UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): September 23, 2026

ARCTURUS THERAPEUTICS HOLDINGS INC.

(Exact name of registrant as specified in its charter)

Delaware	**001-38942**	**32-0595345**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

10285 Science Center Drive
San Diego, California 92121
(Address of principal executive offices)

Registrant's telephone number, including area code: (858) 900-2660

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	**Trading Symbol(s)**	**Name of each exchange on which registered**
Common stock, par value $0.001 per share	**ARCT**	**The Nasdaq Stock Market LLC**

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01. Regulation FD Disclosure.

On September 23, 2026, Arcturus Therapeutics Holdings Inc., a Delaware corporation (the "Company" or "Arcturus") presented an overview of ARCT-810 Phase 2 clinical data, provided an update on its mRNA delivery platform (the "Presentation") and issued a press release which summarizes the Presentation (the "Release").

Copies of the Presentation and Release are furnished herewith as Exhibit 99.1 and Exhibit 99.2, respectively, and are incorporated into this Item 7.01 by reference.

The information in this Item 7.01 of this Current Report on Form 8-K, the Presentation and the Release, shall not be deemed "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liabilities of that section or Sections 11 and 12(a)(2) of the Securities Act of 1933, as amended. The information contained in this Item 7.01, and in the Presentation and the Release, shall not be incorporated by reference into any filing with the Securities and Exchange Commission made by the Company, whether made before or after the date hereof, regardless of any general incorporation language in such filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	**Description of Exhibit**
99.1	Presentation, dated September 23, 2026
99.2	Press Release, dated September 23, 2026
104	Cover Page to this Current Report on Form 8-K in Inline XBRL

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: September 23, 2026

Arcturus Therapeutics Holdings Inc.

By: /s/ Joseph E. Payne
Name: Joseph E. Payne
Title: Chief Executive Officer

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.

In some cases, you can identify forward-looking statements by terms such as "may," "will," "should," "could," "would," "expects," "plans," "anticipates," "believes," "estimates," "projects," "predicts," "potential" and similar expressions (including the negative thereof) intended to identify forward looking statements. Arcturus may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in any forward-looking statements such as the foregoing, and you should not place undue reliance on such forward-looking statements. The forward-looking statements contained or implied in this presentation are subject to other risks and uncertainties, including those discussed under the heading "Risk Factors" in Arcturus' most recent Annual Report on Form 10-K with the SEC and in other filings that Arcturus makes with the SEC. Except as otherwise required by law, we disclaim any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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

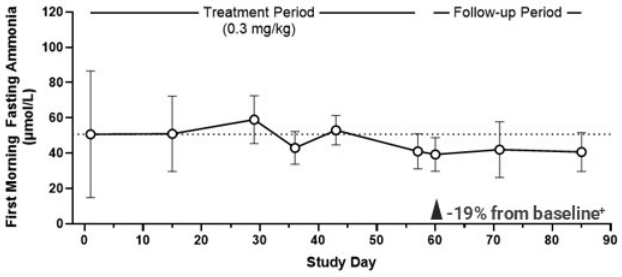
*One participant discontinued after a single dose of ARCT-810 due to a non-serious Grade 2 AE of IV infiltration with a subsequent Grade 2 site injection reaction.

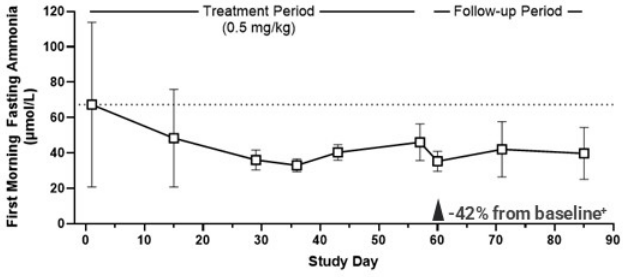
Changes in Clinically Relevant Biomarkers: Ammonia

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

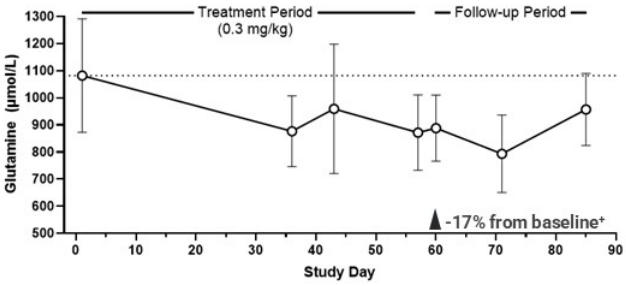
Points represent means ± SD of 3-4 participants. Dotted line indicates mean baseline value. *Mean difference between Day 60 (3 days after last dose) and baseline. Best available data as of 11Sep2026.

