



NEXT GENERATION RNA MEDICINES

—
January 2025

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, the timing for selection of lead candidates, the development, manufacture or commercialization of our pipeline and partnered pipeline assets, the likelihood of success of, and achievement of revenues from, our partnered programs, the planned initiation, design or completion of clinical trials the likelihood that we will obtain clearance from regulatory authorities to proceed with planned 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 clinical data will be sufficient for regulatory approval or completed in time to submit an application for regulatory approval within a particular timeframe, 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, or ability to administer multiple doses of, any of our drug candidates, our manufacturing methods and technologies (including purification, lyophilization and stability of our products), the likelihood that a patent will issue from any patent application, our current cash position and adequacy of our capital to support future operations, and any statements other than statements of historical fact.

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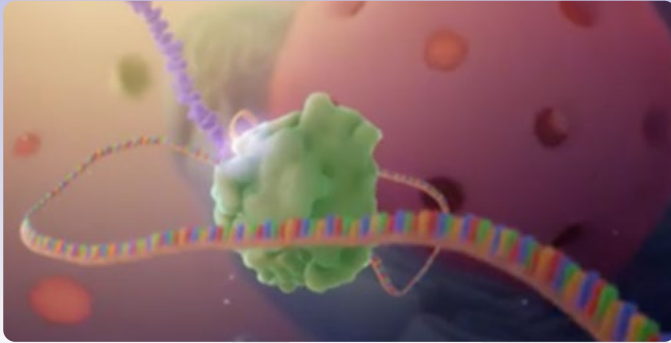
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Arcturus Therapeutics



Global mRNA Medicines Company



KOSTAIVE® Approved in **Japan**
KOSTAIVE® CHMP Positive Opinion in **EU**
Active Clinical Trials on **Five Continents**

Nasdaq: ARCT



Headquarters: San Diego, CA
Founded: 2013

mRNA Medicine Candidates



LUNAR-OTC Ornithine Transcarbamylase Deficiency
LUNAR-CF Cystic Fibrosis
Additional Earlier Stage Programs

