



NEXT GENERATION RNA MEDICINES

—
January 2026

JP Morgan Healthcare Conference

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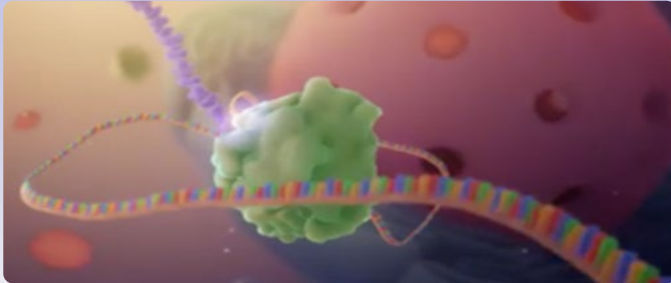
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Arcturus Therapeutics



STARR® mRNA Vaccines



KOSTAIVE®

Approved in **Japan, UK, EU**

LUNAR-H5N1

U.S. Pandemic Flu

PARTNERS

CSL meiji



Nasdaq: ARCT



Headquarters: San Diego, CA

Employees: 100

Founded: 2013

mRNA Therapeutic Candidates



ARCT-810 (LUNAR-OTC)

Ornithine Transcarbamylase Deficiency

ARCT-032 (LUNAR-CF)

Cystic Fibrosis



Proprietary mRNA Technologies Driving Therapeutic Programs

Broad Intellectual Property Portfolio



500+

Patents & Patent Applications



mRNA Technology

- mRNA for protein replacement
- Self-amplifying mRNA (STARR®) low-dose vaccine technology



LUNAR® Delivery

- Hepatocytes – **intravenous**
- Myocytes – **intramuscular**
- Airway Cells – **inhaled**

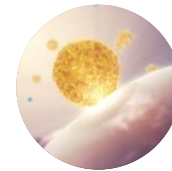
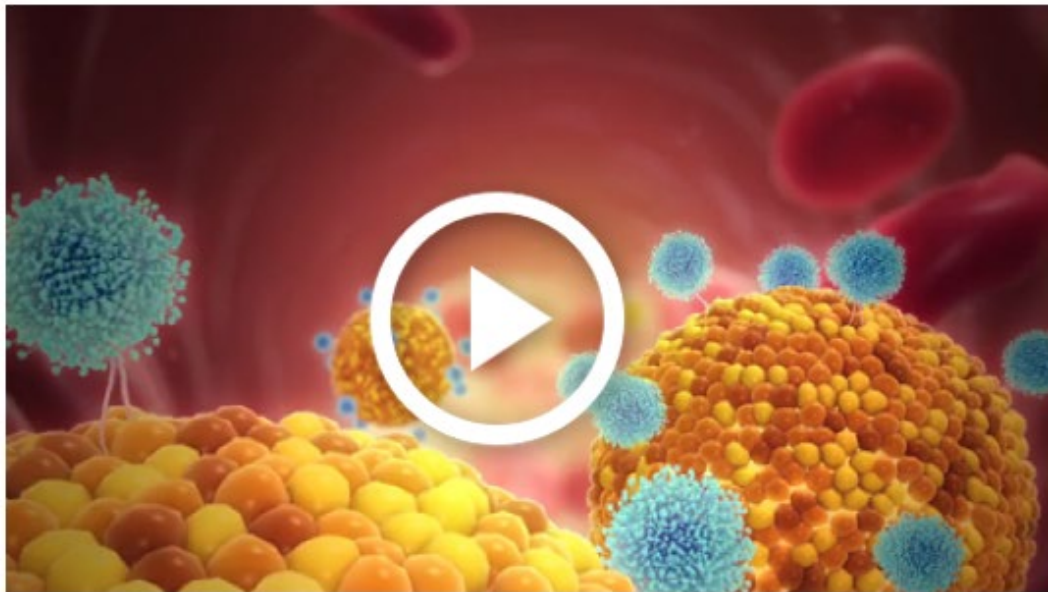


Manufacturing Know-How

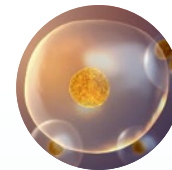
- Drug Substance Production (mRNA & STARR® mRNA)
- mRNA Purification
- Drug Product Production (LUNAR® Lipids + mRNA)
- Fill Finish / Lyophilization