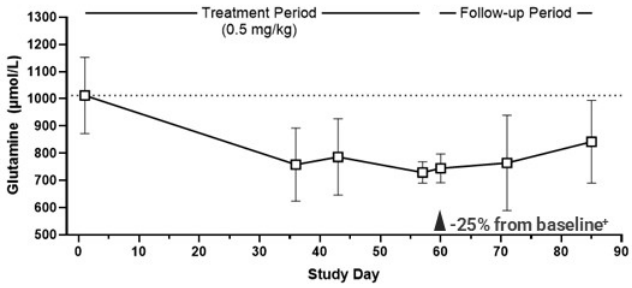
Changes in Clinically Relevant Biomarkers: Glutamine

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



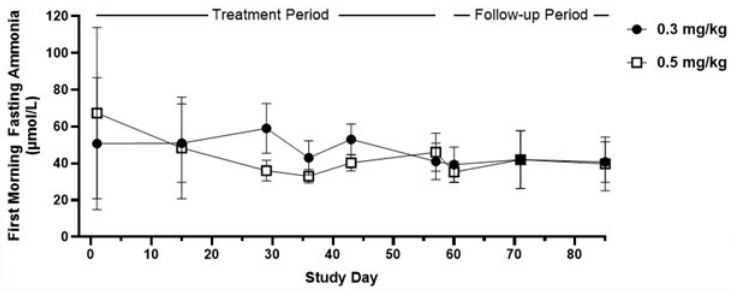


All participants exhibited reduction in glutamine levels following ARCT-810

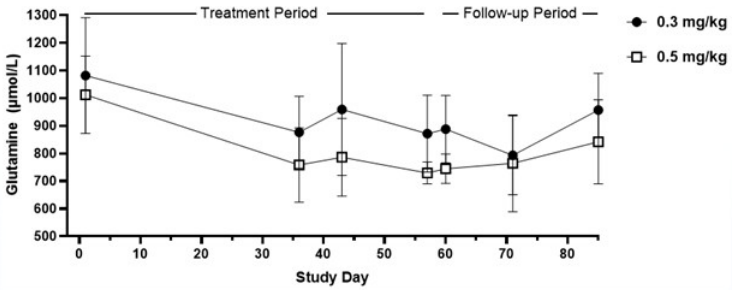
Points represent means ± SD of 3-4 participants. Dotted line indicates mean baseline value. *Mean difference between Day 60 (3 days after last dose) and baseline. Best available data as of 11Sep2026.

Ammonia & Glutamine ARCT-810 Dose Comparison

Ammonia



Glutamine



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

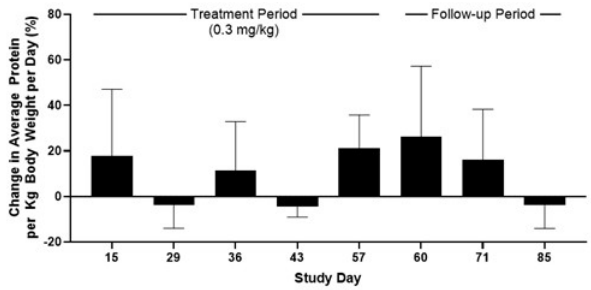
Points represent means ± SD of 3-4 participants. Best available data as of 11Sep2026.