Strategic Partners



Proprietary mRNA Technologies Driving Therapeutic Programs

Broad Intellectual Property Portfolio



400+

Patents & Patent Applications



mRNA Technology

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



LUNAR® Delivery

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

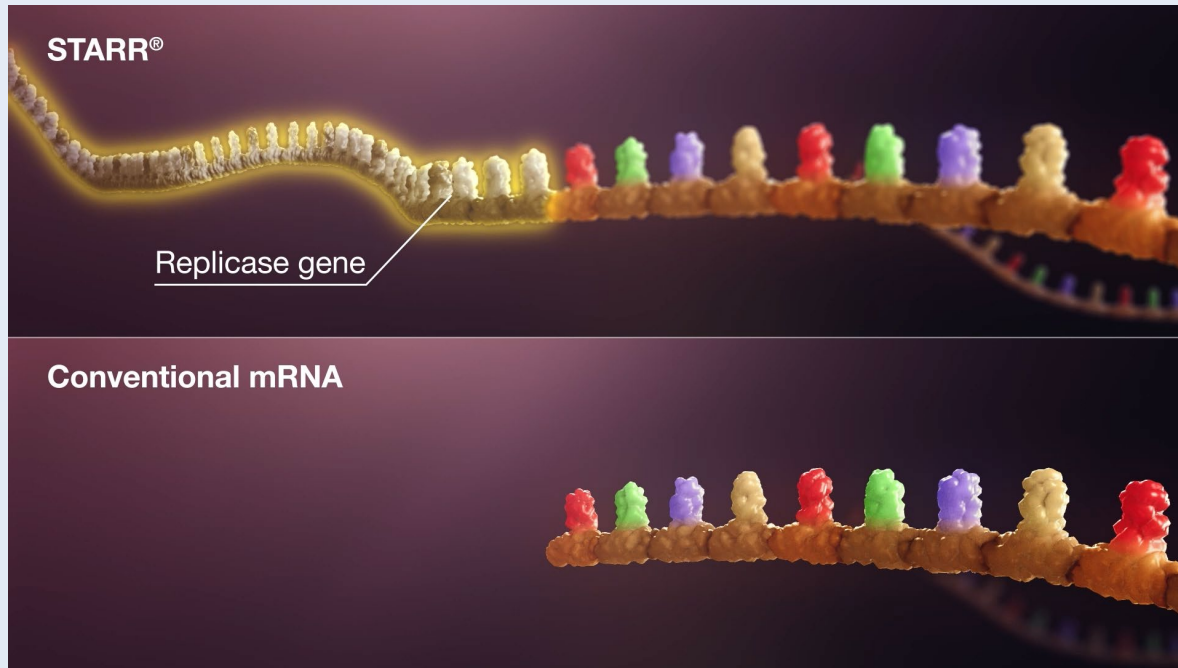


Manufacturing Know-How

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

STARR[®] Self-amplifying mRNA Vaccine

STARR[®] self-replicating RNA-based prophylactic vaccine triggers rapid and prolonged antigen expression within host cells resulting in protective immunity against infectious pathogens



Potential advantages over conventional mRNA Vaccine

Superior immune response: Induces higher neutralizing antibody response and increased immunogenicity

Durable immune response: Requires less frequent boosters due to longer and more durable immune response

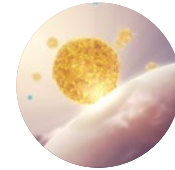
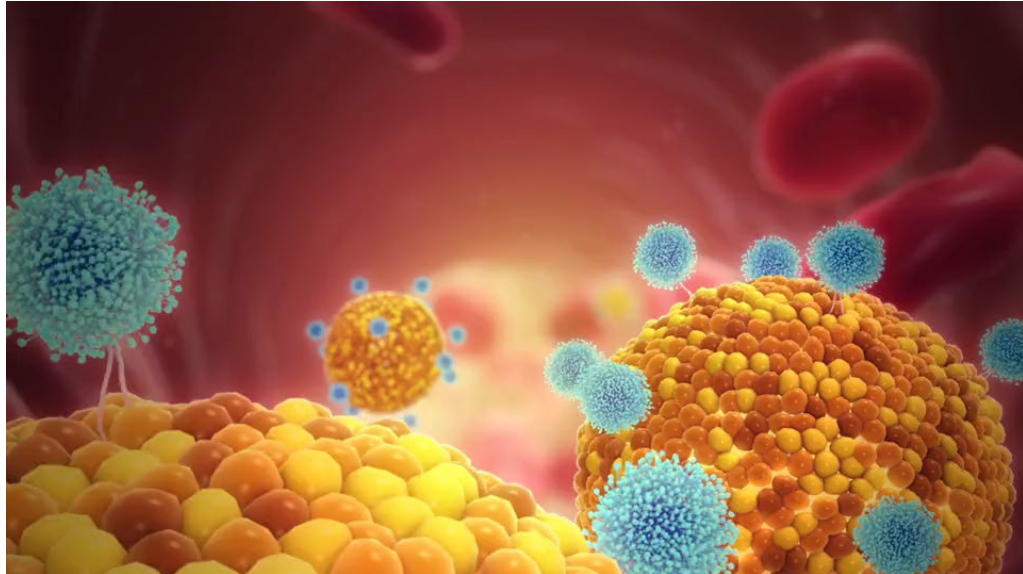
Broad immune response: Demonstrated higher immune response to evolving variants of COVID-19

Lower dose level: Increase the potential for combined vaccines

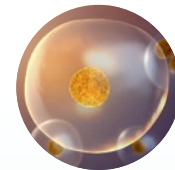
Manufacturing speed: Lower dose levels enabling vaccines do be produced more quickly and simply