LUNAR[®] Lipid Nanoparticle Delivery Technology

Proprietary, Biodegradable, Optimized for Each Cell Type



LUNAR[®] interacts with cell membrane



LUNAR[®] internalized inside endosome





mRNA release via engineered endosomolysis



mRNA translates into protein of interest

Pipeline of Arcturus-Owned mRNA Therapeutic Candidates



Franchise	Candidate	Funded By	Indication	Global Prevalence	Upcoming Milestone
Hepatic	LUNAR [®] -OTC (ARCT-810)		Ornithine Transcarbamylase Deficiency (OTC)	>10,000	Pivotal Trial Strategy Alignment with Regulatory Agencies H1 2026
Respiratory	LUNAR [®] -CF (ARCT-032)		Cystic Fibrosis	>100,000	Phase 2 12-Week Study Initiation H1 2026

Each Arcturus-Owned Program Represents a Significant Commercial Opportunity



LUNAR-CF (ARCT-032)

Inhaled mRNA Therapeutic Candidate
for Cystic Fibrosis

ARCT-032 Background

- An inhaled mRNA therapeutic that can build new CFTR protein in the lung cells of individuals with CF is desired

- Presently in Phase 2 studies, ARCT-032 has been generally safe and well tolerated to date

- Arcturus is preparing to initiate a Phase 2, fourth cohort, study in ~20 CF participants with daily treatment over a period of 12 weeks

- The Cystic Fibrosis Foundation has committed ~\$25 Million to ARCT-032

- ARCT-032 received Rare Pediatric Disease Designation and Orphan Drug Designation from the U.S. FDA and Orphan Medicinal Product Designation from the European Commission (EC)



Cystic Fibrosis

ARCT-032 Market Opportunity



Cystic Fibrosis

- > **>100,000 worldwide prevalence**

- > Caused by mutations in the CFTR gene, resulting in poor chloride transport and dehydrated, sticky mucus in the airways

- > Chronic airway obstruction leads to infection and inflammation, which causes progressive airway damage and ultimately, respiratory failure



Unmet Medical Need

- > Effective CFTR modulators are not approved for treatment of all people with CF

- > Standard of care therapies do not prevent chronic, progressive loss of lung function that ultimately requires lung transplantation or leads to early death



LUNAR-CF Aims to Restore CFTR Function

- > An mRNA replacement therapy has the potential to produce wild-type CFTR in the lungs of CF patients, independent of genotype

- > Functional CFTR protein can restore chloride efflux in the airways, reducing mucus accumulation and airway damage and minimizing the progressive respiratory impairment observed in people with CF

Class I CF

ARCT-032 Initial Target Population



Class I CF Patients

- > **~10,000 Class I CF patients globally**
- > Class I nonsense mutations result in no production of CFTR protein
- > **No treatment option available other than symptomatic care**
- > At risk of developing severe lung disease



Unmet Medical Need

- > Estimated 15% of people with Cystic Fibrosis are potential candidates for ARCT-032
- > 10% with ineligible Class I mutations
- > Up to 5% of patients with incomplete response or unacceptable side effects to CFTR modulators
- > **Ineligibility for CFTR modulators is the greatest area of unmet need in CF**



Potential Uptake

- > Rapid adoption is expected among people with CF who carry ineligible mutations or who are modulator intolerant due to the significant unmet need in this population
- > Those with incomplete response to CFTR modulators represent an important potential patient population

The ~10,000 Class I CF Patient Population Represents the Highest Unmet Need

ARCT-032 Clinical Summary

➤ Phase 1 Study in Healthy Volunteers

- N = 32 across 4 ascending single-dose cohorts
- Safety, tolerability and PK data supported transition to Phase 1b study

➤ Phase 1b Study in Adults with Cystic Fibrosis

- N=7; Each CF participant received two administrations of ARCT-032
- Safety, tolerability and PK data supported transition to Phase 2 study

➤ Phase 2 Study in CF Participants who do not qualify for or benefit from CFTR modulator therapy

- Multiple ascending dose, open-label study
- Safety, tolerability, PK and efficacy at 3 dose levels (5mg, 10mg, 15mg)
- Each participant receives daily treatments of ARCT-032 over a period of 28 days

➤ New 12-Week Study Enrolling a Fourth Cohort Up to 20 CF Participants is Planned to Begin H1 2026

