PRESENTATION

Interim OTC Deficiency Phase 2 Results and LUNAR 2.0™ Next-Generation mRNA Delivery Platform

September 23, 2026

Forward Looking Statements

This presentation contains forward-looking statements. These statements relate to future events and involve known and unknown risks, uncertainties and other factors which may cause our actual results, performance or achievements to be materially different from any future performances or achievements expressed or implied by the forward-looking statements. Each of these statements is based only on current information, assumptions and expectations that are inherently subject to change and involve a number of risks and uncertainties. Forward-looking statements include, but are not limited to, statements about: our strategy, future operations, collaborations, the likelihood of success (including safety and efficacy) and promise of our pipeline (including ARCT-810 and ARCT-2601), the planned initiation, design or completion of clinical trials, the ability to enroll subjects in clinical trials, the timing for receipt of data, the likelihood that preclinical or clinical data will be predictive of future clinical results, the likelihood that interim data or preliminary findings will be predictive of the complete data sets or final conclusions from the Phase 2 study, the likelihood that the Company will continue the Phase 2 Study or the OTC program, the likelihood that ARCT-2601 will proceed into the ongoing Phase 2 Study or any other study, the likelihood that a regulatory agency will agree with assessments of key biomarkers, the likelihood that biomarker results of ARCT-810 will lead to increased urea cycle function, the likelihood that clinical data will be sufficient to proceed into more advanced studies or for regulatory approval, the anticipated timing for regulatory submissions, the timing of, and expectations for, any results of any preclinical or clinical studies or regulatory approvals, the potential administration regimen or dosage and any statements other than statements of historical fact.

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Today's Key Messages

1 ARCT-810 Clinical Evidence

- **Generally safe and well-tolerated** across repeated dosing
- **ALL subjects** maintained **normal ammonia** levels & exhibited **reduction in glutamine** despite generally increased protein intake

2 LUNAR 2.0™: NEW Standard in mRNA Delivery

- **40× higher EPO expression** vs. LUNAR 1.0, in NHPs
- **38× higher OTC expression** vs. the lipid used in ARCT-810, in NHPs
- **More protein from less mRNA** improves dose and interval flexibility

3 ARCT-2601 Utilizes LUNAR 2.0™

- **Preliminary non-GLP package:** no new findings vs. ARCT-810
- **FDA has seen LUNAR 2.0™ data and provided favorable advice**
- **Plan** to integrate -2601 into present ARCT-810 Phase 2 study YE 2026

4 New Platform to Impact Patients and Pipeline

- **Less frequent dosing, lower dose levels, shorter infusions**
- **LUNAR 2.0™** unlocks new target opportunities PKU & Gout
- **AI infrastructure** accelerates innovation and development efficiency

ARCT-810 (LUNAR-OTC)

mRNA Therapeutic Candidate
for Ornithine Transcarbamylase (OTC) Deficiency

ARCTURUS therapeutics

Ornithine Transcarbamylase (OTC) Deficiency

The most common urea cycle disorder

- 10,000 prevalence in U.S./Europe
- The urea cycle converts neurotoxic ammonia to water-soluble urea that can be excreted in urine
- Deficiency in OTC causes elevated blood ammonia, which can lead to neurological damage, coma, and death

Unmet Medical Need

- Present standard of care involves a strict diet (low protein, high fluid intake) plus ammonia scavengers
- Present standard of care does not effectively prevent life-threatening spikes of ammonia
- Severe OTC Deficiency patients are referred for liver transplant, currently the only cure

LUNAR-OTC Aims to Restore Enzyme Function

- Establishing expression of OTC enzyme in liver has potential to restore urea cycle activity to detoxify ammonia, preventing neurological damage and potentially removing need for liver transplantation

ARCT-810 Clinical Trials

Phase 1 – Healthy Volunteers

- Safe and generally well-tolerated in 24 adults

Phase 1b – Single, Ascending Dose Study in OTC Deficiency Adults

- 0.2 – 0.5 mg/kg in 16 adults
- Safe and generally well-tolerated

Phase 2 – Single Dose, Multiple Administrations, Placebo-Controlled Study in OTC Deficiency Adolescents and Adults (UK, EU)

- Enrollment of 6 subjects at the 0.3 mg/kg dose level (x6 IV infusions every 2 weeks) and 2 participants with placebo
- Safe and generally well-tolerated
- Limited glutamine measurements suggested reduction in glutamine compared to placebo

Phase 2 – Multiple doses, Multiple Administrations, Open Label Study (U.S.)

- Examination of 0.3 mg/kg and 0.5 mg/kg doses (x5 IV infusions every 2 weeks)
- More frequent measurements of urea cycle biomarkers and function

ARCT-810 has been consistently safe and well-tolerated with data suggesting improved urea cycle function

U.S. Phase 2 Study Overview

- **Open-label, dose-ascending, multiple dose administration study**
  - 0.3 mg/kg and 0.5 mg/kg, 5 IV infusions every 2 weeks with 4-week follow-up
- **Enrolled adolescents and adults with confirmed OTC deficiency**
  - Participants directed to maintain baseline diet (e.g., protein intake) and medical management (e.g., ammonia scavenger medications)
- **8 participants were enrolled across both dosing cohorts (n=4 each)**

All dosing has been completed with preliminary findings presented here

U.S. Phase 2 Summary of Safety and Tolerability

- **No serious adverse events**
- **Most treatment emergent adverse events (TEAEs) in both 0.3 mg/kg and 0.5 mg/kg dosing cohorts were mild to moderate in severity** – Most common TEAEs were headache (2/8), transaminitis (2/8), and IRRs (2/8)
  - Both Grade 3 non-serious asymptomatic transaminitis events resolved without additional intervention after stopping study drug

	0.3 mg/kg (N=4)	0.5 mg/kg (N=4)
Participants with TEAE, n	4	4
TEAE events, n	14	11
Participants with related TEAE, n	3	4
Related TEAE events, n	8	8
Grade 1	3	6
Grade 2	4[+]	1
Grade 3	1	1
Discontinued due to AE	1[+]	0
Serious AEs, n	0	0
AESIs (hyperammonemia)	0	0
Participants with IRR, n	1	1

ARCT-810 was generally safe and well-tolerated following multiple dose administrations

[+]One participant discontinued after a single dose of ARCT-810 due to a non-serious Grade 2 AE of IV infiltration with a subsequent Grade 2 site injection reaction.