LUNAR[®] - Lipid Nanoparticle (LNP) Delivery Technology

Proprietary, Biodegradable, Optimized for Each Cell Type



LUNAR[®] interacts with cell membrane



LUNAR[®] internalized inside endosome





mRNA release via engineered endosomolysis






mRNA translated 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	Phase 2 (EU & U.S.) Interim Data H1 2025
Respiratory	LUNAR [®] -CF (ARCT-032)		Cystic Fibrosis	85,000-100,000	Phase 2 Interim Data H1 2025

Each Arcturus-Owned Program Represents a Significant Commercial Opportunity

Pipeline of Partnered STARR[®] mRNA Vaccines

Candidate	Partner	Indication	Stage
KOSTAIVE[®] (ARCT-154; zapomeran) Monovalent		COVID-19	MHLW Approved (JP)  Anticipated EMA Approval (EU) 1Q25
KOSTAIVE[®] Bivalent (ARCT-2301) Ancestral / Omicron BA.4/5		COVID-19	Phase 3
KOSTAIVE[®] XBB.1.5 (ARCT-2303) Monovalent: XBB.1.5		COVID-19	Phase 3
LUNAR-FLU Multiple Programs		Seasonal Influenza	Preclinical to Phase 1
LUNAR-H5N1 (ARCT-2304) Pandemic Avian Influenza		Pandemic Influenza	Phase 1



**GREATER THAN
\$4 Billion**

in Potential Milestones &
Profit Sharing/Royalties

CSL: Arcturus Therapeutics Global Vaccine Partner

14.8 Billion
USD Annual Revenue

OPERATING IN
40+ Countries
Worldwide



32,000+
Employees Worldwide

110 Million
influenza doses distributed in FY24



Focused on four strategic technology platforms – plasma protein; recombinant technology; cell and gene therapy; and vaccines



Therapeutic areas of focus of immunology, hematology, respiratory, cardiovascular, transplant, nephrology and vaccines

CSL Seqirus

A World Leader in Flu Vaccines

\$2.13
Billion USD
Annual Revenue*

CSL Seqirus is one of the
Three Core Businesses of CSL

*CSL Full Year Results & ASX Information, August 2024

CSL Vaccine Partnership



Up to \$4.3 billion in Milestone Payments



Collaboration combines CSL's global vaccine commercial and manufacturing infrastructure with Arcturus' expertise in mRNA design and modification, LUNAR[®] lipid nanoparticle (LNP) technology, Drug Substance and Drug Product manufacturing know-how.



Deal terms encompass the development, manufacture, and commercialization of mRNA-based vaccines targeting COVID-19, Influenza and three additional respiratory infectious disease vaccines.

Partnership Terms

CSL

\$200 million

\$1.3 billion

\$3.0 billion

ARCTURUS
therapeutics

Upfront Payment

Development
Milestones

Commercial
Milestones

40% profit sharing for COVID-19 vaccines
(defined as 40% of gross profits, less 40% of development costs)

Up to **double digit royalties** for influenza and three additional infectious disease vaccines



Meiji: Background Information

Meiji Seika Pharma, a Subsidiary of Meiji Holdings Co. Ltd., Funded and Conducted the KOSTAIVE® Phase 3 Comparator Booster Study and Obtained Regulatory Approval in Japan



The Meiji Group provides food and pharmaceuticals indispensable to their customers



\$7.3 Billion USD Net Sales (As of March 31, 2024)



113 Locations Worldwide with 17,270 Employees



Meiji Seika Pharma provides antibacterial drugs, vaccines, central nervous system drugs, and generic drugs



\$1.36 Billion USD Net Sales (As of March 31, 2024)

- Announced investment in ARCALIS
- Submitted application to amend Approval for KOSTAIVE® to include domestic manufacturing sites in Japan in July 2024
- Received approval in Japan for KOSTAIVE® by the MHLW in November 2023
- Entered into agreement with CSL Seqirus April 2023, responsible for obtaining regulatory approval, distribution, sales and marketing of KOSTAIVE® in Japan