Objectives

- Establish safety, tolerability, efficacy in adults with CF who are not on CFTR modulator therapy

Phase 2 Safety and Tolerability Study (Cohorts 1, 2, 3)

- Open-Label, multicenter, multiple ascending dose study
- Daily inhaled treatments of ARCT-032 over a period of 28 days
- First cohort (N = 3; 5 mg) completed dosing
- Second cohort (N = 6; 10 mg) completed dosing
- Third cohort (N = 4; 15 mg) dosing phase near completion

Phase 2 Safety and Preliminary Efficacy Study (Cohort 4)

- Open-label, multicenter, N = 20, Dose = 10 or 15 mg
- Daily inhaled treatments of ARCT-032 over a period of 12 Weeks
- **Planned initiation 1H 2026**



ARCT-032 Phase 2 Interim Data

Mucus Plug Reduction is Important

Arcturus evaluated mucus plug reduction after 28 days of treatment with ARCT-032

High-Resolution CT Scans were analyzed utilizing Thirona's FDA 510(k)-cleared AI Technology

Lung structure changes are important predictor and precursor of lung function improvements

- Studies¹ have shown lung structural abnormalities in subjects with CF are associated with lower FEV1 lung function scores over the next 10 years of their life
- Mucus plugging are among the most predictive of lower FEV1 function
- Chest HRCT scans can provide an early readout of likely long-term success for CF patients

Mucus Plug Reduction Interim Results

- No mucus plug reduction observed at the 5 mg dose level (first cohort)
- Significant mucus plug reductions observed at the 10 mg dose level (second cohort)
- Third cohort (15 mg) is ongoing, near completion of dosing phase

Cohort 2: Mucus Reduction Summary

Subject Number	Dose (mg)	Number of Mucus Plugs % Change @ Day 28	Mucus Volume (mL) % Change @ Day 28
2	10	-38.5%	-67.4%
4	10	-34.9%	-27.5%
6	10	-28.5%	-29.5%
5	10	-9.1%	-6.1%
3	10	23.8%	9.1%
1	10	25.6%	60.9%

4 out of 6 participants in Cohort 2 exhibited Mucus Reduction (each received 10 mg ARCT-032 daily for 28d)

Averaging the four participants that exhibited Mucus Reduction (Patients 2, 4, 6, 5):

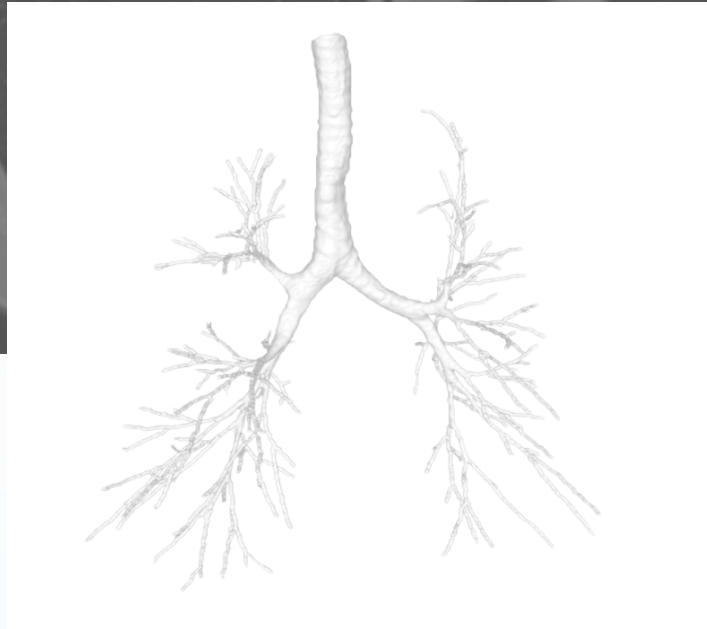
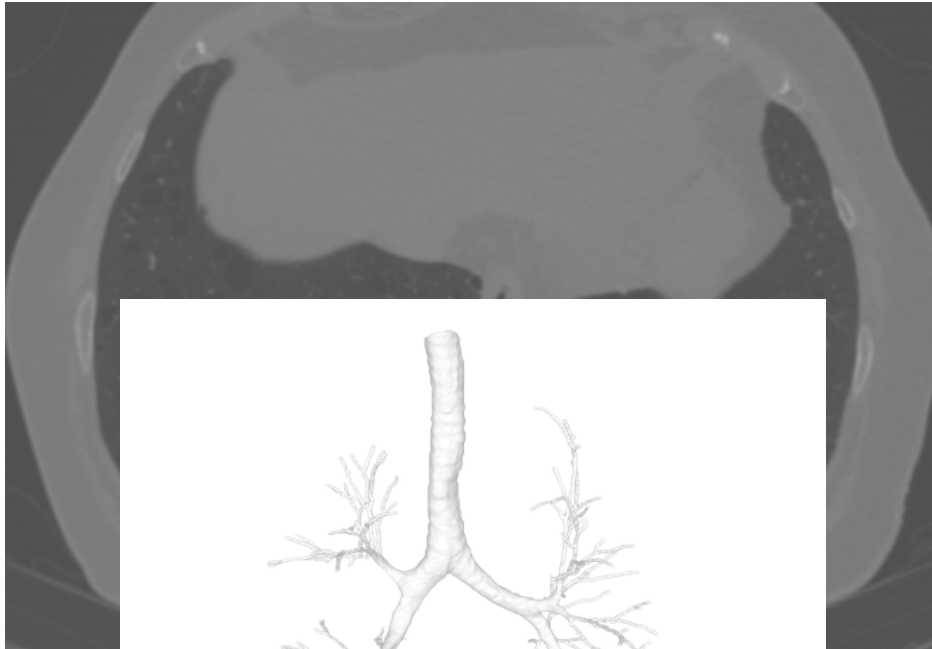
- 27.8% Reduction in Number of Mucus Plugs
- 32.6% Reduction in Mucus Volume