U.S. Phase 2 Efficacy Measures

- **Clinically-relevant biomarkers of urea cycle** – plasma ammonia and glutamine
- **OTC enzyme activity through urea cycle byproduct enrichment** – Relative urea function (RUF)
- **Dietary intake** – Focus on protein intake given its centrality to OTC deficiency clinical management

Participant Baseline Characteristics

	0.3 mg/kg (N=3[+])	0.5 mg/kg (N=4)
Sex n (%)	F 3 (100%)	F 4 (100%)
Race n (%)	White 3 (100%)	White 4 (100%)
Ethnicity (n,%)	Hispanic 1 (33%)	Hispanic 1 (25%)
Age (yrs) Median (Range)	46 (14 – 57)	32 (17 – 42)
BMI (kg/m^2) Median (Range)	24.1 (20.4 – 30.7)	23.5 (17.0 – 24.8)
Nitrogen Scavengers n (%)	2 (67%)	4 (100%)

Expansion of prior Phase 2 study measures to better understand ARCT-810's impact on urea cycle function

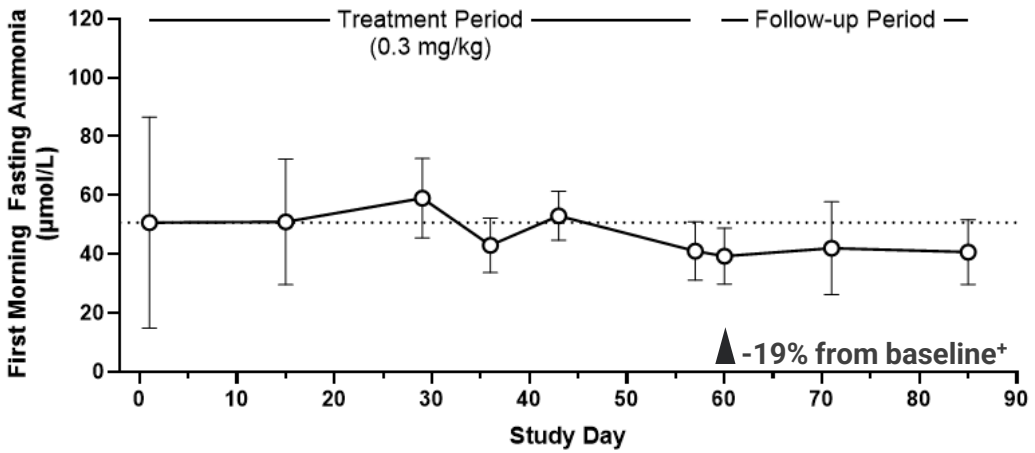
[+]One participant discontinued after a single dose of ARCT-810 due to a non-serious Grade 2 AE of IV infiltration with a subsequent Grade 2 site injection reaction.

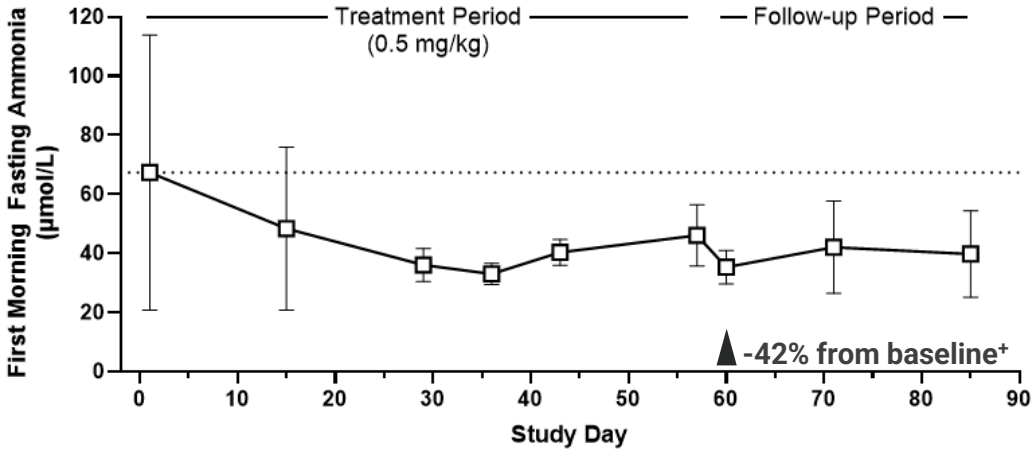
Changes in Clinically Relevant Biomarkers: Ammonia

Objective: Stable first morning fasting plasma ammonia levels with ARCT-810

Results

- 2/7 (29%) participants had elevated ammonia at baseline
- At 0.3 mg/kg and 0.5 mg/kg dose levels, mean ammonia levels were similar or lower than baseline





All participants achieved and maintained normal ammonia levels following ARCT-810

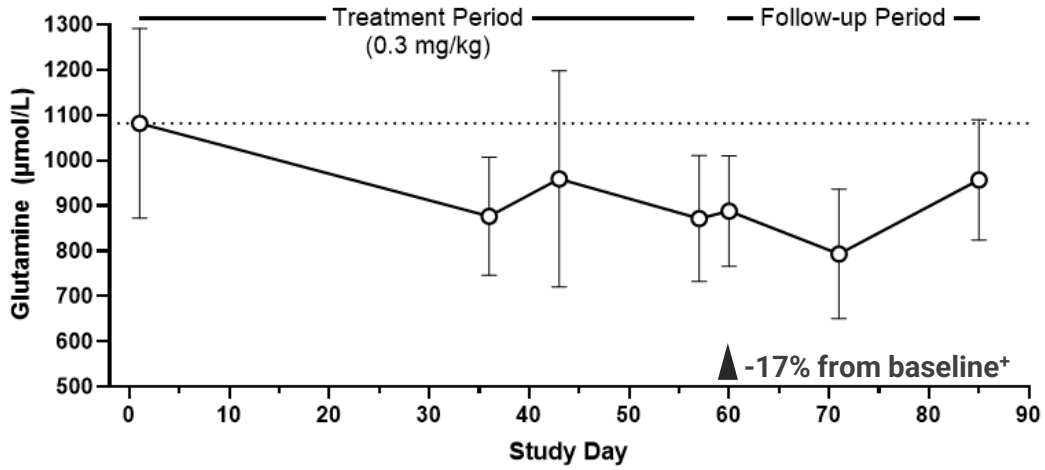
Points represent means ± SD of 3-4 participants. Dotted line indicates mean baseline value. +Mean difference between Day 60 (3 days after last dose) and baseline. Best available data as of 11Sep2026.