Meiji Holdings Co., Ltd., IR Team, Corporate Communications Dept. Data Book, Fiscal Year 2024, October 9, 2024

Meiji Holdings Co., Ltd., IR Team, Corporate Communications Dept. Data Book, H1 of FYE March 2024, November 11, 2024

ARCALIS: Arcturus' Joint Venture mRNA Manufacturing Partner



ARCALIS
Major
Equity
Owners

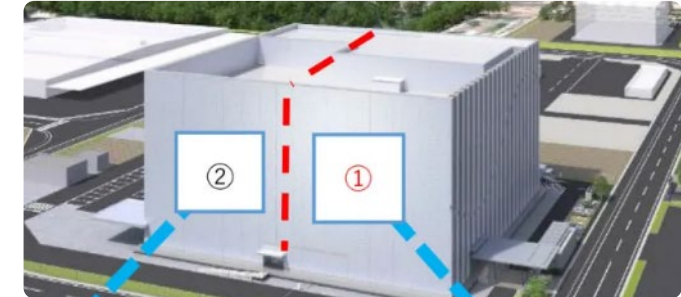
ARCALIS is a CDMO Specializing in Manufacturing of mRNA Vaccines and Therapeutics

- Joint Venture Founded in 2021
- Major Equity Owners: Axcelead & Arcturus & Meiji
- Meiji Seika Pharma is collaborating with ARCALIS for domestic mRNA vaccine production
- Meiji established an equity position in ARCALIS through an investment in November 2024



ARCALIS' cGMP mRNA Drug Substance Manufacturing Plant

- Completed July 2023; Located in Minamisoma City, Japan
- **Capacity:** Up to 5 kg in bulk mRNA drug substance per year
- 78,059 sq ft (7,252 sq m) floor space



ARCALIS' cGMP mRNA Drug Product Manufacturing Expansion

- **Capacity:** 30 L (3 Lines); building to 100 L (2 Lines)



ARCALIS Awarded with \$165 Million in Grants from the Japanese Government

KOSTAIVE® Phase 3 Clinical Studies

KOSTAIVE® Received Approval Nov 2023 from Japan's Ministry of Health, Labor and Welfare (MHLW)

¹ Yoshiaki Oda, Yuji Kumagai, Manabu Kanai, Yasuhiro Iwama, Iori Okura, Takeshi Minamida, Yukihiro Yagi, Toru Kurosawa, Benjamin Greener, Ye Zhang, Judd L. Walson. Immunogenicity and safety of a booster dose of a self-amplifying RNA COVID-19 vaccine KOSTAIVE® versus BNT162b2 mRNA COVID-19 vaccine: a double-blind, multicentre, randomised, controlled, phase 3, non-inferiority trial, *The Lancet Infectious Diseases*, 2023, [https://doi.org/10.1016/S1473-3099\(23\)00650-3](https://doi.org/10.1016/S1473-3099(23)00650-3).

KOSTAIVE® (Monovalent)

Phase 3 Non-inferiority safety and immunogenicity trial

- KOSTAIVE® administered at an 83.3% lower dose than Comirnaty® (N = 828)
- 50% of participants received KOSTAIVE® (5 mcg); 50% of participants received Comirnaty® (30 mcg)
- Conducted in Japan

➤ **Achieved Primary Endpoint** of non-inferiority of neutralizing antibody response against SARS-CoV-2 Ancestral strain compared to Comirnaty®

➤ **Achieved Secondary Endpoint** of superiority of KOSTAIVE® in neutralizing antibody response against SARS-CoV-2 Omicron BA.4/5 variant; increased immunogenicity associated with KOSTAIVE® versus Comirnaty® at Day 29

➤ **Generally safe and well tolerated**

➤ **Phase 3 Study published** in *The Lancet Infectious Diseases*¹

THE LANCET
Infectious Diseases

KOSTAIVE® (Bivalent, ARCT-2301)