After 28 daily doses (10 mg) of ARCT-032:

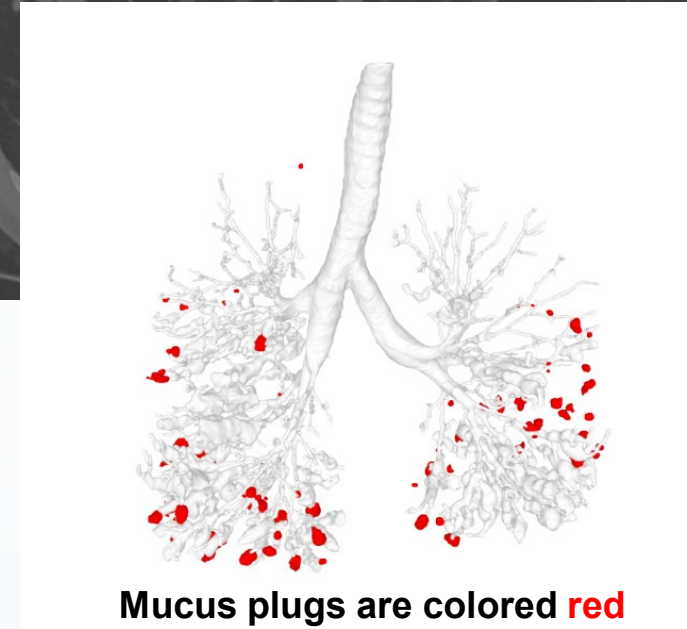
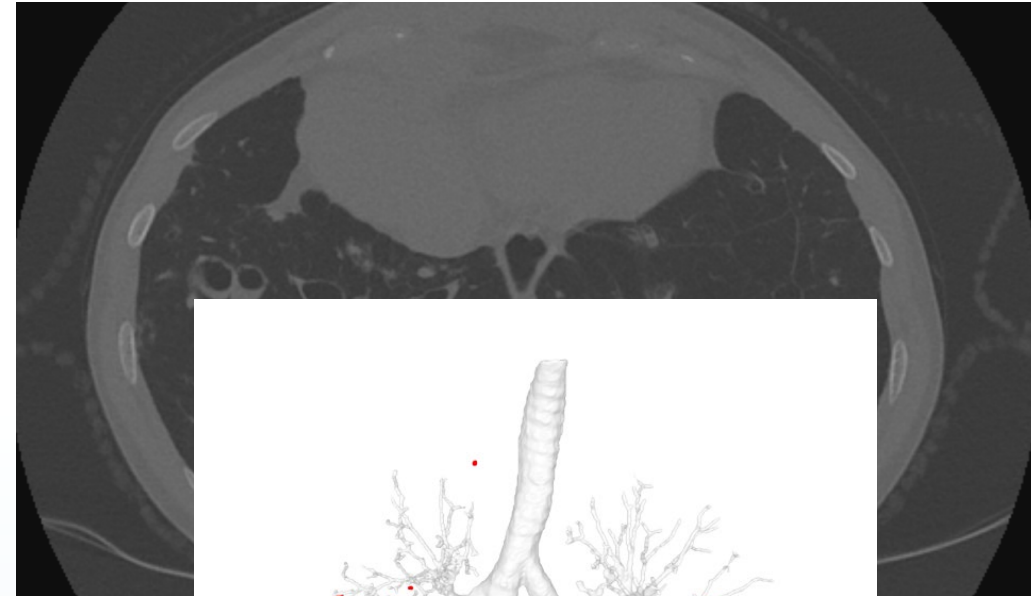
Reduction of mucus plugs and mucus volume is encouraging

