For Immediate Release **May 19, 2021**

Acuitas Announces Publication of Data Demonstrating Durable Low Density Lipoprotein Cholesterol Reduction in Mice and Non-Human Primates After a Gene Editing Treatment in *Nature Biotechnology*

Vancouver, B.C. – Acuitas Therapeutics, a company focused on developing lipid nanoparticle (LNP) delivery systems to enable messenger RNA (mRNA)-based therapeutics, recently announced publication of data from research with European collaborators demonstrating effective and precise in vivo gene editing in mice and non-human primates (NHP). The paper (https://doi.org/10.1038/s41587-021-00933-4), entitled "*In vivo adenine base editing of PCSK9 in macaques reduces LDL cholesterol levels,*" published in the journal *Nature Biotechnology*, describes cutting edge work using Acuitas' proprietary LNP technology to deliver mRNA encoding a Cas9 adenine base editor (ABE) and guide RNA (gRNA) to the liver of mice and primates to enable precise editing of the *PCSK9* gene. Inactivation of the *PCSK9* gene resulted in lowered PCSK9 and low density lipoprotein (LDL) plasma levels. For this work, Acuitas collaborated with Dr. Gerald Schwank of the Translational Genome Editing Laboratory in the Institute of Pharmacology and Toxicology at the University of Zurich.

The ability of base editing to efficiently and precisely introduce defined changes to disease-associated genes in living organisms offers a significant advantage over other gene editing strategies. Furthermore, since the majority of pathogenic mutations in the human genome involve changes that can be directly repaired by ABEs such as those used in this work, these editors represent very promising tools for gene editing therapeutics. In addition to the murine data, this paper demonstrates that base editing technologies delivered in Acuitas' proprietary LNP can modify a disease-related gene in target organs of NHP, a key step to advancing therapeutics towards clinical trials.

The *Nature Biotechnology* paper describes data showing 4 and 50% whole liver editing in mice following administration of 1 and 3 mg/kg of mRNA encoding an ABE and a *PCSK9*-directed gRNA, encapsulated in Acuitas' proprietary LNP. This was concomitant with a >90% reduction in circulating PCSK9 levels and a 60% reduction in LDL in animals receiving the higher 3 mg/kg dose. This compared to 2 and 28% whole liver editing in NHP following administration of 0.75 and 1.5 mg/kg of mRNA/gRNA LNP with a 26-39% and 9-19% reduction in circulating PCSK9 and LDL, respectively, in animals receiving 1.5 mg/kg. Importantly, the LNP showed a high trophism

for hepatocytes with less than 1% on-target editing in all other organs assessed, with the exception of the spleen which showed 7% editing. Furthermore, no major off-target effects were detected in either the transcriptome or the genome of hepatocytes isolated from treated animals.

“The work described in this paper represents a significant achievement in the quest with our partners and collaborators to develop revolutionary therapies, including gene editing medicines. Of significance is our earlier work with nucleic acid LNP-based drugs that showed that NHP studies can accurately predict activity in humans. Based on these data, we are very optimistic that therapeutically relevant and durable editing can be achieved at well-tolerated doses in the clinic,” says Dr. Ying Tam, Chief Scientific Officer at Acuitas. He continues: “More broadly, this validates the utility of mRNA LNP therapeutics beyond vaccines to a wide range of clinical applications including oncology applications.”

About Acuitas Therapeutics

Founded in February 2009, Vancouver-based Acuitas Therapeutics (www.acuitastx.com) is a private biotechnology company that specializes in the development of delivery systems for nucleic acid therapeutics based on lipid nanoparticles. The company partners with pharmaceutical and biotechnology companies and academic institutes to advance nucleic acid therapeutics into clinical trials and to the marketplace. The team works with partners to develop new therapies to address unmet clinical needs based on its internationally-recognized capabilities in delivery technology. Acuitas Therapeutics has agreements in place with several partners to use its proprietary lipid nanotechnology in the development of COVID-19 vaccines. These include Pfizer/BioNTech for COMIRNATY®, which has been approved for Emergency Use in multiple jurisdictions including the U.S., Canada and Europe; and CureVac, which initiated a Phase 2b/3 study in late 2020 and expects to request authorization for Emergency Use in 2021.

-END-