Bivalent KOSTAIVE® (ARCT-2301: ancestral D614G and Omicron BA.4-5)

- Results consistent with monovalent KOSTAIVE®
- Phase 3 clinical booster vaccination study was also conducted in Japan

Bivalent KOSTAIVE® was assessed in comparison with bivalent conventional mRNA vaccine (Comirnaty®):

- Day 29 superiority of neutralizing antibody response against SARS-CoV-2 Ancestral strain was established
- Day 29 superiority of neutralizing antibody response against SARS-CoV-2 Omicron BA.4/5 subvariant was established
- Day 29 neutralizing immune response against SARS-CoV-2 Omicron XBB.1.5 subvariant was higher compared to Comirnaty



Historic Approval of World's First sa-mRNA Product

CSL-Arcturus Collaboration
Results in Groundbreaking
Approval of KOSTAIVE®

Unprecedented approval paves the
way for additional sa-mRNA vaccines

First Arcturus Approval

KOSTAIVE® self-amplifying mRNA
COVID vaccine was **approved in
Japan by the MHLW in
November 2023**

The STARR® vaccine was created,
optimized, clinically developed and
approved in under 4 years



Enduring Vaccine with Strong Clinical Data

**Approval based on positive
clinical data from several
KOSTAIVE® studies**

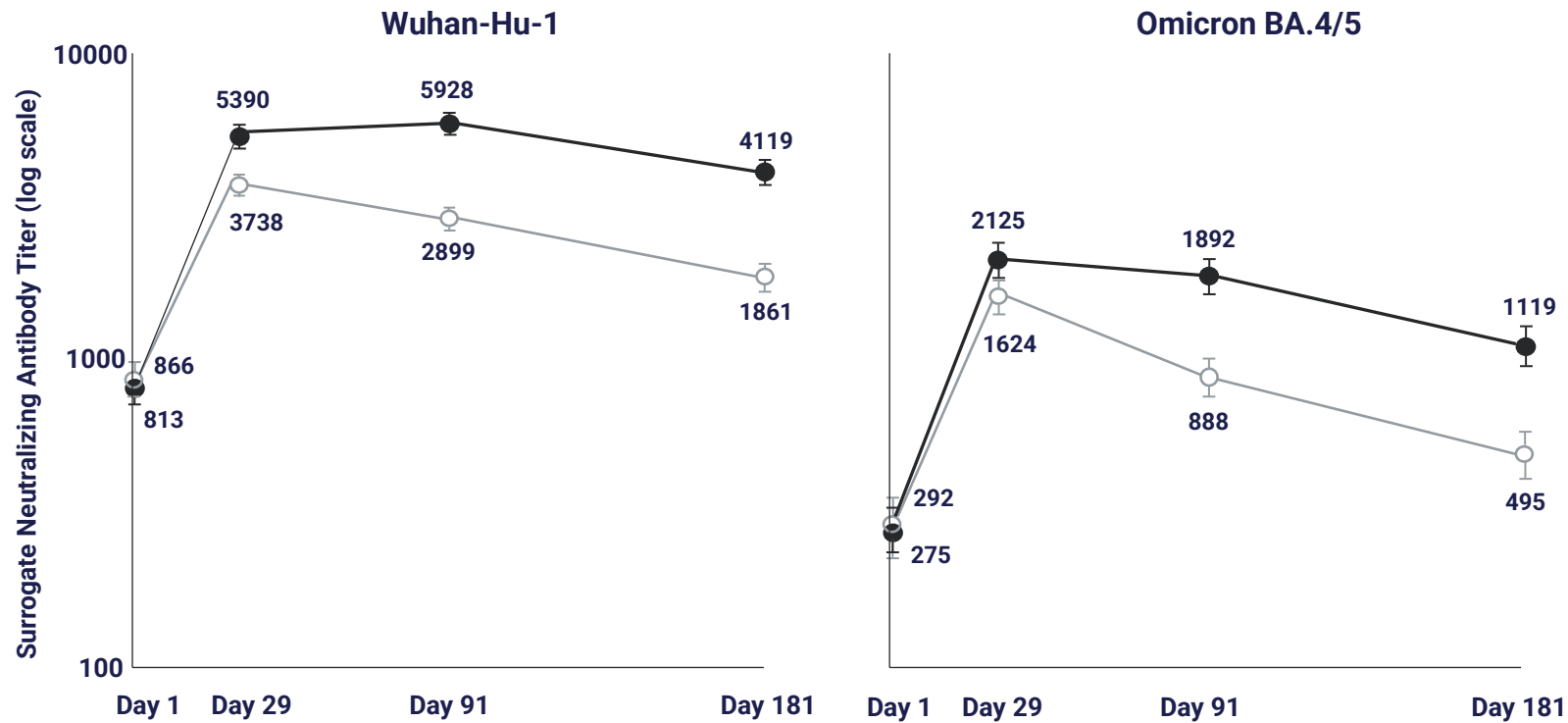
18,000+ subjects have received
sa-mRNA COVID vaccines