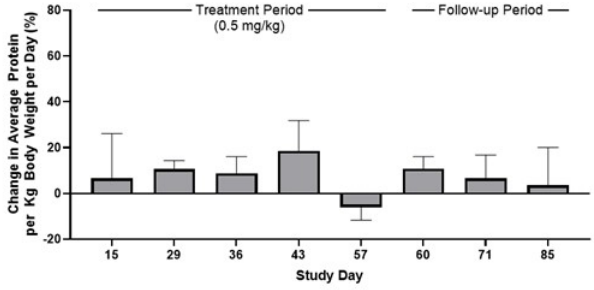
Biomarker Reductions Observed Despite Increased Protein Intake

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

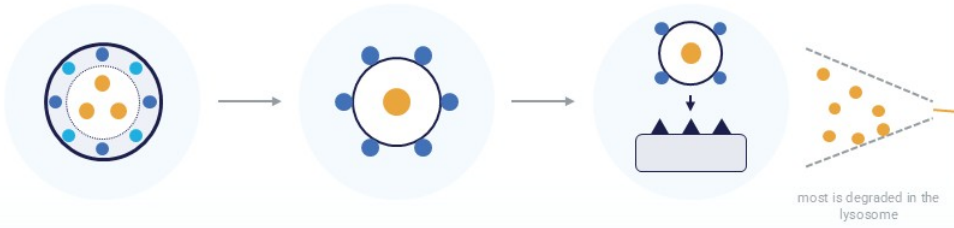
- **The glutamine result is what persuades a metabolic physician:** elevated in every participant despite mostly normal ammonias, down in every participant on drug, and back toward baseline once dosing stopped. That is drug effect, not variability.
- **The clear ammonia decline in the 0.5 mg/kg cohort 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.

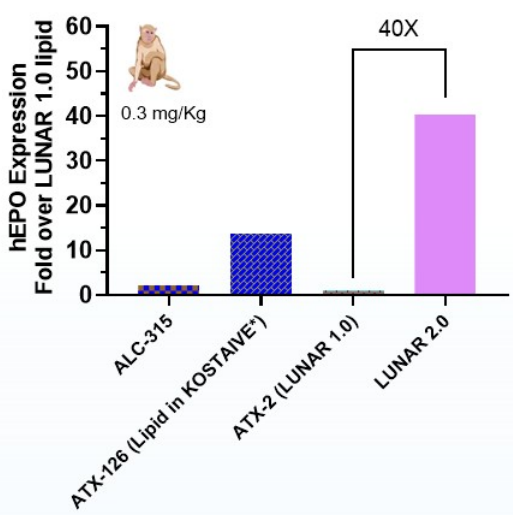
RATE-LIMITING STEP

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

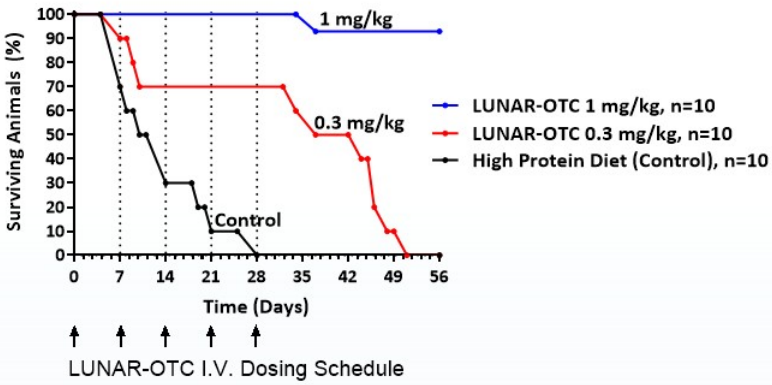
Lipid	Fold Enhancement Over LUNAR 1.0
ALC-315	2.2
ATX-126 (Lipid in KOSTAIVE®)	14
ATX-2 (LUNAR 1.0)	1.0
LUNAR 2.0™	**40**

- 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

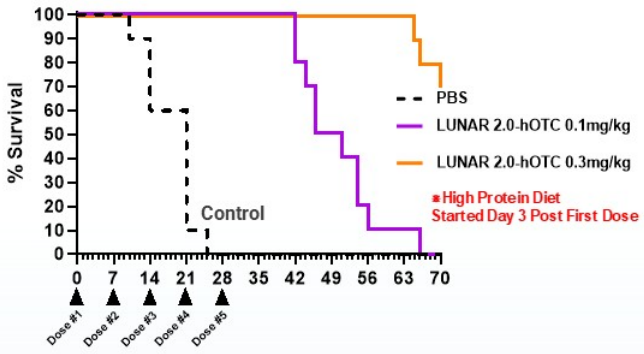
LUNAR 2.0™ produced 40-fold higher hEPO expression in NHPs compared to LUNAR 1.0

