ALC-315™ in Cancer Vaccines

Acuitas' ALC-315™ ionizable lipid — used in the Pfizer-BioNTech COVID-19 vaccine (COMIRNATY®) — was assessed for its cancer vaccine development potential. The research directly compared Acuitas' LNP to lipoplexes and evaluated modified mRNA against the unmodified mRNA predominantly used in current cancer vaccine trials. Key highlights of this data include:

- Using LNP comprised of ALC-315™, unmodified RNA induced a stronger antigen-specific CD8 T-cell response compared to a nucleoside-modified mRNA incorporating N1methylpseudouridine-encoding OVA payload as a model tumour antigen, while maintaining strong immunogenicity at one-tenth of the initially tested dose.

- Using LNP comprised of ALC-315™, mRNA delivered intramuscularly induced equal or superior cellular and humoral immunity compared to intravenously (IV) administered mRNA lipoplexes – an alternative mRNA cancer vaccine format in clinical development – despite mRNA lipoplexes being administered at four-fold higher doses and with more boosts.
- Several potent novel proprietary lipids were identified that achieved equivalent cellular responses to ALC-315™. Further assessment will be conducted to compare potency and activity using syngeneic neoantigen models.

Novel Lipids with Improved Activity for Prophylactic Vaccine Development

Acuitas identified and validated six novel lipids that induce higher virus-specific immunogenicity compared to ALC-315™. Key findings related to these novel lipids include:

- The six novel lipid candidates induced equivalent neutralizing antibody titres at a five-fold lower dose than ALC-315™.
- The lipid candidates demonstrated favorable reactogenicity profiles comparable to ALC-315™, while eliciting stronger cellular- and B-cell responses.
- Innate immune responses induced by LNP correlated with their reactogenicity, but not with adaptive and innate immune responses.
- Several lipid candidates achieved higher *in vivo* expression in secondary lymphoid organs and reduced liver expression compared to ALC-315™.

Impact of Body Weight and Medications on mRNA-LNP Safety in Monkeys

As the industry continues using larger nonhuman primates in translational work, Acuitas sought to understand how body weight, premedications (steroid, H1 and H2 blockers), and concomitant medications (meloxicam) impact LNP activity and tolerability. The study was conducted in monkeys using an IV-administered mRNA-LNP encoding human IgG. Key highlights of this data include:

- LNP tolerability is reduced in larger monkeys (>6 kg).
- Premedications helped reduce the elevation of liver transaminases.
- Premedications improved tolerability but reduced the level of IgG mRNA expression.
- Platelet count decreases were greatest in large monkeys and monkeys given meloxicam.

More information on posters presented at the mRNA Health Conference and Vaccine R&D Conference can be found here.

About Acuitas Therapeutics

Acuitas Therapeutics, Inc. is a Vancouver-based company focused on developing and optimizing lipid nanoparticle (LNP) delivery systems for nucleic acid-based therapeutics. They collaborate with pharmaceutical and biotech companies, academic researchers, and global health organizations to advance a broad range of medicines for a variety of diseases.

Acuitas' clinically validated LNP technology has had a profound global impact — most notably enabling the Pfizer-BioNTech COVID-19 vaccine, **COMIRNATY®**, which has protected billions of people in more than 180 countries. Our technology also enables **ONPATTRO®** by Alnylam Pharmaceuticals, the first FDA-approved RNAi therapeutic for treating the rare and fatal disease transthyretin amyloidosis. More recently, Acuitas' LNP technology has delivered other groundbreaking firsts: the **first in-human proof of concept** for genome base editing and the **first personalized CRISPR therapy.**

Today, they are advancing next-generation LNP to support a variety of therapeutic modalities. This includes targeted LNP for extrahepatic and *in vivo* CAR T-cell therapies, epigenetic medicines to modulate gene expression without altering DNA, multivalent vaccines for infectious diseases — such as malaria, HIV/AIDS, and tuberculosis — as well as oncology vaccines, including personalized cancer vaccines.

For more information, visit www.acuitastx.com.

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