Partner **Meiji Seika Pharma**
advanced the MHLW approval
and is the exclusive distributor
of KOSTAIVE® in Japan



KOSTAIVE[®]: More Durable Immune Response

Phase 3 Persistence Data Comparing KOSTAIVE[®] (5 mcg) to Comirnaty[®] (30 mcg)



THE LANCET Infectious Diseases

Oda Y et al. Lancet Infect Diseases; February 1, 2024
DOI: (10.1016/S1473-3099 mcg(mcg 24)00060-4)

KOSTAIVE[®] sa-mRNA Booster Shows Higher Durability of Immune Response Compared to Approved mRNA Vaccine

- KOSTAIVE[®] (5 mcg)
- COMIRNATY[®] (30 mcg)

COMIRNATY[®] is the brand name of BNT162b2

LUNAR-H5N1 (ARCT-2304)

Avian Influenza Program
U.S. Pandemic Preparedness Initiative

LUNAR-H5N1 (ARCT-2304)

Received Clearance from
FDA to Begin H5N1
Pandemic Flu Vaccine
Clinical Trial in Nov 2024

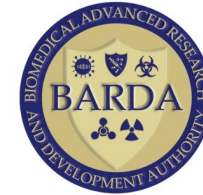
Initiated Phase 1 dosing in
December 2024

Third STARR[®] mRNA
Vaccine Candidate to Enter
Clinical Development

LUNAR-H5N1

Phase 1 Randomized placebo-controlled trial (NCT06602531)

- Designed to enroll approximately 200 healthy adults
- 120 participants 18-59 years old; 80 participants 60-80 years old
- Clinical study is fully funded by BARDA



➤ Primary objective

Evaluate safety and immune responses of three different dose levels and two different vaccination schedules of ARCT-2304 vaccine

➤ ARCT-2304

Utilizes clinically validated LUNAR[®] delivery and STARR[®] mRNA platform technologies. STARR mRNA has demonstrated in multiple clinical trials its ability to elicit a robust immune response at very low dose levels, with extended persistence of neutralizing antibodies compared to approved conventional mRNA vaccines

H5N1 Influenza

H5N1 influenza is a significant concern in animal health. To date, H5N1 flu has affected over 10,000 wild birds, nearly a thousand dairy cows, and over 130 million poultry. Elevated H5N1 infections in animals have led to increasing numbers of human infections including two confirmed severe cases in the United States and one death. Most of the confirmed 67 human infections were due to exposure of U.S. dairy and poultry workers to infected dairy cows and poultry

LUNAR-CF (ARCT-032)

Inhaled mRNA Therapeutic Candidate
for Cystic Fibrosis

Cystic Fibrosis

ARCT-032 Market Opportunity



Cystic Fibrosis

- > 85,000 - 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

- > Highly effective CFTR modulators are not approved for treatment of all people with CF and may not be tolerated in others