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



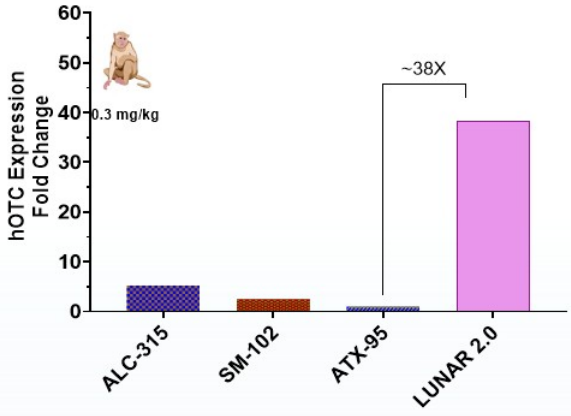
ARCT-2601 utilizes LUNAR 2.0™

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**

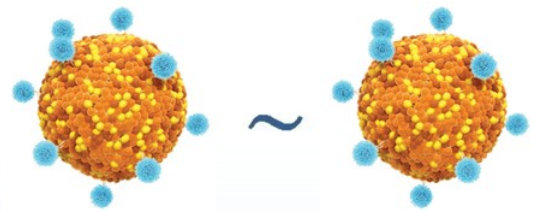
- NHPs (n=3) treated, and PBS control; IV 60-min infusion @ 0.3 mg/kg
- Liver biopsies 48h post-infusion analyzed for hOTC via mass spec

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	PROPOSED — NEAR TERM	FUTURE — SYRINGE PUMP
3 Hours *infusion time*	**1 Hour** *infusion time*	**< 5 Min** *infusion time*
VOLUME 250 mL	VOLUME 40 mL	VOLUME 5 mL
DOSE 0.5 mg/kg	DOSE 0.3 mg/kg	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.

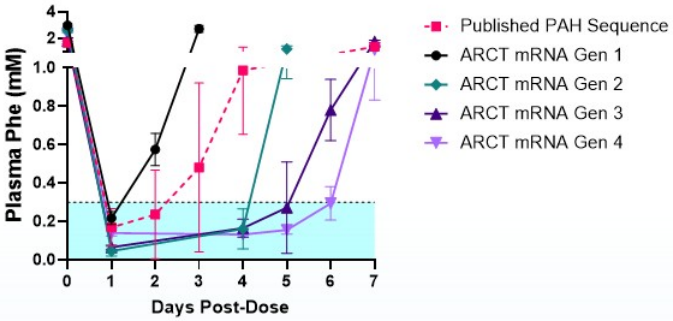
LUNAR 2.0 | Hepatocyte delivery

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

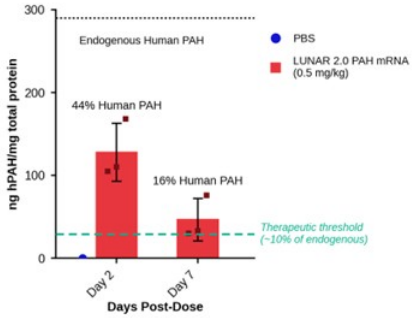
Why PKU Now? Two-Stage Platform Optimization Story

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

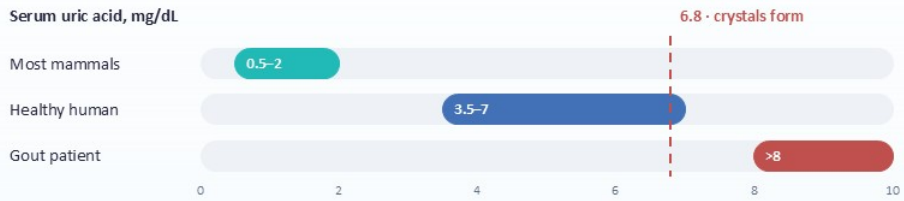
Uric acid is dissolved and excreted

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

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

ARCT-810 generally safe and well tolerated, demonstrating encouraging activity across key urea cycle biomarkers in ongoing Phase 2 study

