

Acuitas Therapeutics

NON-CONFIDENTIAL PRESENTATION



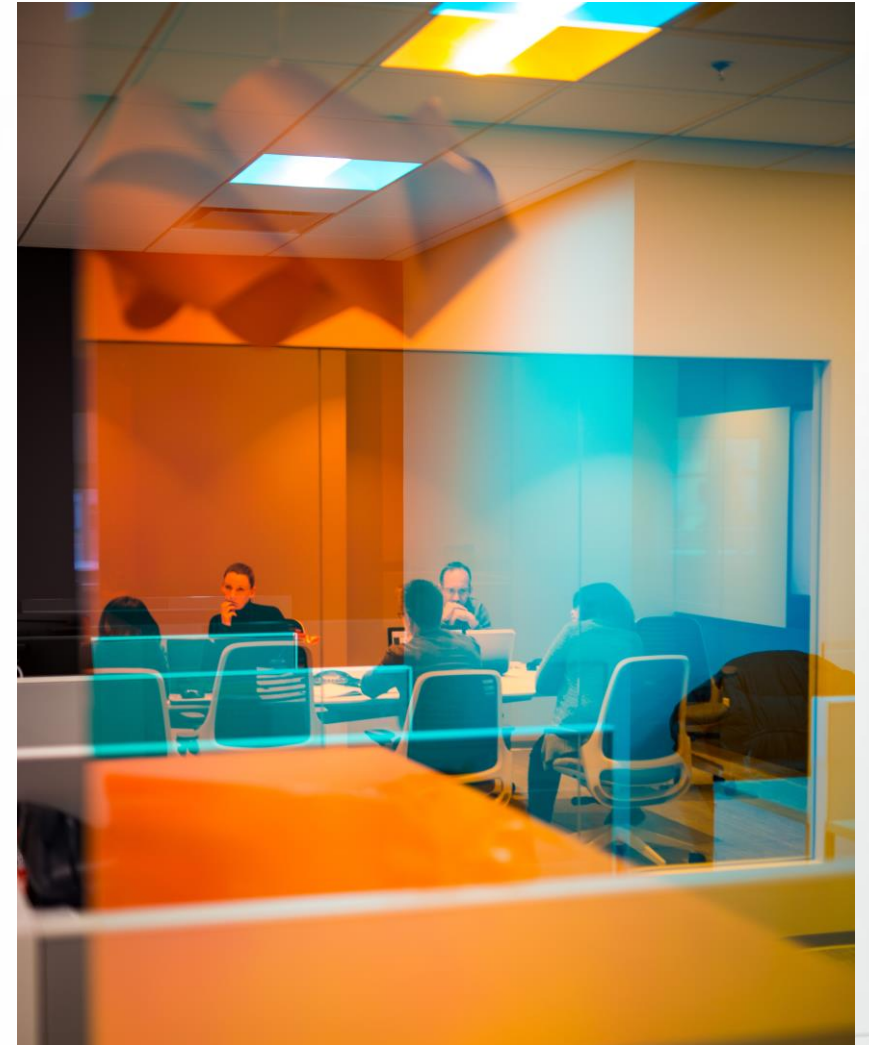
Vision

Acuitas is the premier LNP technology provider globally, enabling our partners to advance new therapeutics to address unmet clinical needs



Mission

- ▶ To provide our partners with the best LNP delivery technology for nucleic acid therapeutics
- ▶ To support our partners to rapidly advance new therapeutics to address unmet medical needs
- ▶ To continually innovate to maintain and strengthen our LNP technological lead



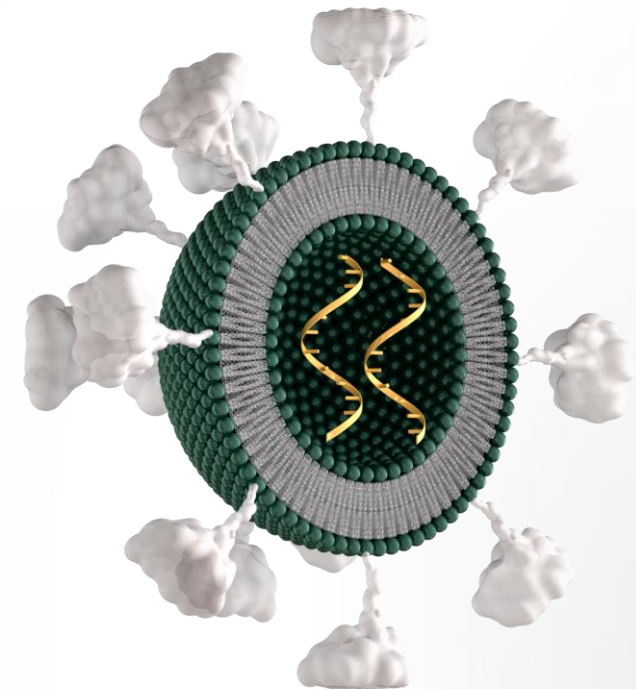
Company Background

- ▶ Privately held biotechnology company
- ▶ Founded February 2009; based in Vancouver, British Columbia
- ▶ Highly experienced team developing lipid nanoparticle delivery systems
- ▶ Facilities for chemistry, formulation and preclinical studies



LNP Technology: Clinically Validated

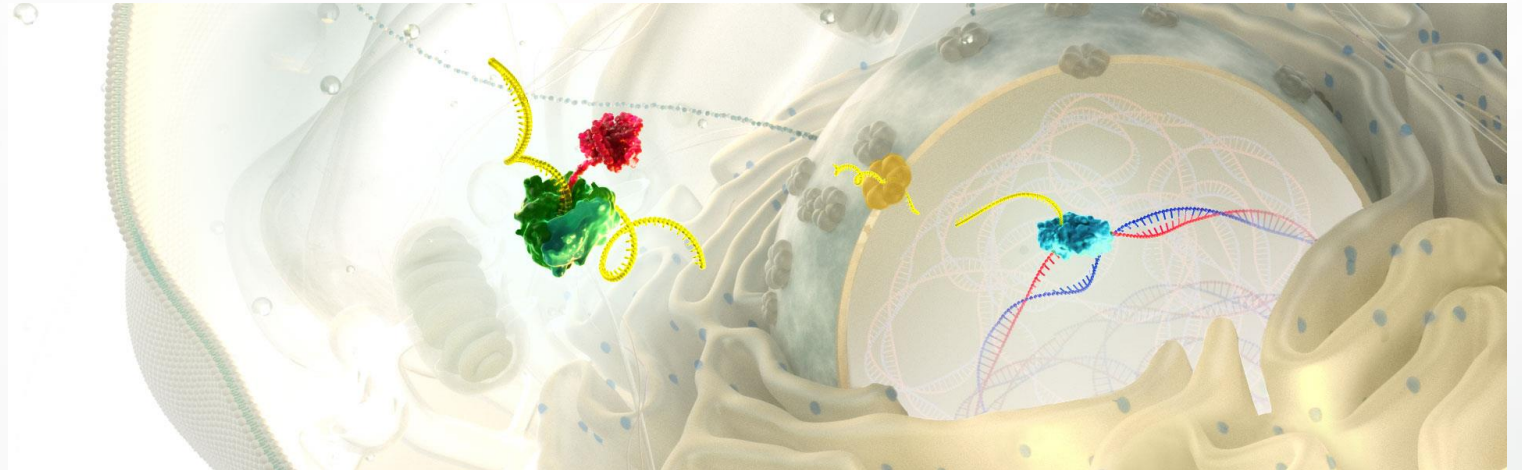
- ▶ Acuitas LNP formulation used in ONPATRO® (Alnylam collaboration)
 - ▶ First Approved RNAi product (2018)
 - ▶ Approved in US, Europe, Japan & elsewhere
- ▶ Acuitas LNP formulation used in COMIRNATY® (BioNTech-Pfizer collaboration)
 - ▶ First authorized mRNA therapeutic (2020)
 - ▶ First authorized COVID-19 vaccine
 - ▶ Emergency Use Authorization in US, Canada, EU, UK & elsewhere