HRCT Imaging Background

Example of Adult Healthy Lung



Example of Adult Class I CF Lung

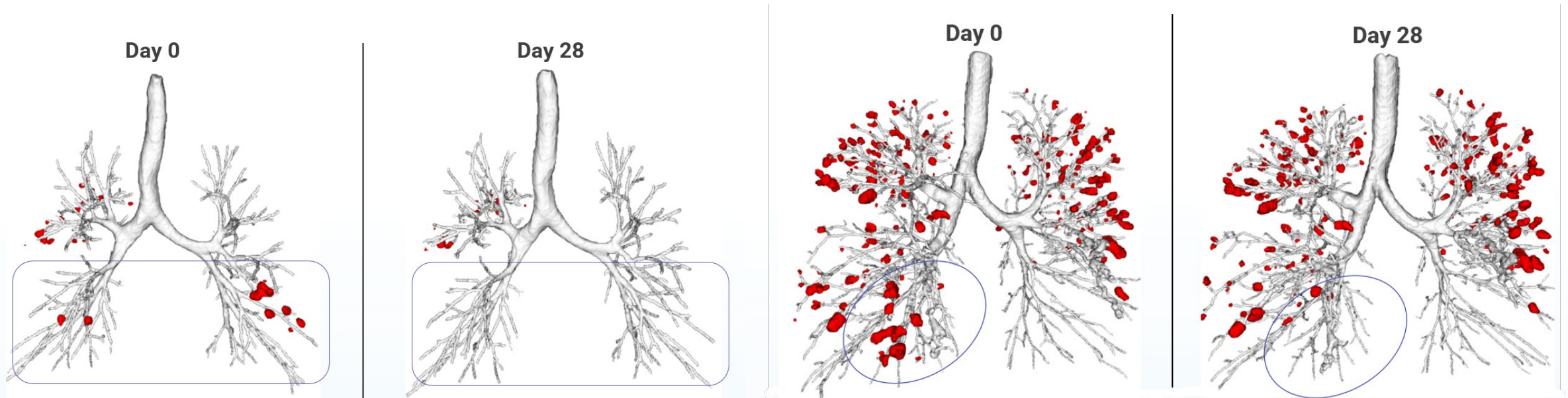


Mucus plugs are colored **red**

HRCT Scans of Selected Class I CF Participants

Cohort 2: Patient 2

Cohort 2: Patient 5



Reduction of mucus plugs after 28 days of treatment with ARCT-032

ARCT-032: Summary of Phase 2 Interim Data

- **ARCT-032 continues to be safe and well tolerated at all tested dose levels**
- **Meaningful trends of clinical activity observed via high HRCT scans** – After 28 days of treatment with ARCT-032 (10 mg), 4 out of 6 Class I CF participants exhibited encouraging reduction in numbers of mucus plugs and mucus volume
- **Larger (N = 20) and longer duration (12 wks) study is planned to begin H1 2026** – The HRCT mucus reduction and supporting lung function data from the second cohort (10 mg), combined with additional data collected from the ongoing third cohort (15 mg), will guide dose selection

¹Reference <https://ir.arcturusrx.com/static-files/48940714-0106-400d-a4a9-15acb88da82e> for full Phase 2 interim data presentation

LUNAR-OTC (ARCT-810)