LUNAR 2.0™ produces greater than 30-fold higher protein expression in multiple NHP studies – unlocks new therapeutic opportunities

ARCT-2601, an OTC deficiency therapeutic candidate utilizing LUNAR 2.0™, to be integrated by YE 2026 into ongoing Phase 2 study as advised by the FDA

Arcturus to acquire myNEO, an AI discovery company, to improve mRNA design quality, accelerate innovation, and enhance target identification capability

Presentation at 4:30 p.m. ET today

SAN DIEGO--(BUSINESS WIRE)--September 23, 2026--Arcturus Therapeutics Holdings Inc. (the "Company," "Arcturus," Nasdaq: ARCT), a messenger RNA medicines company focused on the development of liver and respiratory therapeutics, today announced encouraging interim Phase 2 results from ARCT-810 in ornithine transcarbamylase (OTC) deficiency and introduced LUNAR 2.0™, the Company's next-generation mRNA delivery platform, and additional liver pipeline programs.

"The ARCT-810 Phase 2 interim results validate Arcturus' mRNA liver therapeutics platform and the introduction of LUNAR 2.0™ marks the beginning of a new and exciting chapter for Arcturus," said Joseph Payne, President and CEO of Arcturus. "We are very pleased that ARCT-2601, utilizing LUNAR 2.0™, is positioned to be efficiently integrated into our ongoing OTC deficiency Phase 2 study later this year."

"The greater than 30-fold improvement demonstrated by the next-generation platform is exciting and has the potential to translate into a more effective and more convenient therapy," said Dr. Marshall Summar, former founding member and Executive Committee member of the NIH Urea Cycle Disorders Consortium, a recognized expert in rare diseases and OTC deficiency. "I believe ARCT-2601 has the potential to become a new standard of care for OTCD patients, particularly in severe onset, if approved, and I am excited to see the potential impact of Arcturus' next-generation mRNA delivery platform across other programs."

"Validating clinical data, a compellingly differentiated LUNAR 2.0™ mRNA delivery platform, and a proprietary AI computational engine, support the continued advancement of Arcturus' growing mRNA therapeutics pipeline, including ARCT-2601, and the initiation of new programs, such as Phenylketonuria (PKU) and Gout," said Dr. Pad Chivukula, Chief Scientific Officer of Arcturus.

ARCT-810 Phase 2 Interim Results

- Generally safe and well tolerated
- Reduced and/or maintained first morning fasting ammonia within the normal range, including during increased protein intake by participants
- Reduced glutamine, achieving normal range in some participants

In the Phase 2 study to date, ARCT-810 was generally safe and well tolerated, reduced and/or maintained first morning fasting ammonia within the normal range, including during increases in protein intake by participants; reduced glutamine, with participants at the 0.5 mg/kg dose level achieving mean glutamine values within the normal range during treatment. Weight gain was observed in all participants.

LUNAR 2.0™

LUNAR 2.0™ is the Company's next-generation mRNA delivery platform that incorporates improved lipids and an enhanced formulation process specific to these lipids. In non-human primates (NHPs), LUNAR 2.0™ demonstrated a 40-fold improvement compared to LUNAR 1.0 in expressing human erythropoietin (hEPO). In a separate NHP study, LUNAR 2.0™ exhibited 38-fold more potency than ATX-95, the key lipid in ARCT-810, in expressing human ornithine transcarbamylase (hOTC). LUNAR 2.0™ unlocks new therapeutic opportunities previously inaccessible, including Phenylketonuria (PKU) and Gout.

ARCT-2601 Utilizes LUNAR 2.0™

ARCT-2601 is Arcturus' next-generation investigational mRNA therapeutic for OTCD. To date, ARCT-2601 has demonstrated a similar safety profile to ARCT-810 in non-GMP pre-clinical studies. The U.S. Food and Drug Administration provided favorable feedback and regulatory-path clarity for ARCT-2601, following a Type C meeting in June this year. Based on the data and the feedback from the FDA, Arcturus plans to initiate dosing of ARCT-2601 near year-end in participants with OTCD, ages 12 years and older, under an amended Phase 2 protocol that integrates ARCT-2601 into the current ARCT-810 Phase 2 study. Based on data in non-human primates, ARCT-2601 is anticipated to provide benefits of lower and/or less frequent dosing.