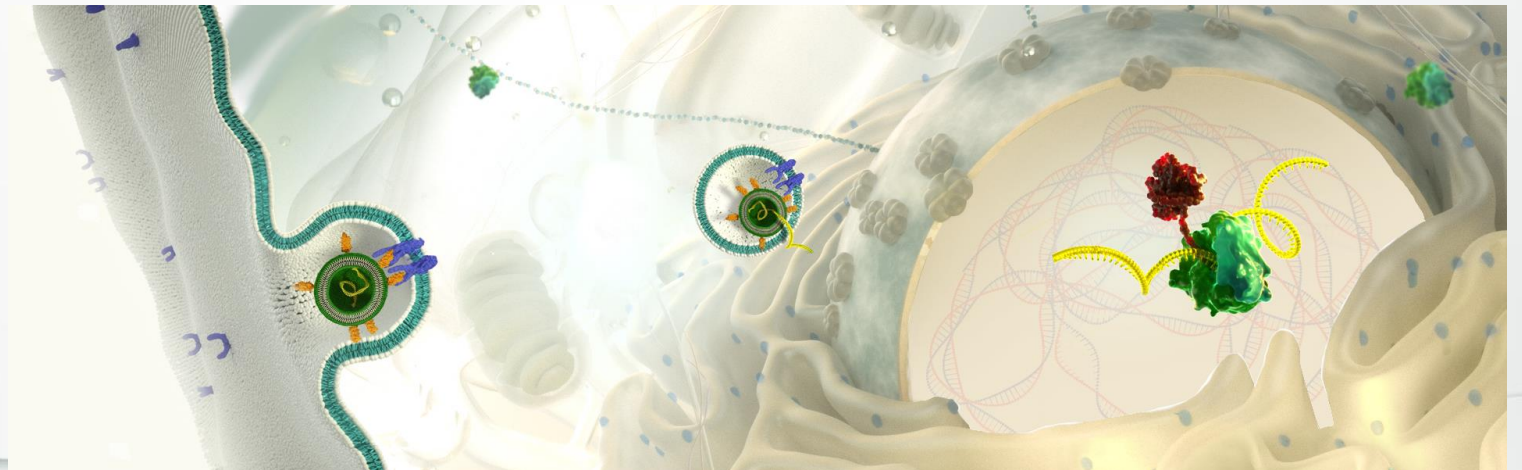
Therapeutic Opportunity: mRNA Therapy

- Delivery of novel proteins to treat disease

Normal cell: Genomic DNA transcribed to mRNA



mRNA Therapy: Synthetic mRNA delivered in LNP



Therapeutic Opportunities

▶ Vaccines

- ▶ Intracellular expression of viral or bacterial proteins generating protective immune response
- ▶ Expression of tumour antigens (personalized vaccines)

▶ Antibodies

- ▶ Expression of prophylactic or therapeutic antibodies to treat current and emerging diseases

▶ Protein Replacement therapeutics

- ▶ Expressing a human protein to address genetic disorders such as haemophilia & cystic fibrosis

▶ Genome Editing/Base Editing

- ▶ Expressing a genome editing or base editing protein to modify human gene expression

Acuitas Capabilities

CMC

- ▶ Chemistry
- ▶ LNP Formulation & Characterization

Preclinical

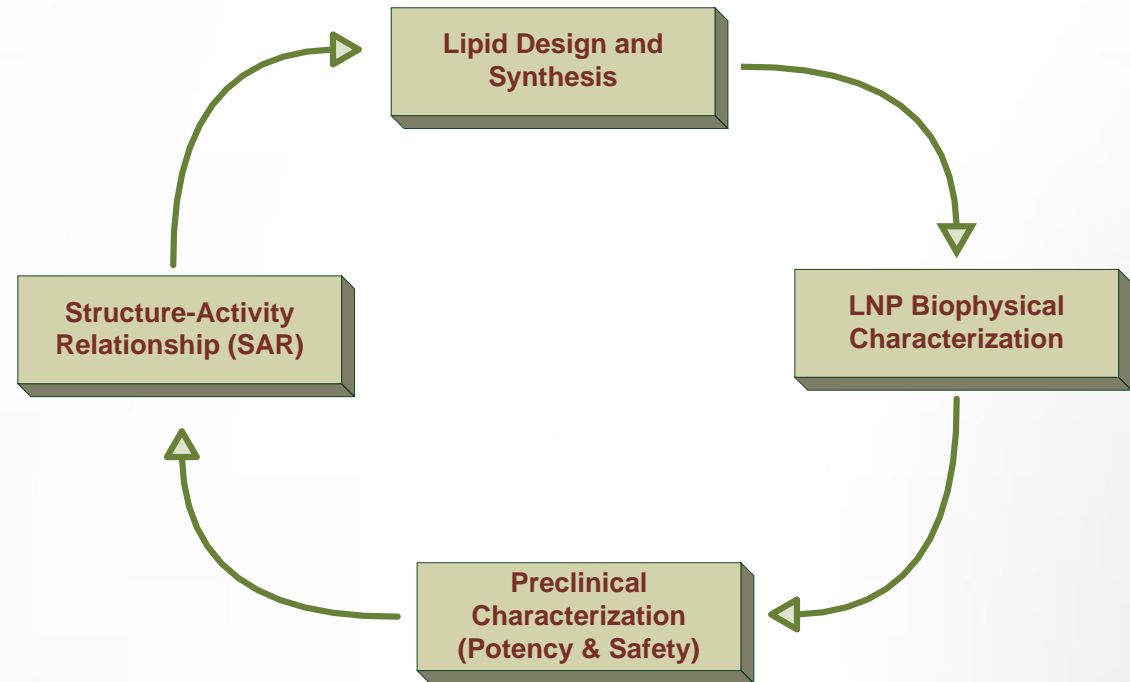
- ▶ Pharmacodynamic studies
- ▶ Safety studies
- ▶ PK/ADME