Systemically Delivered mRNA for
Ornithine Transcarbamylase (OTC) Deficiency

Ornithine Transcarbamylase (OTC) Deficiency

ARCT-810 Market Opportunity



The most common urea cycle disorder

- ~10,000 prevalence in U.S./ EU
- 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 **progressive 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 Summary

- **Phase 1 Study in Healthy Volunteers**
 - Completed dosing up to 0.4 mg/kg, total participants N = 24, generally safe and well tolerated

- **Phase 1b Single Ascending Dose Study in OTCD Adults**
 - Completed enrollment and dosing of all cohorts (N=16)
 - Dose cohorts were 0.2, 0.3, 0.4 and 0.5 mg/kg; no serious or severe adverse events

- **Phase 2 (UK & EU) Single and Multiple Ascending Dose, Placebo-controlled Study in OTCD Adolescents & Adults**
 - Completed enrollment of 8 participants at the 0.3 mg/kg dose level
 - Up to 6 bi-weekly doses for each participant with the following endpoints
 - Primary Endpoints: Safety and tolerability
 - Secondary Endpoints: PK and PD (ureagenesis assay, plasma ammonia: 24-hr profile and peak level)
 - Exploratory Endpoints: Plasma amino acids and OTC enzyme activity; urine orotic acid

- **Phase 2 Ongoing Open Label Study (U.S.)**
 - Enrolling adults and adolescent participants with more severe disease
 - Multiple dose levels to be evaluated
 - Each participant is expected to receive five intravenous infusions administered over two months

- **ARCT-810 received Orphan Drug Designation, Fast Track Designation & Rare Pediatric Disease Designation from the U.S. FDA and Orphan Medicinal Product Designation from the European Commission (EC)**

Objectives

- Establish safety and tolerability in OTC deficient adolescents and adults
- Evaluate biomarker responses – glutamine, ammonia, ureagenesis

European Phase 2 Study – Completed (N = 8; 6 ARCT-810 / 2 placebo)

- Randomized, placebo-controlled
- 0.3 mg/kg ARCT-810; up to six biweekly IV infusions
- Entry criteria: Patients with stable disease

U.S. Phase 2 Study – Ongoing (up to N = 6)