Arcturus to Acquire myNEO

Arcturus has entered into a definitive agreement to acquire myNEO, subject to customary closing conditions. The transaction is expected to close in October. Arcturus has been working closely with myNEO since 2024. The acquisition brings a differentiated computational engine, supported by proprietary intellectual property, intended to fortify Arcturus' AI infrastructure by improving mRNA design quality and enhancing target identification capabilities.

Presentation: Today at 4:30 p.m. ET

- Domestic: 1-800-347-6865
- International: 1-203-518-9757
- Conference ID: Arcturus
- Webcast: Link

About Ornithine Transcarbamylase Deficiency

Ornithine transcarbamylase (OTC) deficiency is the most common urea cycle disorder. Urea cycle disorders are a group of inherited metabolic disorders of the liver that make it difficult for affected patients to remove toxic waste products as proteins are digested. OTC deficiency caused by mutations in the X-linked OTC gene, leads to a non-functional or deficient OTC enzyme and usually affects males more severely. OTC is a critical liver enzyme which catalyzes a metabolic process that converts toxic ammonia to urea that is excreted by the kidney. This conversion does not occur properly in patients with OTC deficiency and, aside from the risk of high ammonia levels, leads to increased blood concentrations of glutamine with low to normal levels of citrulline and increases in urine orotic acid. High blood ammonia levels in OTC deficiency may cause health crises with seizures, progressive neurocognitive impairment, coma, and death. Severe cases of OTC deficiency usually present early in life, but patients with less severe symptoms may be diagnosed as adolescents and adults. There is currently no cure for OTC deficiency, apart from liver transplant. However, liver transplantation comes with significant risks of surgical and postsurgical complications such as organ rejection, and recipients must take immunosuppressant drugs for the rest of their lives. The current standard of care for OTC deficiency patients is well-controlled but may not prevent chronic neurotoxic effects and is challenging to maintain, consisting of a low-protein diet, substitution of essential amino acids and treatment with nitrogen scavenging medications that keep the ammonia from rising to acutely toxic levels. These treatments do not address the underlying cause of disease. In Europe and the U.S., approximately 10,000 people have OTC deficiency.

About ARCT-810

ARCT-810 is an intravenously administered investigational mRNA therapeutic designed to express normal functional OTC enzyme in the liver of individuals with OTC deficiency. ARCT-810 has received Orphan Medicinal Product Designation and an approved pediatric investigation plan (PIP) from the European Medicines Agency (EMA), and Orphan Drug Designation, Fast Track Designation along with Rare Pediatric Disease Designation from the U.S. Food and Drug Administration (FDA) for the treatment of OTC deficiency. ARCT-810 is based on Arcturus' proprietary mRNA design methodologies, lipid platform and manufacturing and formulation processes. ARCT-810 also utilizes Arcturus' extensive and proprietary lipid library and employs the Company's LUNAR® delivery platform to deliver OTC mRNA to hepatocytes.

About ARCT-2601

ARCT-2601 is a next-generation intravenously administered investigational mRNA therapeutic designed to express normal functional OTC enzyme in the liver of individuals with OTC deficiency. ARCT-2601 incorporates LUNAR 2.0™ including improved lipids and an enhanced formulation process specific to these lipids that have demonstrated greater than 30-fold improvement compared with LUNAR 1.0 in nonhuman primate studies. ARCT-2601 is based Arcturus' proprietary mRNA design methodologies, lipid platform and manufacturing and formulation processes.

About First Morning Fasting Ammonia as a Biomarker

Hyperammonemia is responsible for the neurocognitive morbidity associated with OTCD. Maintenance of normal ammonia levels or reduction in ammonia levels is therefore a key goal for OTCD therapeutics including ARCT-810. A post hoc analysis including >1,000 ammonia results from 114 patients with urea cycle disorder (UCD) who were enrolled in four short-term ammonia scavenger switchover studies, demonstrated that first morning fasting plasma ammonia is the least variable of ammonia measurements and fasting ammonia correlates well with ammonia $AUC_{0\text{-}24,}$ a predictor of risk of hyperammonemia crises in UCD patients (Lee et al., 2015).