Clinical & Regulatory

- ▶ Clinical translation
- ▶ Regulatory support
- ▶ Clinical support

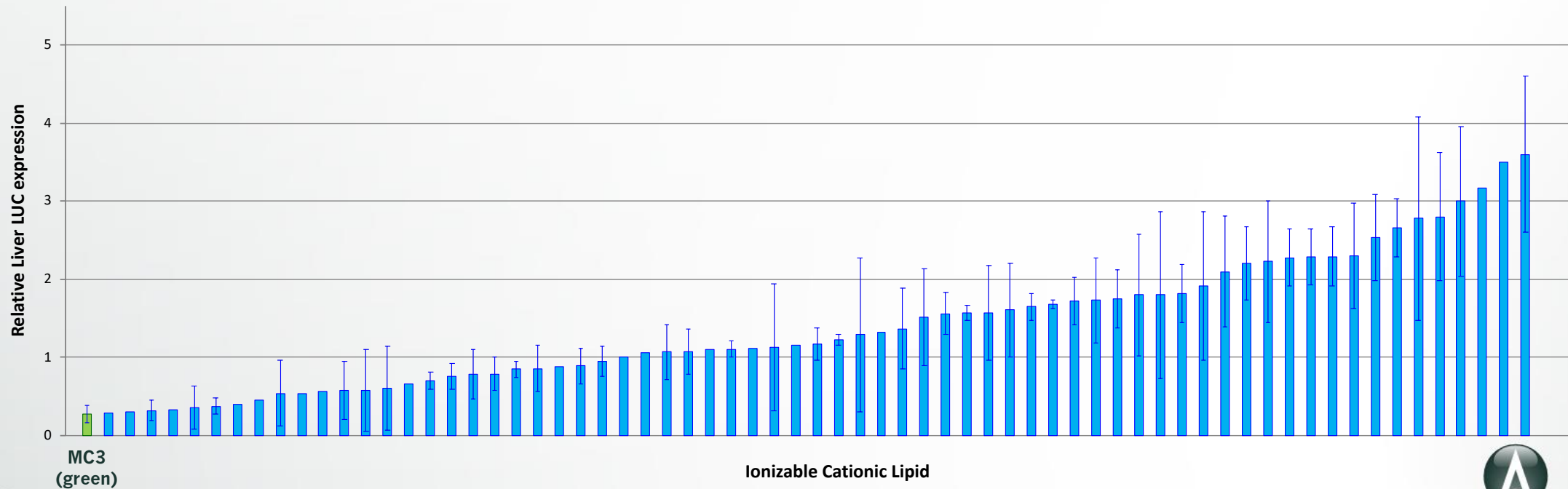
mRNA-LNP Technology Development: Objectives & Process

- ▶ Enhance potency and safety profile for LNP carriers
- ▶ Enable broad range of mRNA therapeutic applications
- ▶ Iterative approach to identify improved LNP compositions



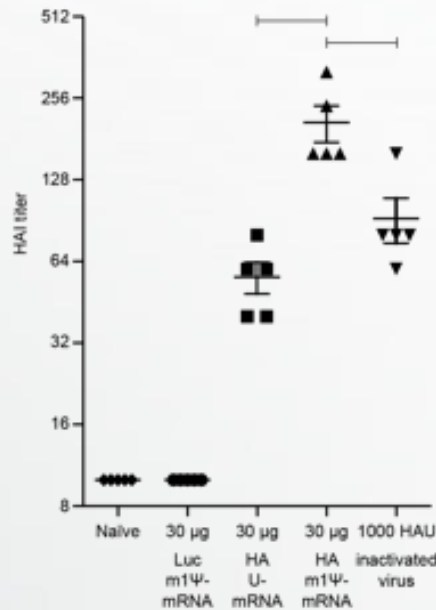
mRNA-LNP Technology: Potency Enhancement

- ▶ Screening program combined with key SAR relationship analysis results in substantial improvement in LNP potency.
- ▶ Relative activities of LNP with different cationic lipids