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

- > 8% of CF patients have genotypes making them ineligible for modulators¹

- > Additional 10% of CF patients are eligible but not prescribed modulators¹



LUNAR-CF Aims to Restore CFTR Function

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

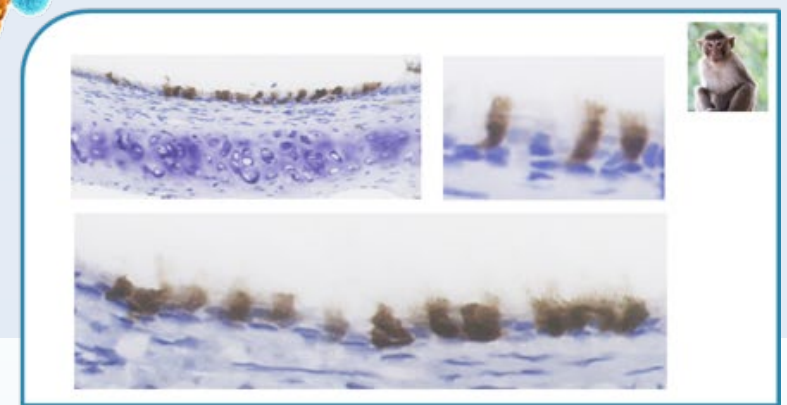
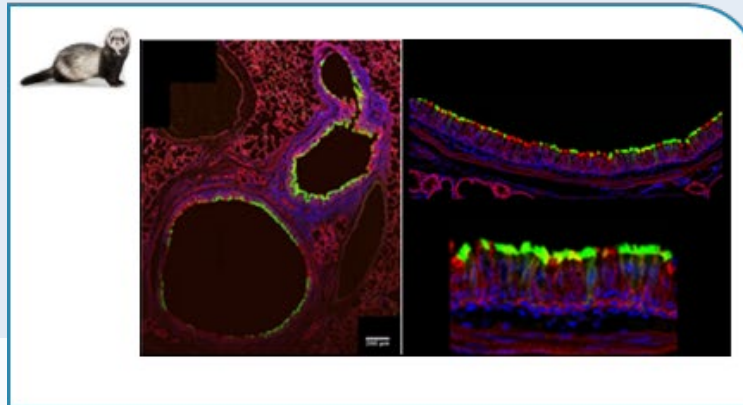
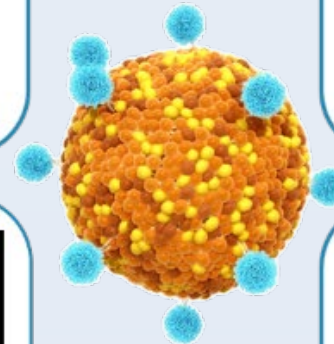
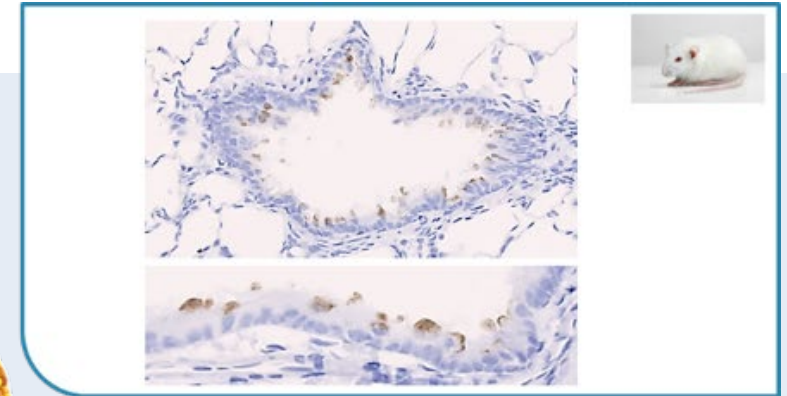
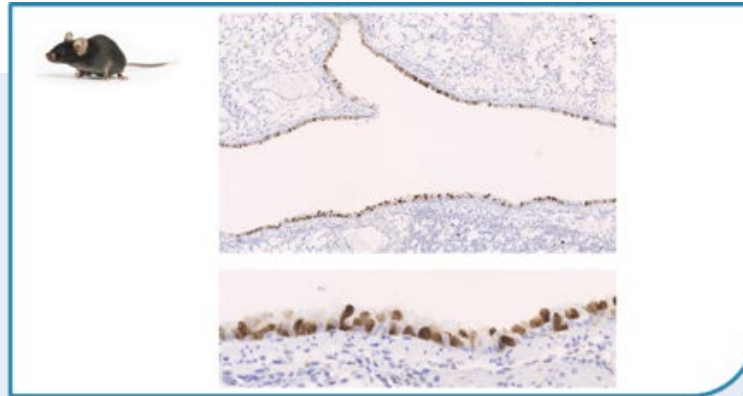
- > Functional CFTR protein can restore chloride efflux in the airways, reducing mucus accumulation and airway damage and minimizing the progressive respiratory impairment observed in people with CF