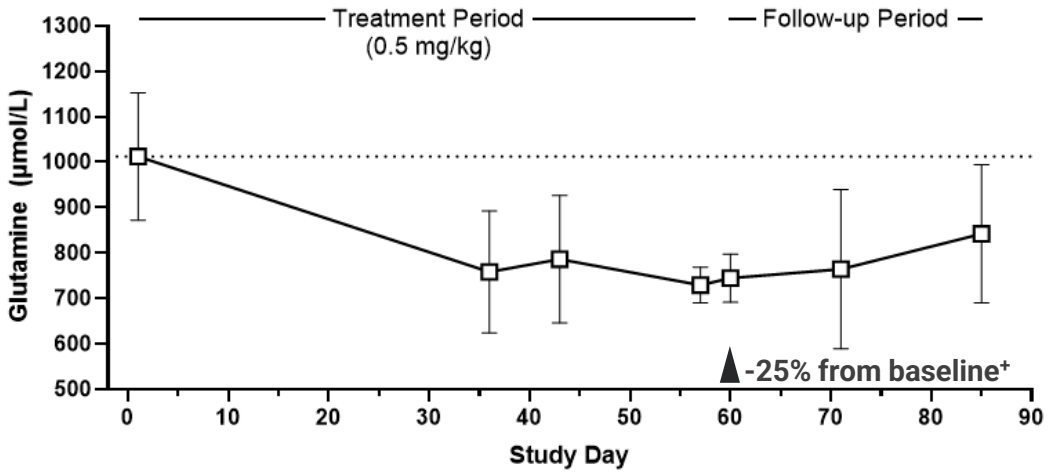
Changes in Clinically Relevant Biomarkers: Glutamine

Objective: Reduction in plasma glutamine levels following ARCT-810

Results

- 7/7 (100%) participants had elevated glutamine at baseline
- At 0.3 mg/kg and 0.5 mg/kg dose levels, mean glutamine levels were lower than baseline



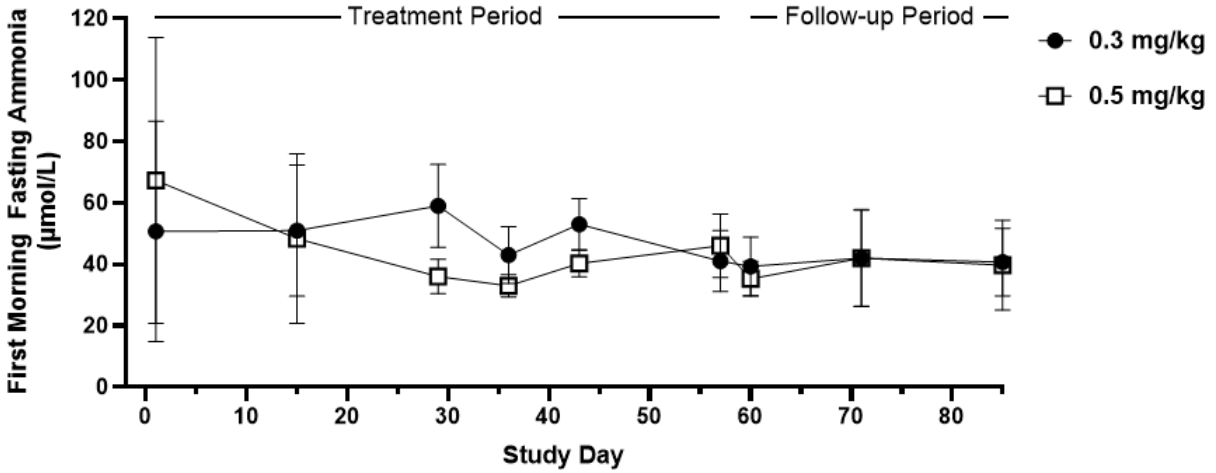


All participants exhibited reduction in glutamine levels following ARCT-810

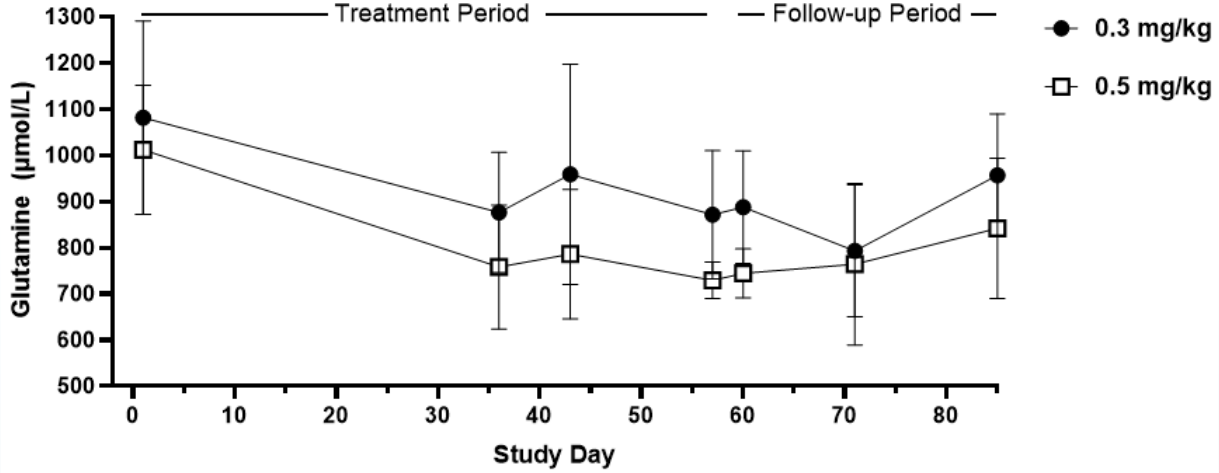
Points represent means ± SD of 3-4 participants. Dotted line indicates mean baseline value. +Mean difference between Day 60 (3 days after last dose) and baseline. Best available data as of 11Sep2026.

Ammonia & Glutamine ARCT-810 Dose Comparison

Ammonia



Glutamine



Consistent reductions observed at both 0.3 & 0.5 mg/kg ARCT-810 doses studied

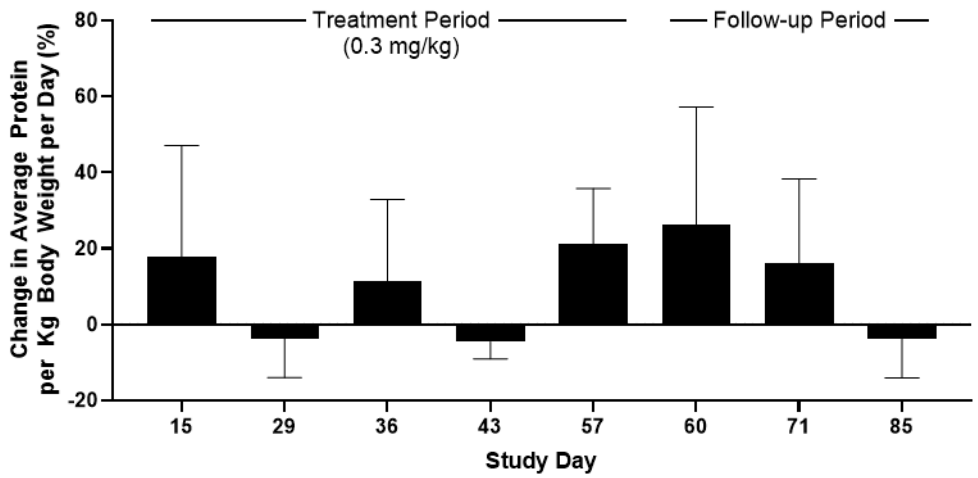
Points represent means ± SD of 3-4 participants. Best available data as of 11Sep2026.