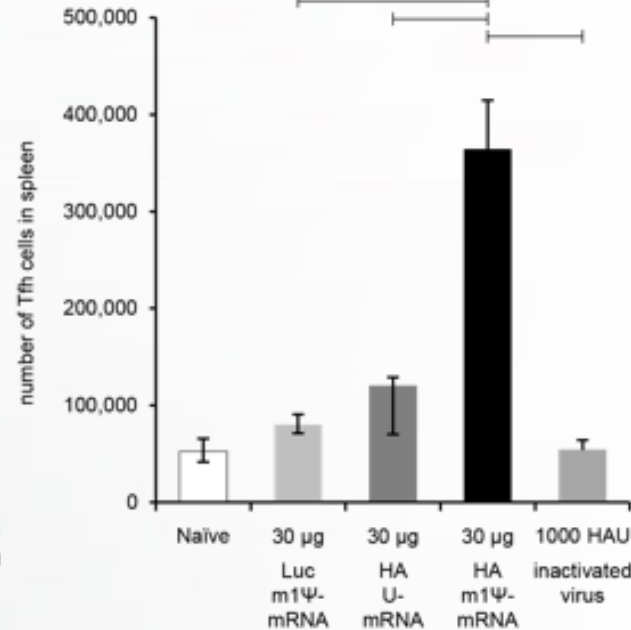


mRNA Vaccines: Acuitas Experience

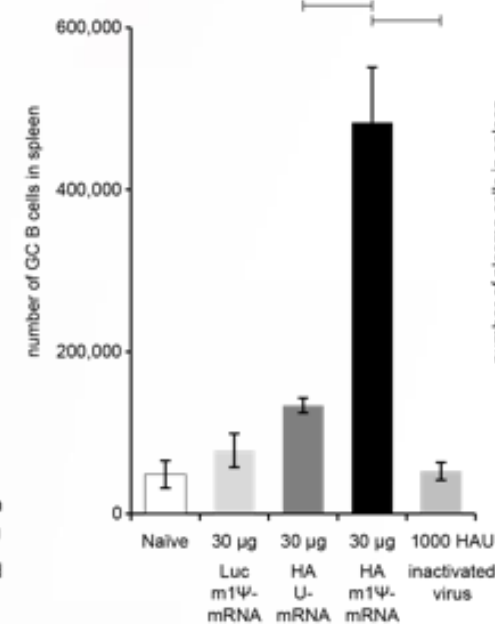
Antibody Titres



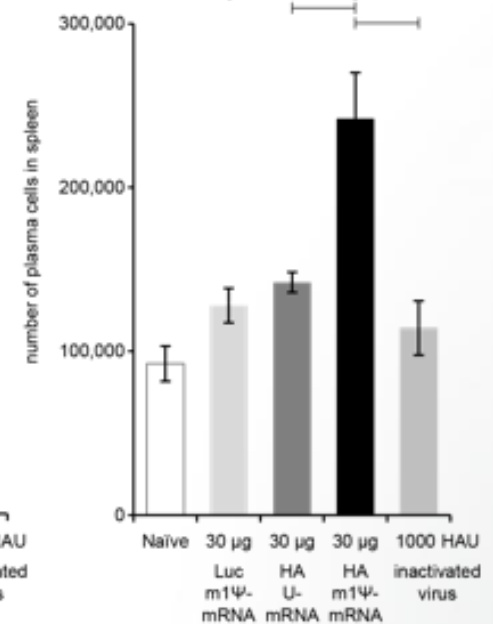
Splenic CD4+ Tfh-Cells



Germinal Centre B-cells



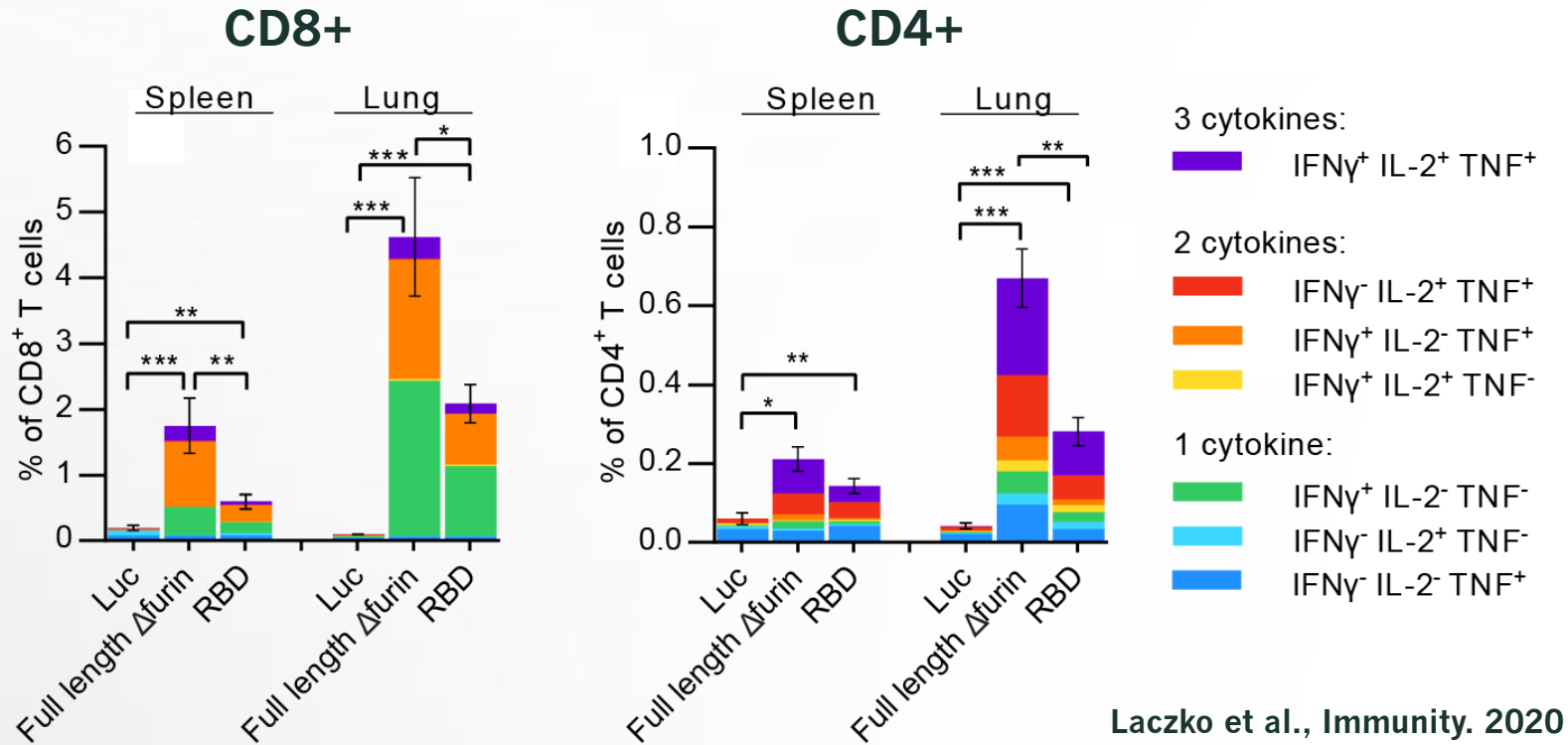
Plasma B-Cells



Pardi. et al., Immunity. 2018

- Extremely potent antibody responses induced by mRNA LNP vaccines against numerous pathogens including influenza and Zika driven by induction of T-follicular helper cells and germinal center and plasma B-cells

COVID-19 mRNA Vaccines: Acuitas Experience



- i.m. Immunization with mRNA-LNP encoding full length or receptor binding domain of SARS-CoV2 spike protein induces Th1-biased multifunctional T-cell responses in spleen and lung

