May 20, 2026

Acuitas Therapeutics Highlights In Vivo CAR T Cell Engineering and Ionizable Lipid Quality Attributes at the 2026 ASGCT Annual Meeting

- *Targeted extended circulation LNP incorporating DARPins achieved complete B cell depletion in nonhuman primates through highly specific* in vivo *CD8+ T cell engineering*
- *Robust study quantifies relationship between aldehydes as a key driver of mRNA-lipid adduct formation and mRNA-LNP product performance* in vivo

Vancouver, B.C. – Acuitas Therapeutics, the global leader in lipid nanoparticle (LNP) delivery systems for the acceleration of partners' clinical development, concluded its participation at the American Society of Gene & Cell Therapy (ASGCT) 2026 Annual Meeting. The company presented a suite of new research, highlighted by advancements in extrahepatic targeting for *in vivo* CAR T-cell therapy and new insights into LNP performance.

"The research presented by Acuitas at ASGCT 2026 showcases our holistic approach to pave the way for highly specific and re-dosable genetic medicines," commented Chief Scientific Officer Ying Tam, Ph.D. "From the successful *in vivo* engineering of CAR T cells to elucidation of the mechanisms behind RNA-lipid adducts, these data advance the industry standard in LNP delivery — a standard validated by the compelling data presented this week by partners who are relying on Acuitas' LNP to power their own therapeutic breakthroughs."

In Vivo CAR T Cell Generation via CD8-Targeted LNP

A cornerstone of Acuitas' ASGCT presence was data on a novel targeted extended circulation LNP (ecLNP) developed to deliver CAR-encoding mRNA to CD8+ T cells. In collaboration with Athebio to incorporate Athebody® designed ankyrin repeat proteins (DARPins) — engineered binding proteins used for cell-specific targeting — Acuitas demonstrated the ability to precisely target CD8+ T cells *in vivo*.

Key findings from the data include:

- The ecLNP composition increased plasma half-life from 15 minutes to 2 hours in murine models. Additionally, with the addition of DARPins, the ecLNP formulation showed a 10-fold reduction in liver expression compared to standard LNP

- In nonhuman primates (NHP), administration of ecLNPs encapsulating CD20 CAR mRNA resulted in CAR expression on more than 60% of circulating CD8+ T-cells
- These CD8+ CAR T-cells led to the complete and sustained depletion of B cells not only in peripheral blood, but also in bone marrow and lymphoid tissues (spleen and lymph nodes) at doses as low as 0.25 mg/kg

Improving Product Quality by Understanding RNA-LNP Adduct Formation

Acuitas also shared critical data regarding the chemical stability of mRNA-LNP products as it relates to purity of the underlying ionizable lipid raw materials, specifically focusing on the mechanisms of RNA-lipid adduct formation. These adducts are undesired bonds formed between ionizable lipid impurities and mRNA, which inhibits translation and therefore protein levels. Often undetected by traditional mRNA purity assays, adduct formation can have significant detrimental impacts on the long-term stability and performance of LNP-delivered mRNA therapeutics.

"RNA-lipid adduct formation is an important issue affecting LNP-delivered therapies," said Dr. Chris Barbosa, Vice President of Technology Development at Acuitas. "Understanding the chemical drivers of RNA-lipid adduct formation and quantifying the impact on product performance through this study is an important step that allows us to control critical impurities and set targets for our approved lipid manufacturers. This ensures that our partners receive LNP delivery vehicles with the highest possible integrity and potency for clinical use."

Key insights from the study include:

- Aldehydes as process impurities or degradation products of ionizable lipids are the main driver of RNA-lipid adduct formation. Acuitas has developed and implemented a wide array of analytical methods, including Ion-Pairing Reversed Phase (RP-IP) chromatography and Liquid Chromatography Mass Spectrometry (LCMS), to detect and measure adduct-forming impurities.
- The presence of lipid adducts directly correlates with a decrease in protein expression. In murine models, a clear correlation was observed between increased adduct levels and decreased serum IgG expression. The presence of high levels of these aldehyde impurities and lipid adducts did not impact liver tolerability.

- Adduct formation is highly dependent on time, temperature and the impurity profile of the specific lot of ionizable lipid used. Thorough screening of incoming raw materials for aldehyde content will help ensure the quality and efficacy of the final LNP drug product.

Deepening Insights into LNP-Immune System Interactions

Beyond targeting and LNP quality, Acuitas presented research aimed at improving the clinical safety profile of LNP-based medicines:

Human Whole Blood Assay to Identify Compounds to Mitigate Infusion-Related Reactions

To better understand infusion-related reactions, Acuitas developed an optimized whole blood assay to assess the contribution of LNP and mRNA to immune stimulation, possible mechanisms of immune stimulation, and to identify mitigating drugs that are more specific than steroids. Clinically relevant mitigating agents, such as baricitinib (a JAK1/2 inhibitor) and pegcetacoplan (a complement inhibitor), effectively dampened immune stimulation in high inflammatory response donors, potentially enabling long-term repeated dosing without the long-term effects of steroid use.

Decoding Inter-Animal Variability in NHP Models

To evaluate the significant inter-animal variability frequently observed in preclinical models, Acuitas analyzed the liver transcriptome of 20 NHPs following intravenous infusion of human IgG mRNA-LNP. While treatment resulted in a broad 18-fold potency distribution, this variability showed no correlation with body weight, liver transaminase elevations, or individual pharmacokinetic profiles. Differential upregulation of genes involved in immune modulation were identified, including FOSL1, CCL18 and DHRS9. Multiple factors influence individual pharmacodynamic responses to mRNA-LNP.

More information on the presentation and posters presented at the ASGCT can be found here.

About Acuitas Therapeutics

Acuitas Therapeutics Inc., the global leader in lipid nanoparticle (LNP) delivery systems for nucleic acid therapeutics, is a Vancouver-based company collaborating 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. Its 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, Acuitas is advancing next-generation LNP to support a variety of therapeutic modalities. This includes targeted LNP for extrahepatic therapies such as in vivo CAR T-cells, gene editing therapies across multiple DNA editing technologies, epigenetic medicines to modulate gene expression without altering DNA, and 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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