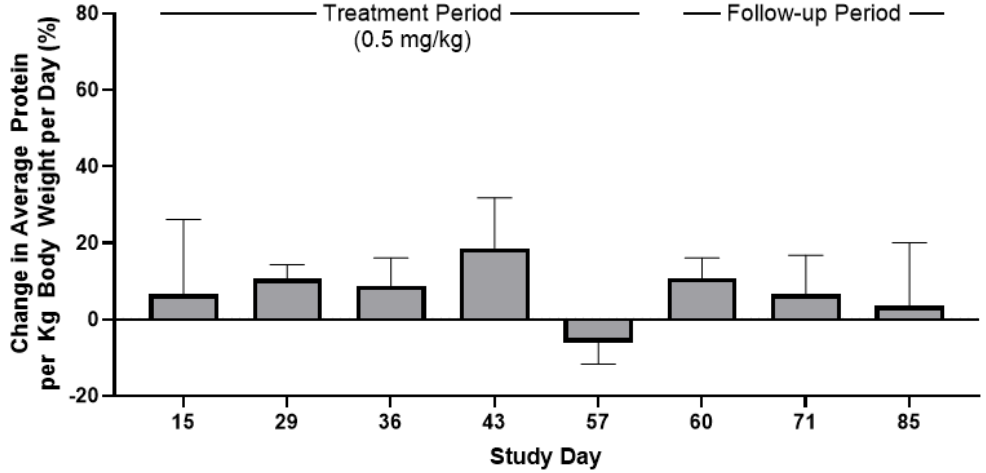
Biomarker Reductions Observed Despite Increased Protein Intake

Objective: Stable protein intake (within 25% of baseline)

Results

- At 0.3 mg/kg and 0.5 mg/kg dose levels, mean protein intake generally increased above baseline
- 5/7 (71%) participants had ≥1 timepoint that exceeded 25% baseline protein intake
  - All participants gained weight over course of study





Increased protein intake + reductions in ammonia & glutamine → suggests increased urea cycle activity

Columns represent means ± SD of 3-4 participants. Best available data as of 11Sep2026.

U.S. Phase 2 Study Summary

- **Multiple doses of ARCT-810 at both dose levels was generally safe and well-tolerated** – Similar safety profiles between 0.3 mg/kg and 0.5 mg/kg
- **Evidence suggesting ARCT-810 increases urea cycle function –** As detected by clinically-relevant biomarkers of urea cycle activity (ammonia and glutamine)
- **Increases in protein intake suggests ARCT-810 may allow for better protein tolerance** – Important clinical outcome

ARCT-810 shows good safety profile and evidence of improvements in urea cycle function

Key Opinion Leader, Dr. Marshall Summar

Marshall Summar, M.D., Former founding member and Executive Committee member of the NIH UCD Consortium, a recognized expert in rare diseases and OTC deficiency, will participate in the presentation.

- Previously Chief of the Division of Genetics and Metabolism, Director of the Rare Disease Institute and the Margaret O'Malley Chair of Genetic Medicine at Children's National Hospital, Emeritus Professor of Pediatrics at George Washington University. Dr. Summar is an internationally recognized expert in urea cycle disorders (UCDs) with over four decades of clinical, research, and policy leadership. He is a founding member and Executive Committee member of the NIH UCD Consortium, where he led national UCD diagnostic and treatment consensus efforts. For more than 20 years, he served on the Scientific Advisory Board of the National UCD Foundation and has advised numerous academic and industry initiatives. He is the author of over 40 UCD-related publications, including GeneReviews®, clinical guidelines, and multinational natural history studies. As an inventor, he holds patents for ammonia diagnostics and UCD-related technologies and has led translational research in critical care and neonatal disease. In recognition of his long-standing contributions to rare disease research and clinical infrastructure, he received the National Organization for Rare Disorders Lifetime Achievement Award in 2022

KOL Perspective: ARCT-810 Phase 2 Data

- **The glutamine result is what persuades a metabolic physician:** elevated in every participant despite mostly normal ammonias, down in every participant on drug, and back toward baseline once dosing stopped. That is drug effect, not variability.
- **The clear ammonia decline in the 0.5 mg/kg cohort was a surprise:** these were stable patients on unchanged scavenger doses, where a flat line is the expected result.
- **Adoption should be brisk rather than cautious:** the safety profile is clean and the biochemistry is legible to treating physicians, so I would expect 25% or more of eligible patients to be early adopters.

ARCT-810 is safe, tolerated, and effective, and the treating community is prepared to use it

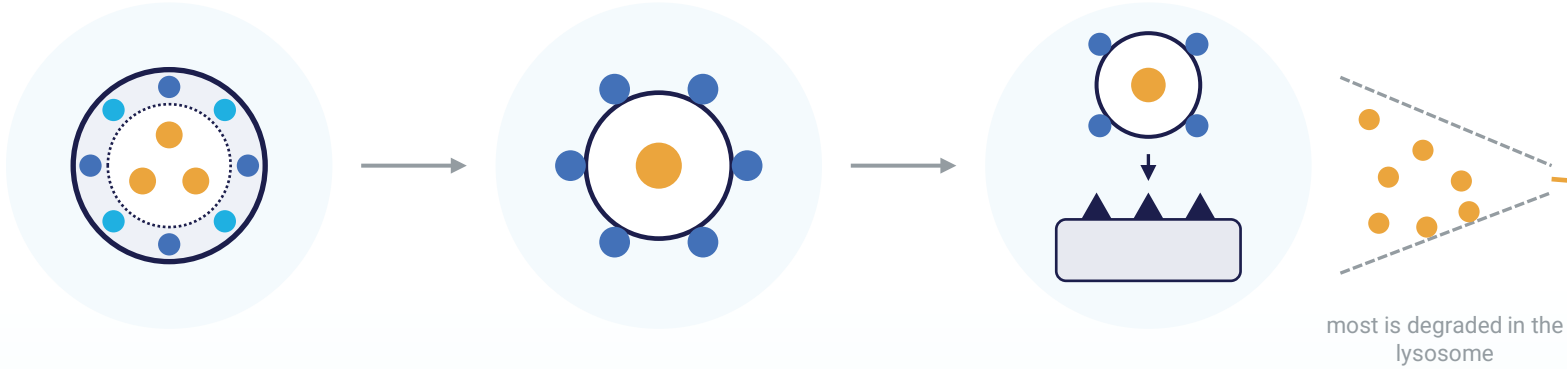
ARCTURUS® therapeutics

ADVANCES IN LUNAR DELIVERY PLATFORM

LUNAR 2.0™

How IV mRNA–LNP Medicines Work

ApoE carries the particle to the hepatocyte — but escaping the endosome is where the pathway is lost