COVID-19 mRNA Vaccines: Acuitas Experience

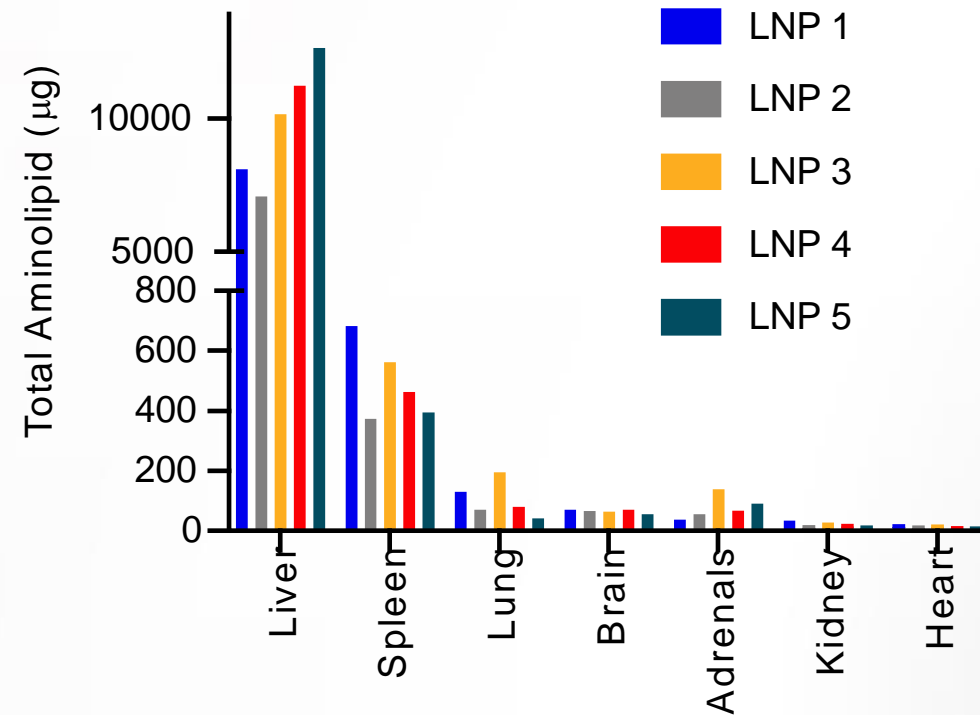
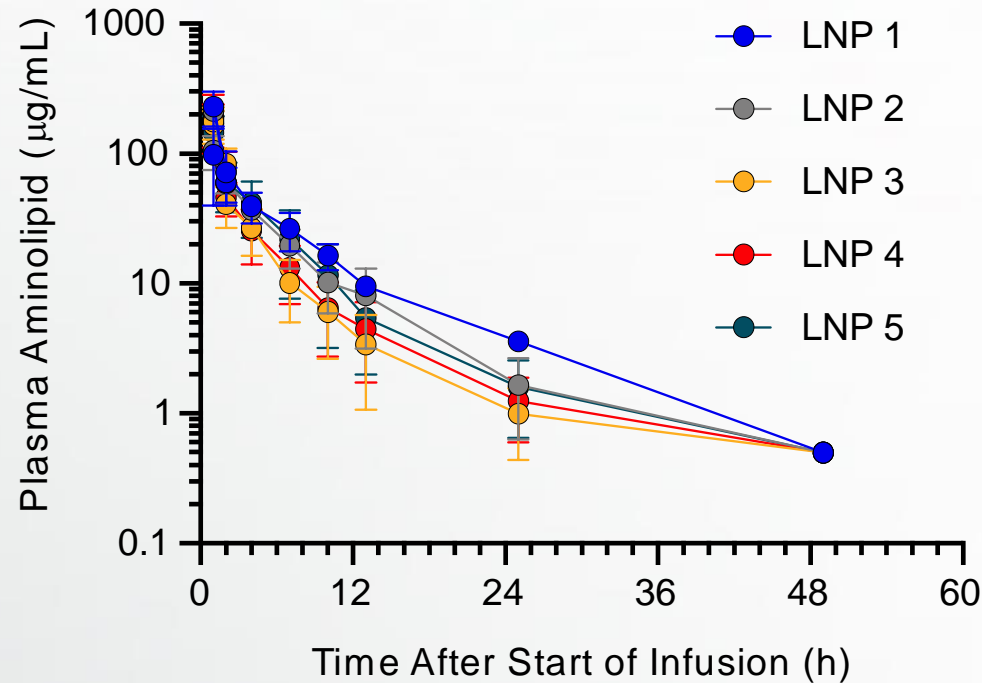
- ▶ Phase I results for rabies vaccine (CureVac) Jan 2020
 - ▶ Strong immune response at 1 µg mRNA dose
- ▶ Collaborations on COVID-19 vaccine development
 - ▶ BioNTech-Pfizer
 - COMIRNATY® authorized for Emergency Use Dec 2020
 - ▶ CureVac
 - Phase 2a/3 study initiated Dec 2020
 - Filing for Emergency Use authorization expected 1H 2021

Core Internal Research: NHP Program

► Objectives

- Characterize mRNA-LNP biodistribution, pharmacokinetics, pharmacodynamics & safety
- Optimize mRNA-LNP carriers for expression of therapeutic proteins & gene editing/base editing clinical candidates

Characterization in NHP: Pharmacokinetics & Biodistribution

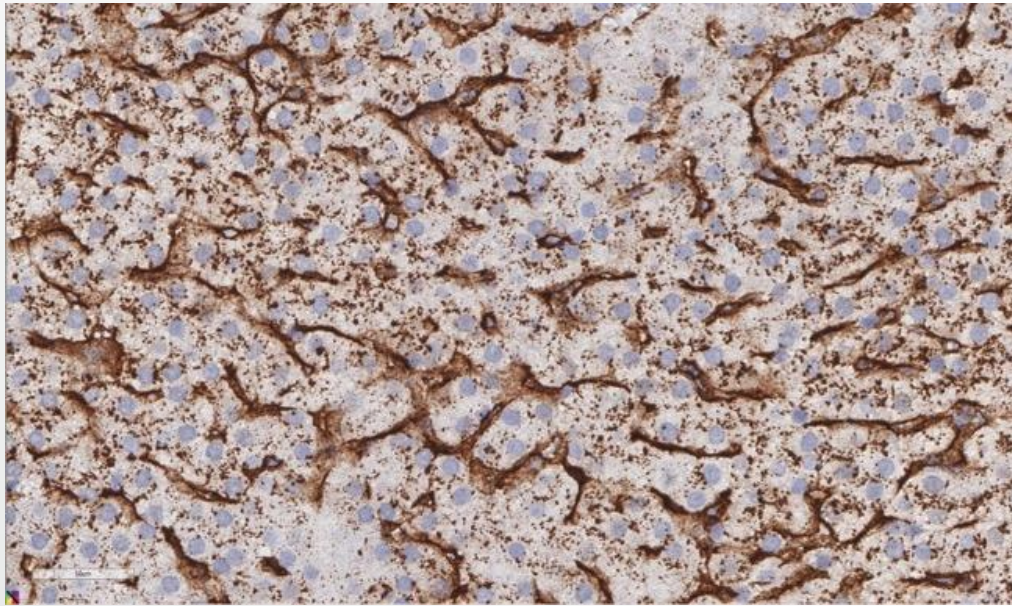


- Rapid clearance from blood compartment
- Distribution primarily to liver & spleen

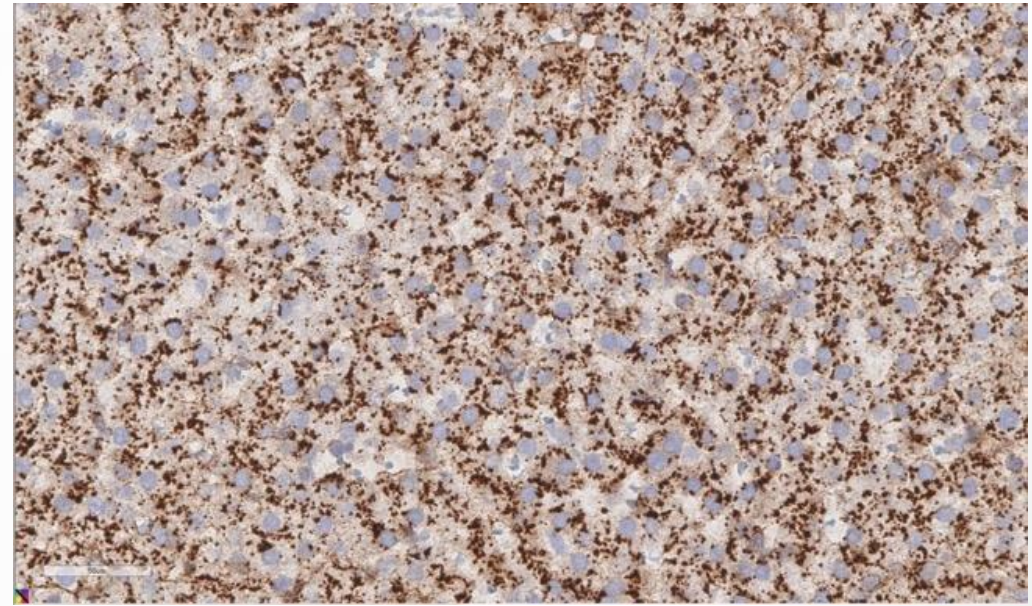
Cell Specific Uptake: Hepatocytes

In Situ Hybridization (mRNA)