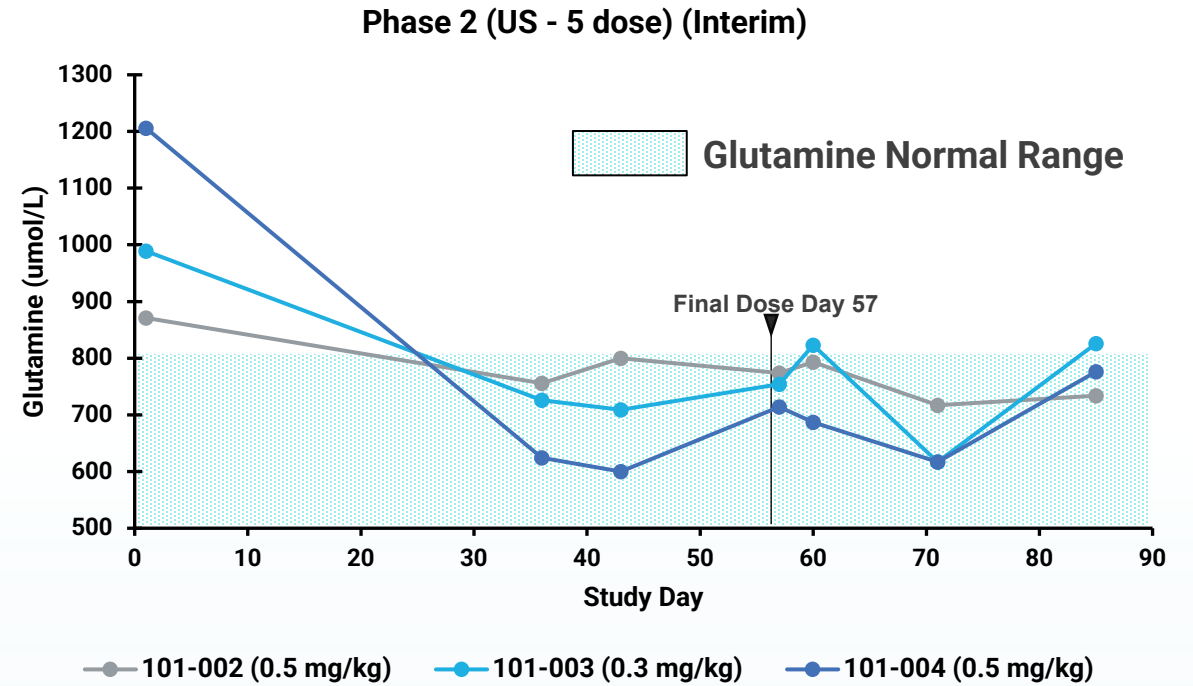
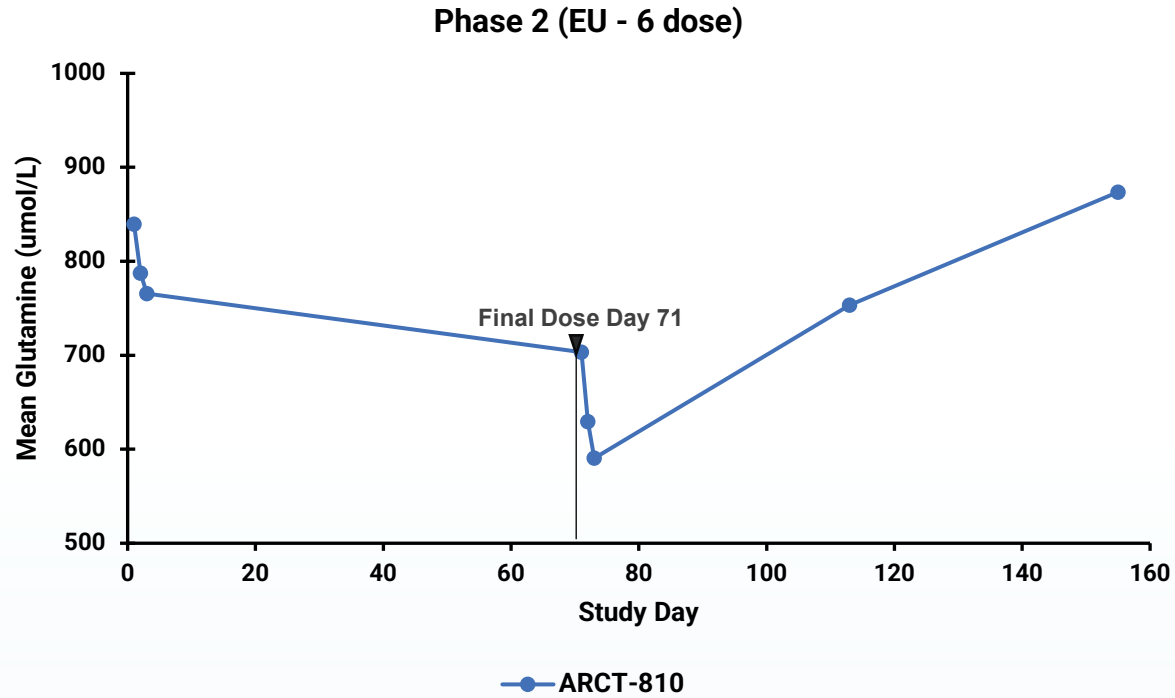
- Open-label, multiple ascending dose study
- 0.3 mg/kg and 0.5 mg/kg; five biweekly IV infusions of ARCT-810
- Entry criteria: Patients with more severe disease
- More frequent and optimized biomarker timepoints
- Includes ¹⁵N-ureagenesis assay



ARCT-810 Phase 2 Interim Data

Glutamine Normalization Following ARCT-810 Administration

Glutamine normal values range from ~400 to 800 $\mu\text{mol/L}$



Interim data show significant reduction in glutamine levels following ARCT-810 administration
High glutamine levels are normalized during treatment course
Approximately one month after the final dose, glutamine levels elevate above normal

ARCT-810 Significantly Increases ^{15}N -Ureagenesis

Interim Phase 2 Data U.S. Open Label Study (N = 3):

Mean Relative Ureagenesis Function (RUF) increased +14.7% from baseline to 28 days post-fifth dose-- from 29.0% (SD 9.1%) to 43.7% (SD 21.7%)