Four-lipid particle

An ionizable lipid, DSPC, cholesterol and PEG–lipid encapsulate the mRNA.

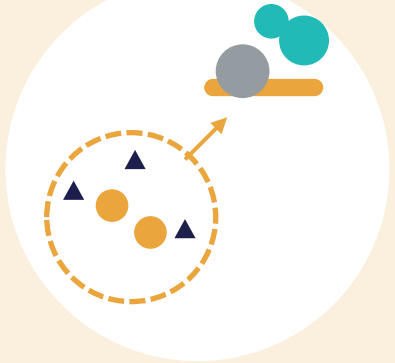
ApoE corona forms

After IV dosing the PEG sheds and plasma ApoE adsorbs onto the surface.

Hepatocyte uptake

ApoE binds LDLR on the hepatocyte and the particle enters by endocytosis.

RATE-LIMITING STEP

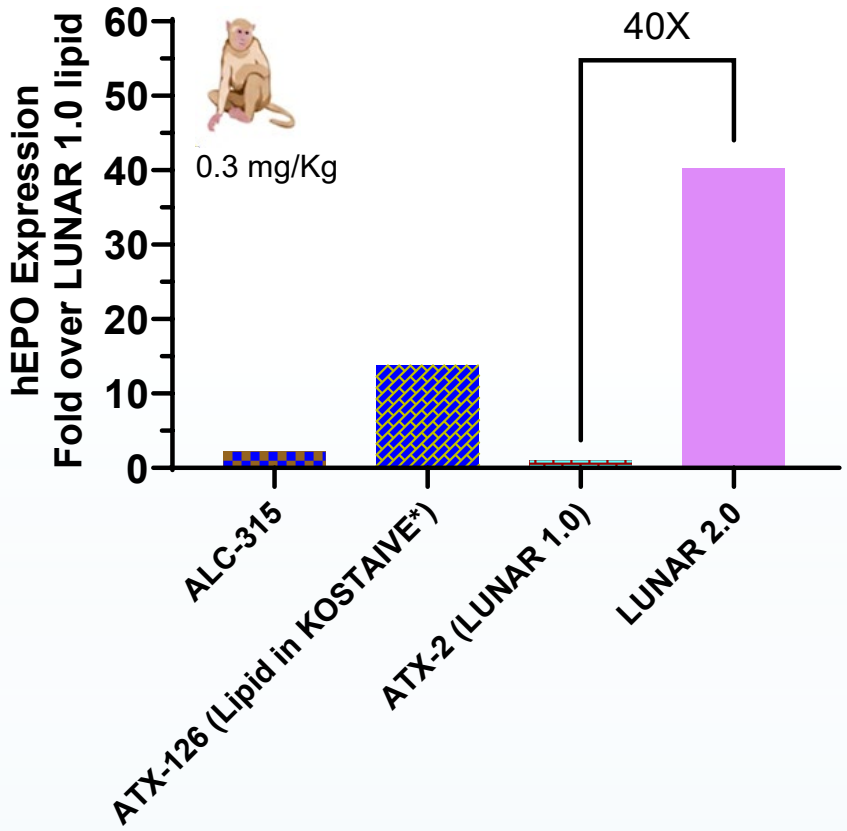


Endosomal escape

The endosome acidifies, the ionizable lipid protonates and mRNA is released to the ribosomes — but most of it never gets out.

Endosomal escape is bottleneck — only ~2-5% of internalized mRNA reaches the ribosome

LUNAR 2.0™ Next Generation LNP: 40-Fold Higher Expression



Relative Fold Enhancement in Human EPO Protein Expression

Lipid	Fold Enhancement Over LUNAR 1.0
ALC-315	2.2
ATX-126 (Lipid in KOSTAIVE®)	14
ATX-2 (LUNAR 1.0)	1.0
LUNAR 2.0™	**40**

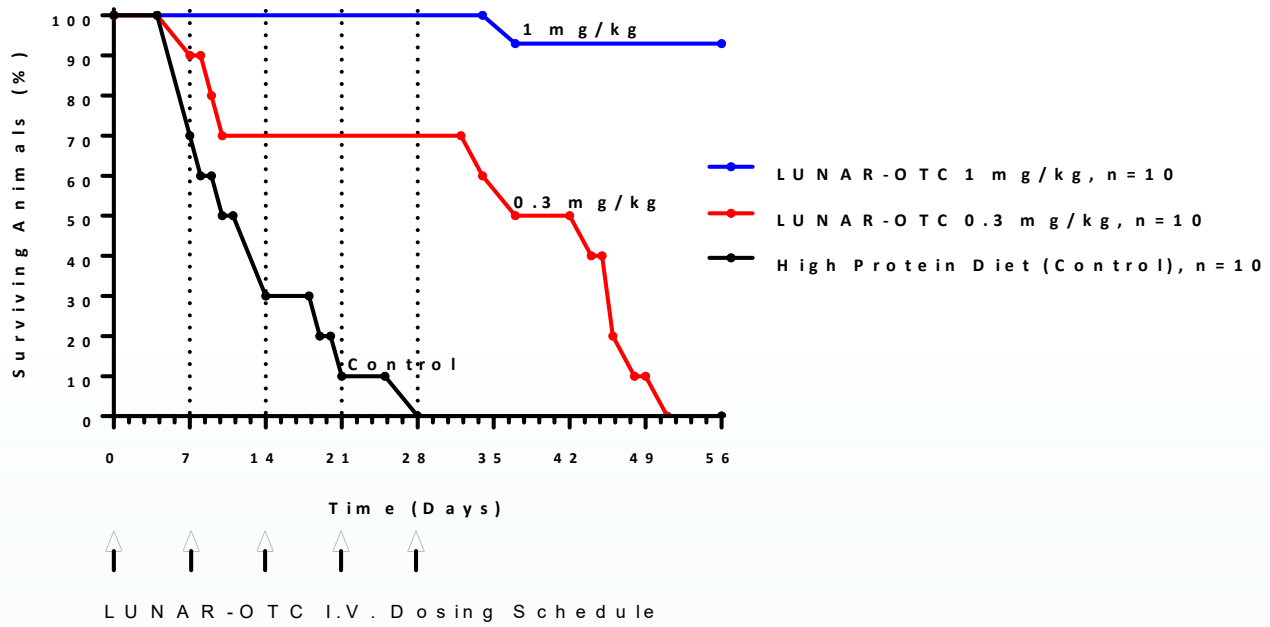
- NHPs (n=3) treated, IV 60-min infusion @ 0.3 mg/kg)
- Plasma concentration 48 hours post infusion
- Only the ionizable lipid differs between arms — same hEPO mRNA, same dose, same infusion