First Generation LNP



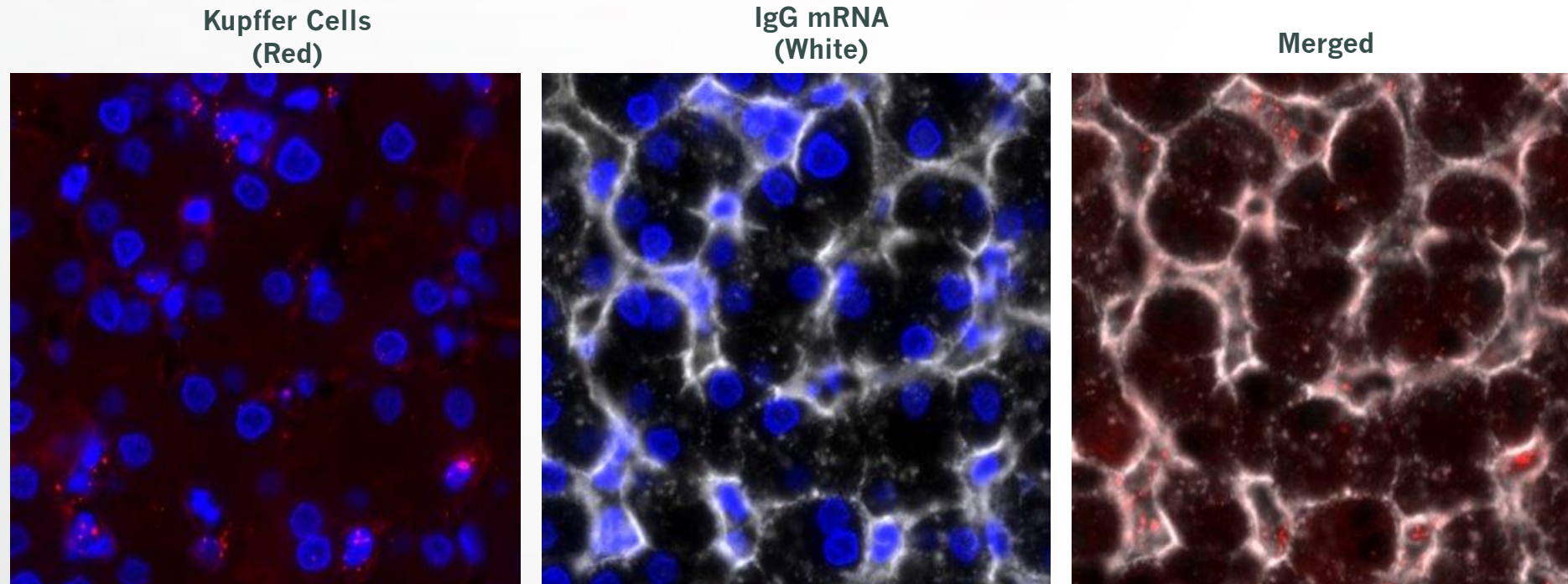
Next Generation LNP



- ▶ New generation LNP have broad liver distribution with little retention in sinusoids
- ▶ Effective delivery of mRNA to hepatocytes

Cell Specific Uptake: Kupffer Cells

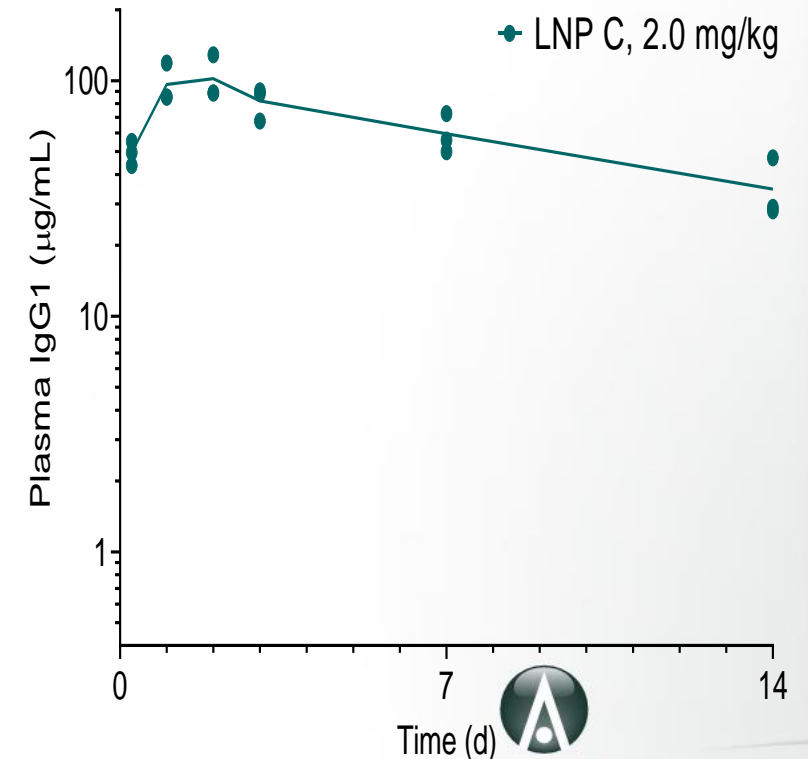
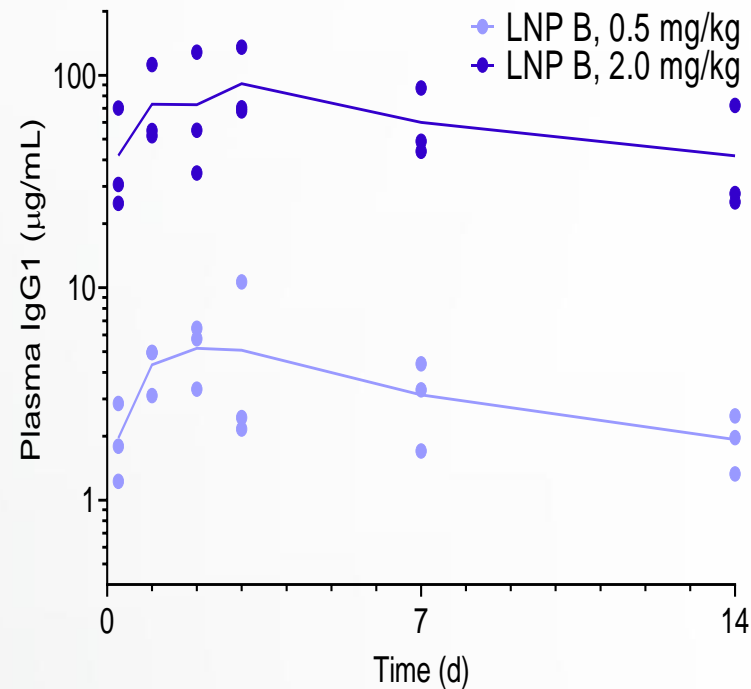
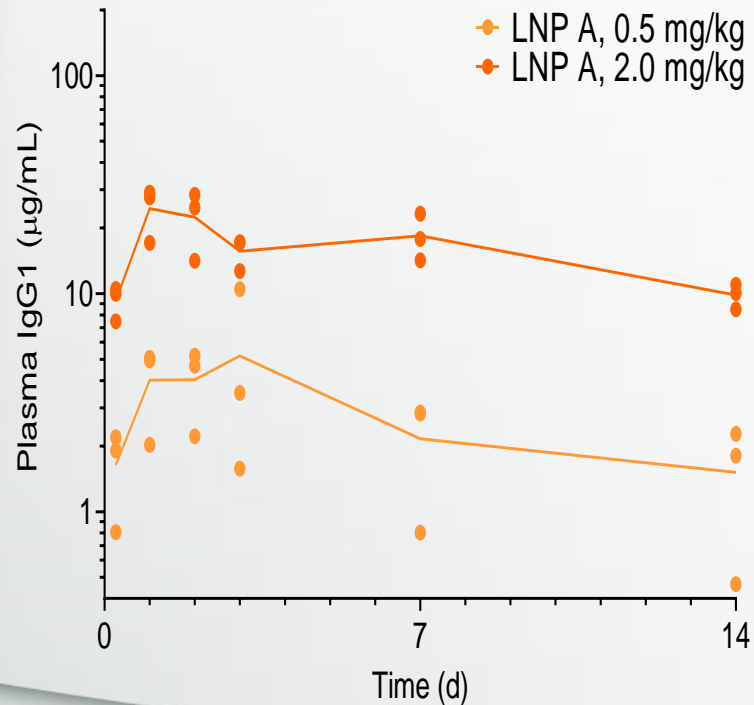
In Situ Hybridization (mRNA): Kupffer Cells