Mean RUF increase is statistically significant

-- p-value = 0.026, LMM analysis

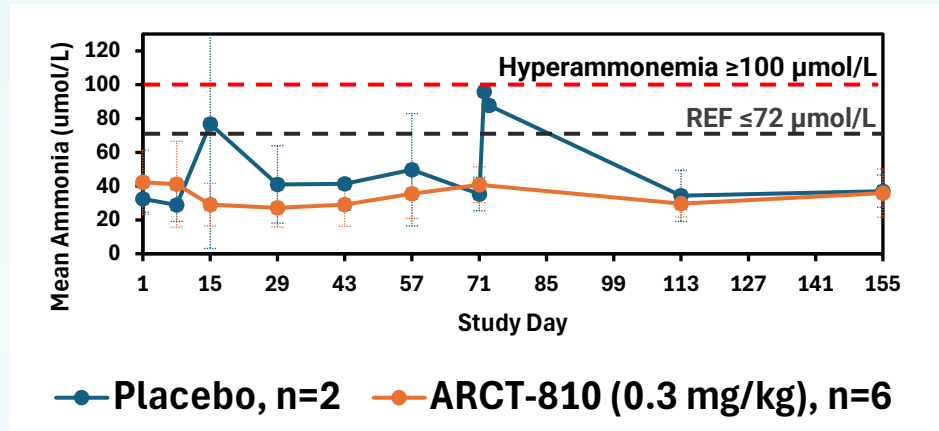
Two of three participants achieved > 50% RUF

Data suggest ARCT-810 progressively increases functional OTC enzyme in the liver resulting in improved urea cycle function

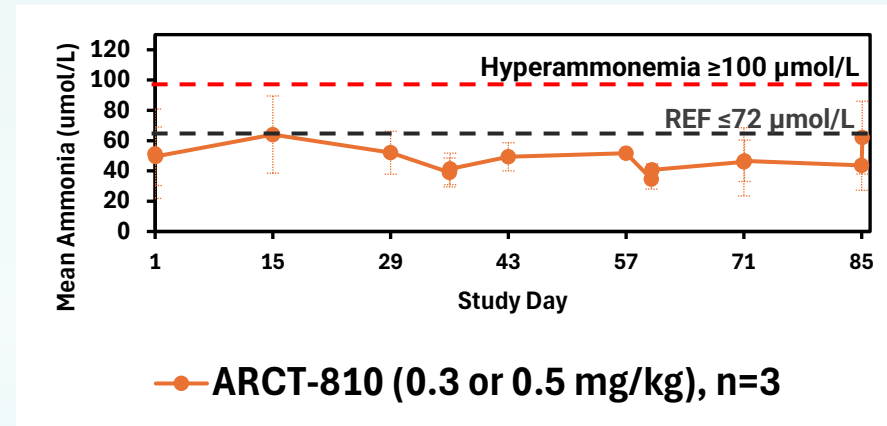
Encouraging ^{15}N -Ureagenesis data provide additional support and confidence in the favorable glutamine results

ARCT-810: Ammonia Stable and Within Normal Range

Phase 2 (Europe)



Interim Phase 2 (U.S.)



Ammonia levels stabilized within normal range following two administrations of ARCT-810 and remained stable for approximately 28 days after completion of dosing

Ammonia data add robustness to the favorable glutamine and ureagenesis data

ARCT-810: Summary of Phase 2 Interim Data¹

- **Significant and consistent reduction in glutamine levels in both Phase 2 studies** – from abnormal to normal levels
- **Significant increase in ¹⁵N-ureagenesis in the U.S. Phase 2 study** – additional evidence of urea cycle improvement
- **Ammonia – stable and within normal range**
- **ARCT-810 continues to be safe and well tolerated at all tested dose levels**

Planned alignment with regulatory agencies around pivotal trial strategy for both severe pediatric and stable adult populations – H1 2026

¹Reference <https://ir.arcturusrx.com/static-files/f01ce22c-25cd-4886-850d-18e8db4484b8> for full Phase 2 interim data presentation

Key Near Term Objectives H1 2026

Arcturus mRNA Therapeutic Clinical Programs

ARCT-810 (OTC Deficiency)

Establish clarity and alignment with FDA on the regulatory development paths

- For severe pediatric OTC Deficient patients (0-6 years of age)
- For OTC deficient adolescents and adults with stable disease

ARCT-032 (CF)

Receive approval to proceed with the Phase 2 fourth cohort (N = 20)

- Initiate enrollment and dosing of daily treatment for 12-weeks

Q & A