LUNAR 2.0™ produced 40-fold higher hEPO expression in NHPs compared to LUNAR 1.0

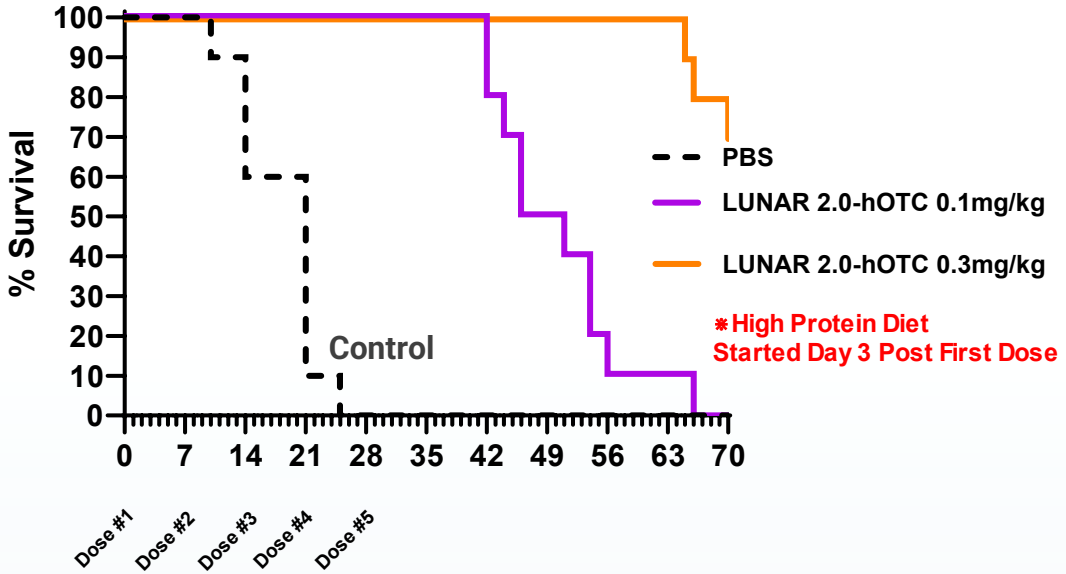
LUNAR 2.0™

ARCT-2601 Highly Effective in OTC-Deficient Model

Survival in OTC-deficient mice on a high-protein diet



ARCT-810 utilizes ATX-95



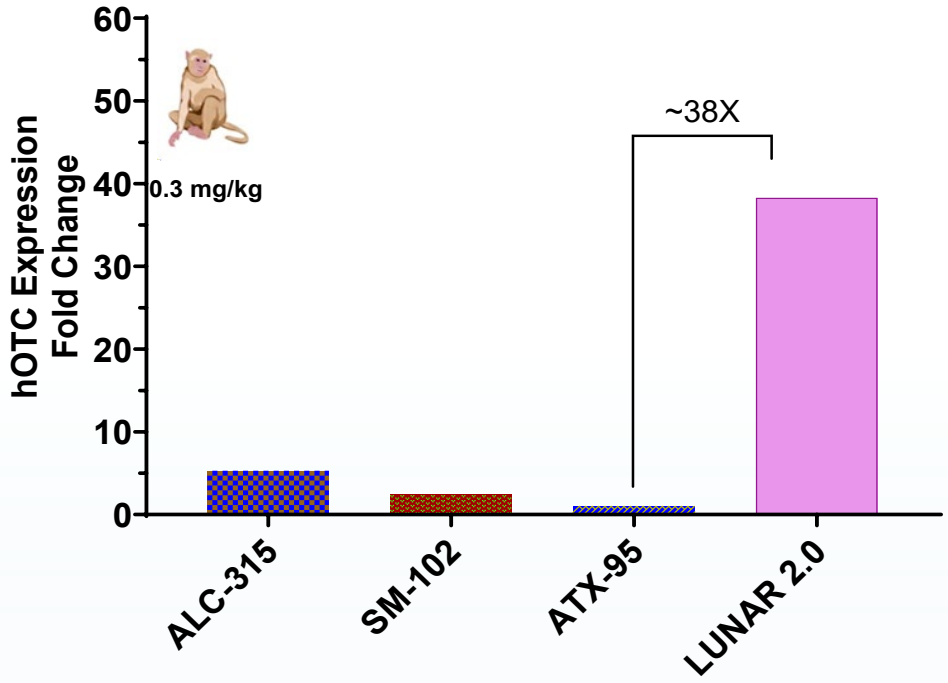
ARCT-2601 utilizes LUNAR 2.0™

ARCT-2601 (LUNAR-OTC 2.0) treatment exhibits dose-dependent survival in lethal OTCD murine model

LUNAR 2.0™

ARCT-2601: 38-Fold Higher hOTC Expression in NHP

compared to ATX-95 (Lipid in ARCT-810)



Relative Fold Enhancement in Human OTC Protein Expression

Lipid	Fold Enhancement Over ATX-95
ALC-315	5.3
SM-102	2.5
ATX-95 (used in ARCT-810)	1.0
LUNAR 2.0™ (used in ARCT-2601)	**38**

- NHPs (n=3) treated, and PBS control; IV 60-min infusion @ 0.3 mg/kg
- Liver biopsies 48h post-infusion analyzed for hOTC via mass spec

LUNAR 2.0™ exhibits 38-fold higher hOTC expression in NHPs compared to ATX-95 (Lipid in ARCT-810)