- Minimal mRNA uptake into Kupffer cells

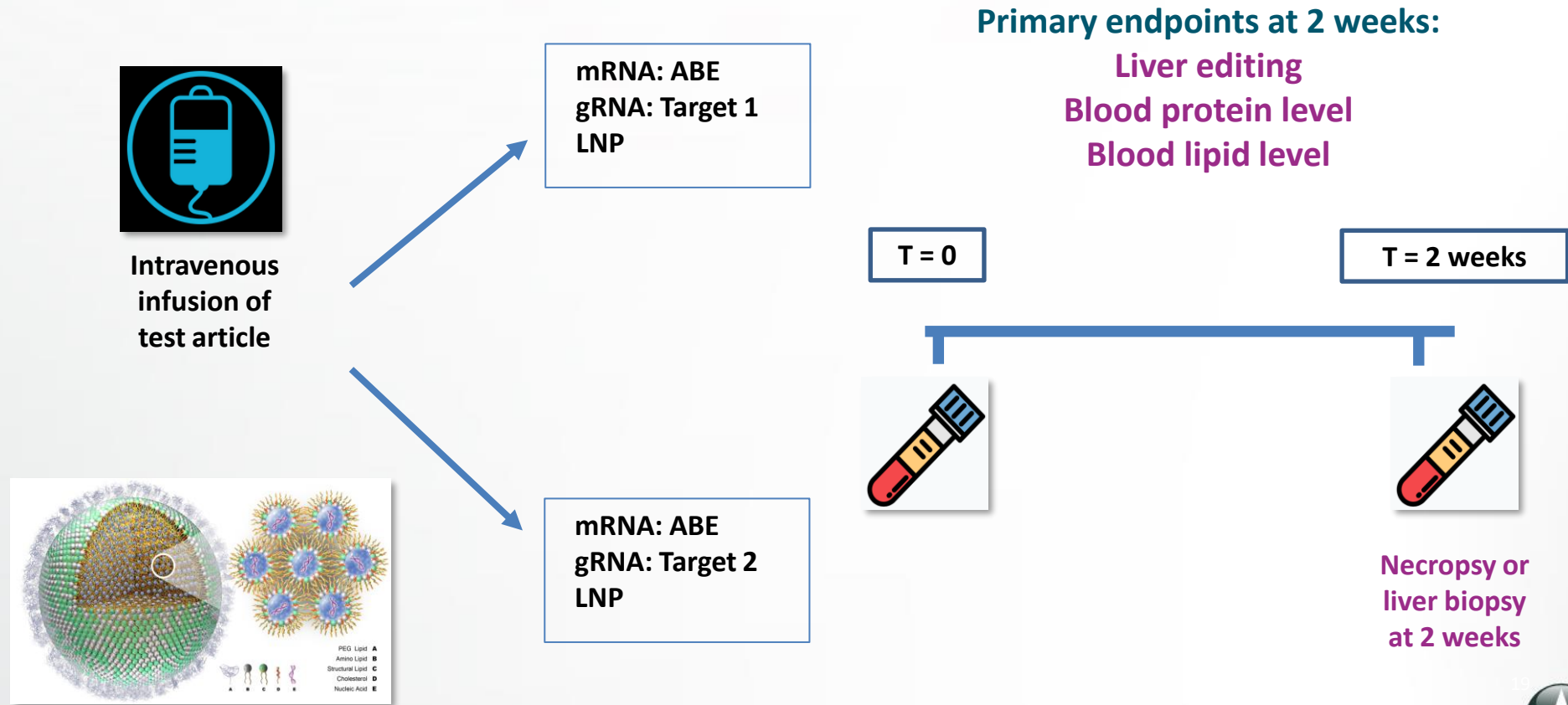
mRNA Monoclonal Antibodies

- High levels of protein (IgG) expression associated with homogeneous mRNA delivery in liver