About Glutamine as a Biomarker

Glutamine is an important biomarker used by clinicians to monitor urea cycle function in OTC deficient patients. Glutamine reflects the body's nitrogen buffering capacity. In urea cycle disorders, excess nitrogen is initially incorporated into glutamine, allowing glutamine to rise steadily as a compensatory mechanism before ammonia levels begin to spike. This role makes glutamine a more stable and predictive biomarker in patients who are not experiencing hyperammonemia. Glutamine assessments have significantly lower intra-subject variability than ammonia (15% vs. 56%), making it more reliable for monitoring metabolic control in stable conditions (Lee et al., 2016).

About Arcturus

Founded in 2013 and based in San Diego, California, Arcturus Therapeutics Holdings Inc. (Nasdaq: ARCT) is a messenger RNA medicines company focused on the development of liver and respiratory therapeutics with enabling technologies: (i) LUNAR® lipid-mediated delivery, (ii) STARR® mRNA technology (sa-mRNA) and (iii) mRNA drug substance along with drug product manufacturing expertise. Arcturus developed KOSTAIVE®, the first self-amplifying messenger RNA (sa-mRNA) COVID vaccine in the world to be approved. Arcturus' strategic collaborations include Thermo Fisher Scientific for ARCT-032 manufacturing and development, BARDA for pandemic influenza initiatives, and ARCALIS, a Japanese joint venture focused on manufacturing mRNA vaccines and therapeutics. Arcturus' pipeline includes programs in cystic fibrosis (CF), ornithine transcarbamylase (OTC) deficiency, phenylketonuria (PKU) and Gout. Arcturus' versatile RNA therapeutics platforms can be applied toward multiple types of nucleic acid medicines including messenger RNA, small interfering RNA (siRNA), circular RNA, antisense RNA, self-amplifying RNA, DNA, and gene editing therapeutics. Arcturus' technologies are covered by its extensive patent portfolio (over 500 patents and patent applications in the U.S., Europe, Japan, China, and other countries). For more information, visit www.ArcturusRx.com. Please connect with us on X and LinkedIn.

Forward Looking Statements

This press release contains forward-looking statements that involve substantial risks and uncertainties for purposes of the safe harbor provided by the Private Securities Litigation Reform Act of 1995. Any statements, other than statements of historical fact included in this press release, are forward-looking statements, including those regarding strategy, future operations, the likelihood of success of the Company's pipeline (including ARCT-810 and ARCT-2601), the likelihood that the interim results of ARCT-810 Phase 2 will be predictive of future clinical results, the likelihood that preclinical data, including the data generated for ARCT-2601, will be predictive of future preclinical or clinical results, the continued advancement of the Company's OTC deficiency program or ARCT-2601, the potential of LUNAR 2.0 to enable the Company to pursue other therapeutic opportunities, the likelihood that the Company will advance new programs with LUNAR 2.0 such as PKU or Gout, the Company's plan to integrate ARCT-2601 into the Phase 2 study and the timing therefor, the potential effectiveness and dosing interval of ARCT-2601, the potential of ARCT-2601 to become a new standard of care, the relative significance or predictiveness of different biomarkers, the likelihood that ARCT-2601 will provide benefits of lower and/or less frequent dosing, the anticipated closing of the acquisition of myNEO and the timing therefor, and the impact of general business and economic conditions. Arcturus may not actually achieve the plans, carry out the intentions or meet the expectations or projections disclosed in any forward-looking statements such as the foregoing and you should not place undue reliance on such forward-looking statements. These statements are only current predictions or expectations, and are subject to known and unknown risks, uncertainties, and other factors that may cause our or our industry's actual results, levels of activity, performance or achievements to be materially different from those anticipated by the forward-looking statements, including those discussed under the heading "Risk Factors" in Arcturus' most recent Annual Report on Form 10-K, and in subsequent filings with, or submissions to, the SEC, which are available on the SEC's website at www.sec.gov. Except as otherwise required by law, Arcturus disclaims any intention or obligation to update or revise any forward-looking statements, which speak only as of the date they were made, whether as a result of new information, future events or circumstances or otherwise.

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