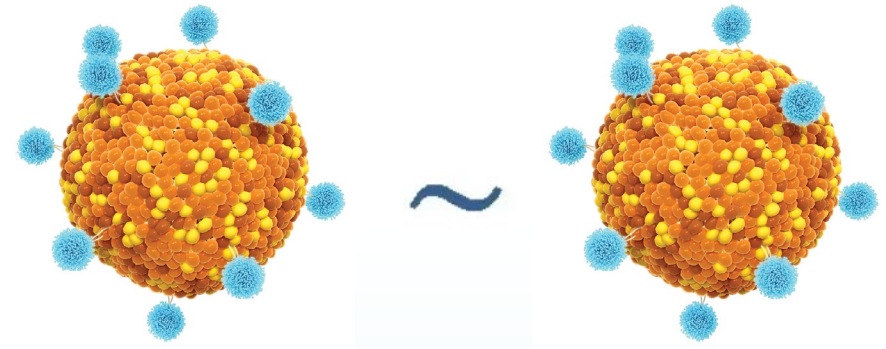
ARCT-2601 (LUNAR-OTC 2.0) Preliminary Safety Data

Three non-GLP preclinical studies, head-to-head against ARCT-810: no new findings

RODENT SAFETY STUDY · NON-GLP
No new findings versus ARCT-810

NHP TOLERABILITY STUDY · NON-GLP
No new findings versus ARCT-810

BIODISTRIBUTION
New LUNAR 2.0™ lipid clears faster



ARCT-2601
LUNAR-OTC 2.0

ARCT-810
LUNAR-OTC

No new safety signals vs. ARCT-810 — and the new LUNAR 2.0™ lipid clears faster

ARCT-2601: FDA Feedback and Regulatory Plan

FDA Type C Meeting on ARCT-2601 Development: Conducted June 2026

- FDA agreed to leverage platform CMC, non-clinical and clinical data to accelerate the development
- FDA agreed to include ARCT-2601 as an arm in the current ongoing ARCT-810 Phase 2 study
- Evaluate preliminary safety, PK, and biomarker data for ARCT-2601 in a small number of patients
- Proceed to an adequate and well-controlled pivotal trial if the initial data are favorable

ARCT-2601 Regulatory / Clinical Plan

- IND Filing 4Q 2026: Evaluate ARCT-2601 in ongoing ARCT-810 Phase 2 study with 3–6 patients
  - Ages ≥12, with elevated baseline ammonia levels
- Advance to a Phase 2/3 pediatric study in H2 2027
  - Ages 0–6, neonatal-onset and severe late-onset patients with unmet medical needs

ARCT-2601 to be integrated into ongoing Phase 2 study as advised by the FDA

LUNAR 2.0™ – Opens Door to Reduced Infusion Time

Better LNP potency × higher concentration → collapses dose volume → collapses clinic time

The Challenge: mRNA-LNP therapeutics targeting the liver must be infused IV

CURRENT

3 Hours

infusion time

VOLUME
250 mL

DOSE
0.5 mg/kg

PROPOSED — NEAR TERM

1 Hour

infusion time

VOLUME
40 mL

DOSE
0.3 mg/kg

FUTURE — SYRINGE PUMP

< 5 Min

infusion time

VOLUME
5 mL

DOSE
0.15 mg/kg

36×	**shorter clinic time** *(3 hr → 5 min)*	**50×**	**lower infusion volume** *(250 mL → 5 mL)*	**7×**	**fewer drug product vials** *(7 vials → 1 vial)*	**RTU**	**ready-to-use** *(no dilution required)*

Engineering mRNA Therapeutics with AI

Arcturus' differentiated computational engine improves design quality, accelerates development, and de-risks pipeline

1 WHAT WE ACQUIRE

Published algorithms, a live platform, and the team behind them

Validated algorithms
neoMS presentation and neoIM immunogenicity prediction — published, peer-reviewed

Platform in production
Ten AI modules on one IVD-ready ImmunoEngine workflow, live with pharma partners

The team behind it
Ghent computational immunology group — a capability we would spend years hiring into San Diego

Advanced Prediction

2 WHAT ARCTURUS GAINS

Better candidates, designed faster and with fewer wasted cycles

- **mRNA & construct design**
  myRNA and myCONSTRUCT into LUNAR and STARR
- **Immunogenicity risk**
  myADA and myEPITOPE screening on expressed protein payloads
- **Targets beyond oncology**
  myPATHOGEN, mySELF and mySURFACE seed starts
- **Translational data**
  myINSIGHTS for biomarker discovery and response prediction

Speed • Quality • Efficiency

3 WHERE IT SHOWS UP FIRST

PKU and Gout demonstrate the near-term application

- **Screen before selection**
  Epitope and ADA-risk screening pre-selection
- **PKU**
  Protein replacement where ADA risk is primary
- **Gout**
  Expressed enzyme payload with the same immune exposure
- **Portfolio read-through**
  Extends to every expressed protein payload in the portfolio

PKU | Gout

Arcturus AI infrastructure accelerates innovation across mRNA therapeutic pipeline

Expansion of Liver Disease Franchise: PKU

LUNAR-PKU: Arcturus's strategy to treat phenylketonuria (PKU)

1 DISEASE BACKGROUND

PKU is a rare inborn error of metabolism

Phenylketonuria results from defective phenylalanine (Phe) metabolism caused by mutations in the enzyme phenylalanine hydroxylase (PAH).

Rare IEM | PAH mutation

2 THERAPEUTIC APPROACH

IV-administered mRNA restores PAH activity

mRNA encoding the PAH enzyme replaces deficient or defective intracellular enzyme activity in patients with PKU.

mRNA-encoded PAH

3 DELIVERY PLATFORM

LUNAR 2.0™ LNP delivers mRNA to the liver

LUNAR 2.0 increased potency combined with mRNA modification enables efficient hepatocyte delivery and franchise expansion into PKU.