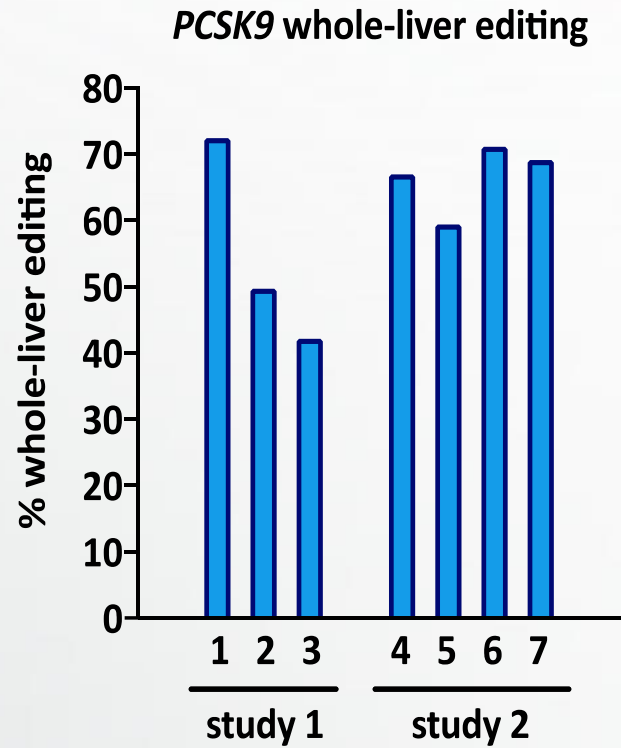


mRNA-LNP Clinical Applications: Base Editing Candidates

NHP Study Design

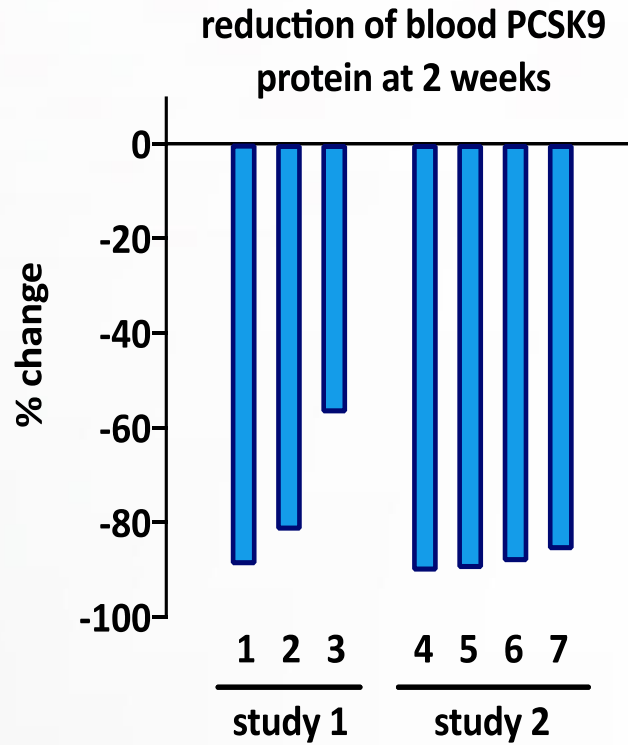


PCSK9 Base Editing: Pharmacodynamics



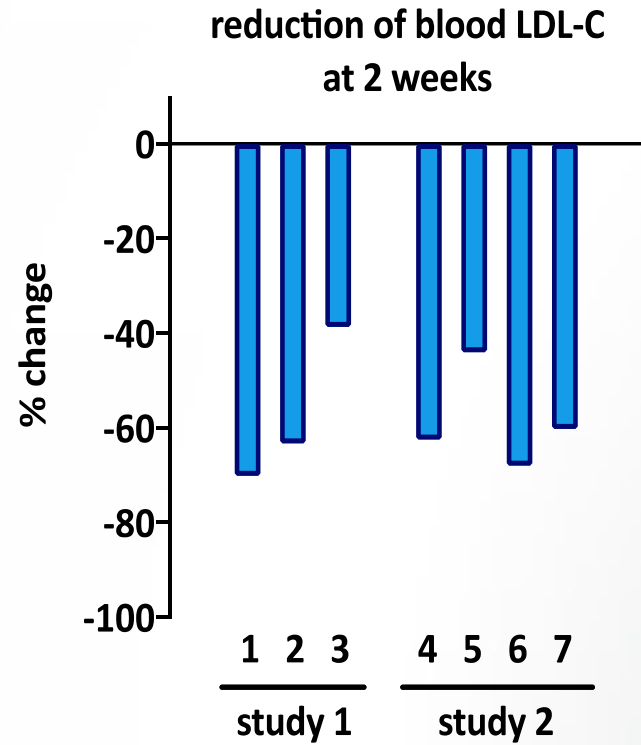
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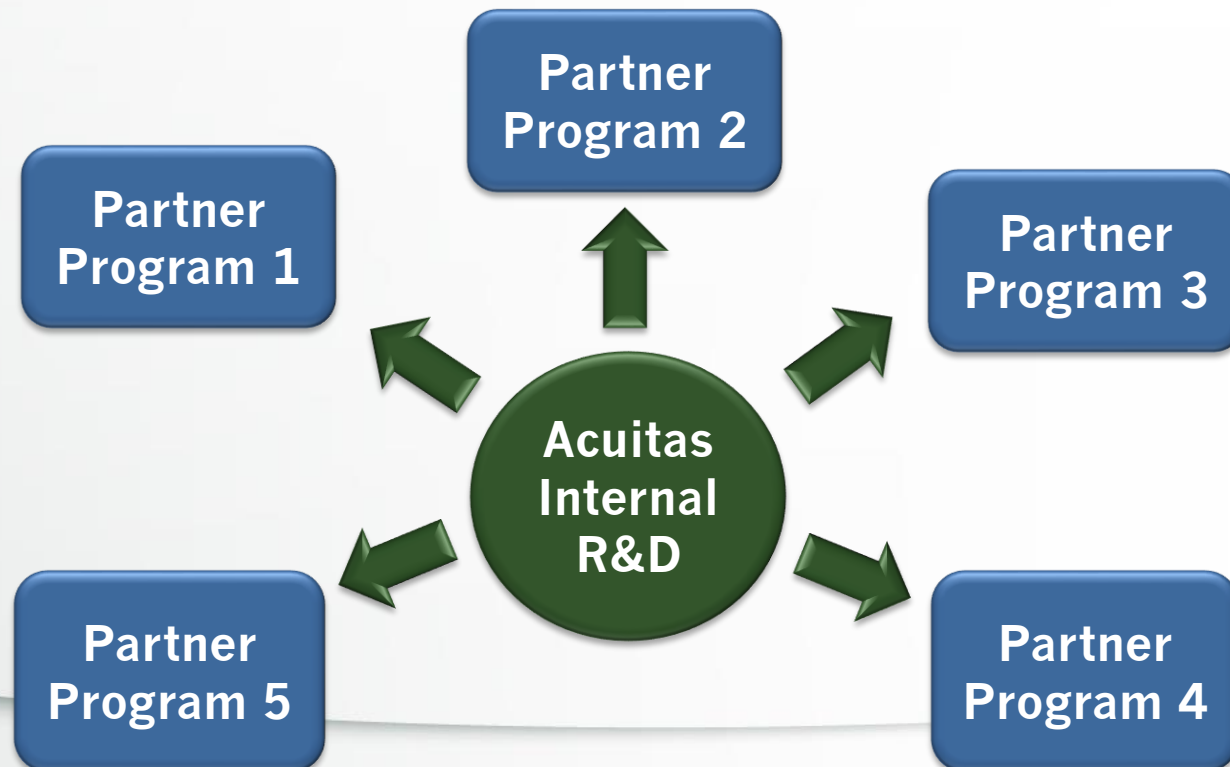
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What makes Acuitas the Leader?

- ▶ Highest potency LNP carriers for mRNA therapeutics
- ▶ Broad IP portfolio providing commercial rights for mRNA-LNP therapeutics
- ▶ Broad partnership experience in mRNA therapeutics field
 - ▶ Multiple partnered products authorized or in clinical development
- ▶ Strong academic collaborations with KOLs
 - ▶ Expanding clinical opportunities for mRNA therapeutics
 - ▶ Strong publication record in leading scientific journals

Acuitas Business Model

- ▶ Partner with multiple pharmaceutical/biotechnology companies to advance mRNA-LNP therapeutics
- ▶ Maintain leadership position in LNP Technology while supporting partner development programs



Contact Information

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