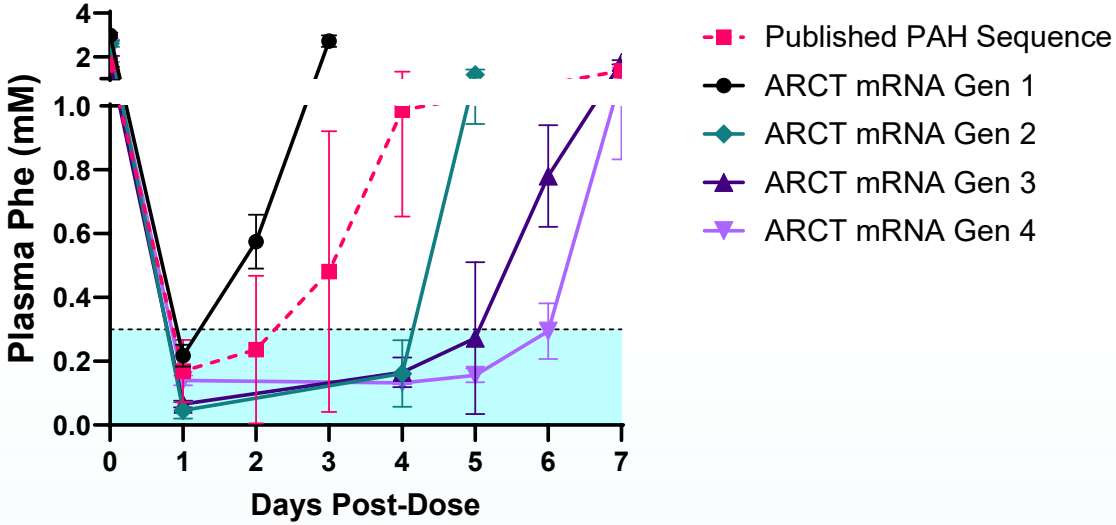
LUNAR 2.0 | Hepatocyte delivery

LUNAR 2.0™ potency plus mRNA modification enable expansion into PKU, a liver disease with high unmet need

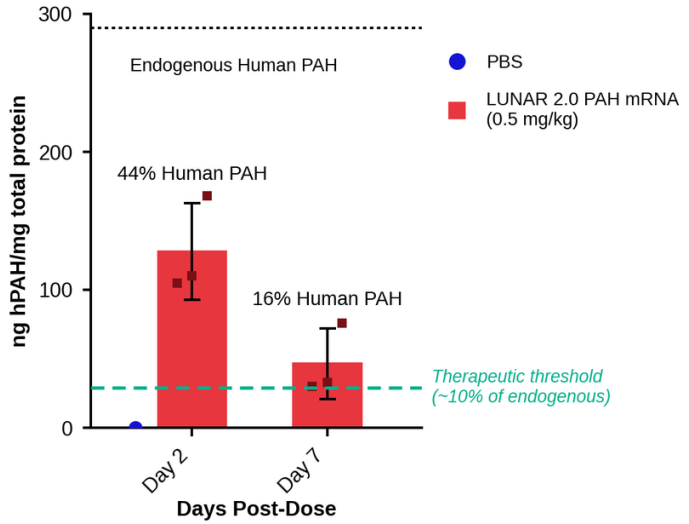
Why PKU Now? Two-Stage Platform Optimization Story

From 24 hours → 6-7 days durability through mRNA + LNP engineering

PAH mRNA-LNPs
1 mg/kg i.v. in PKU Mice



Optimized PAH Expression in NHP Liver



STAGE 1 · Arcturus mRNA Optimization

6-7 days efficacy with improved PAH mRNA

STAGE 2 · PAH Protein Expression in NHP Liver

Optimized mRNA + LUNAR 2.0 lipid leads to robust protein expression in NHP liver at day 2 & day 7 post-IV dose

Single-Dose Durability Achieved Via Coordinated mRNA + LNP Optimization

Gout is a Disease Caused by a Missing Enzyme

Humans lost the gene to make uricase ~15 million years ago

Mammals: uricase ON

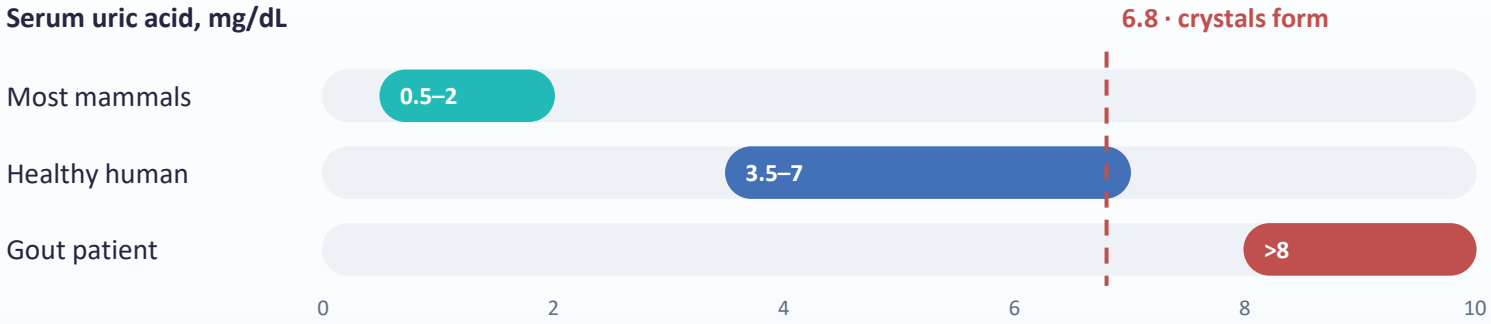
Uric acid is dissolved and excreted

Humans: gene switched OFF

Uric acid builds up → crystals in joints → gout

Arcturus: mRNA turns it back ON

The liver makes uricase, restores ability to excrete uric acid



9.2M U.S. gout patients

200K fail every oral drug

$13.5B uricase market by 2034

Restoring uricase is restoring native biology — a liver-expressed enzyme delivered by LUNAR 2.0

LUNAR 2.0™ Key Takeaways

1 POTENCY

> 30X Improvement

higher liver protein expression than LUNAR 1.0 in NHP

2 ARCT-2601 (OTC Deficiency)

Phase 2: YE 2026

Highly potent in NHPs, no new preclinical safety signals;
FDA-aligned to integrate ARCT-2601 into present ARCT-810 Phase 2 study

3 FUTURE PATIENT CONVENIENCE

Lower Dose → < 5 Min

4 FRANCHISE EXPANSION

PKU · Gout

LUNAR 2.0 + engineered mRNA open the next liver indications

More protein from less mRNA — lower doses, shorter infusions, new indications

KOL Perspective: The LUNAR 2.0™ Platform and ARCT-2601

- **A greater than 30-fold potency gain is a change in kind, not degree:** it moves the objective from supporting the urea cycle to correcting it, and it buys headroom on both dose and interval.
- **Once-monthly dosing is the variable that determines real-world benefit:** in a disease of daily vigilance, interval drives enzyme persistence, and persistence is what changes outcomes.
- **I expect ARCT-2601 to become the standard of care, particularly in severe onset OTC deficiency,** and the same platform reads through to a long list of liver-based rare diseases, where roughly 70% of patients are children. Even if gene editing reaches it's promise patients will still need a significant treatment window and to date edited patients have still required pharmacologic support.

ARCT-2601 should set the standard in OTC deficiency and extend well beyond it

Q & A