¹ Cystic Fibrosis Foundation. (2024). 2023 CYSTIC FIBROSIS FOUNDATION PATIENT REGISTRY HIGHLIGHTS. In <https://www.cff.org/medical-professionals/patient-registry>.

LUNAR[®]-mRNA in Healthy Animals (four different species)

Successful delivery to airway epithelium; transduction demonstrated by Brown and Green staining

LUNAR[®] Delivery to Airway Epithelium is Demonstrated in Rodent and Non-Rodent Species

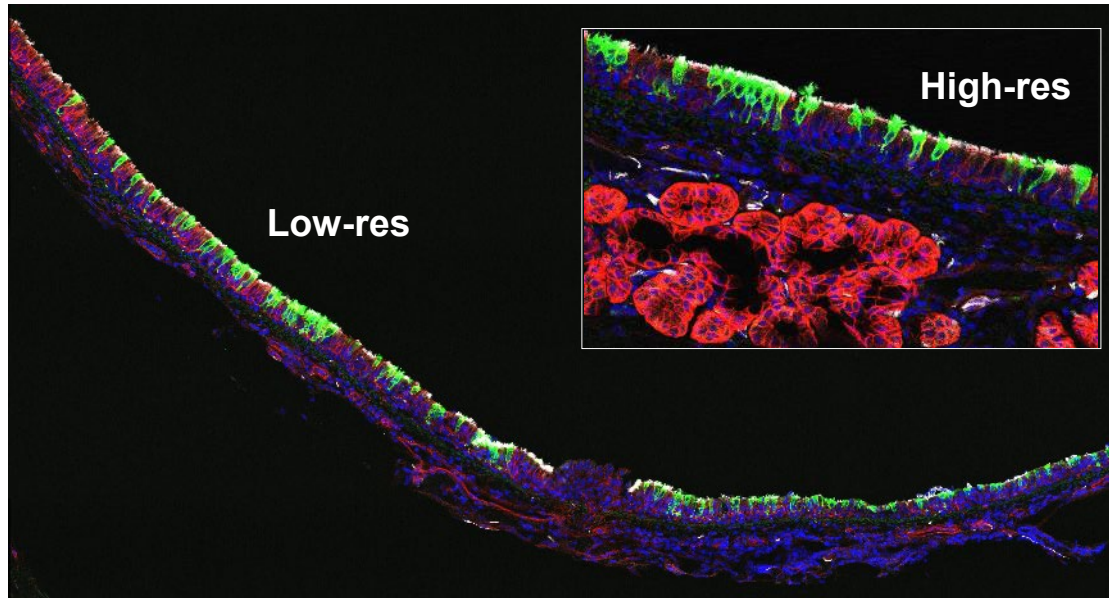


LUNAR[®]-mRNA in Cystic Fibrosis Ferret Model

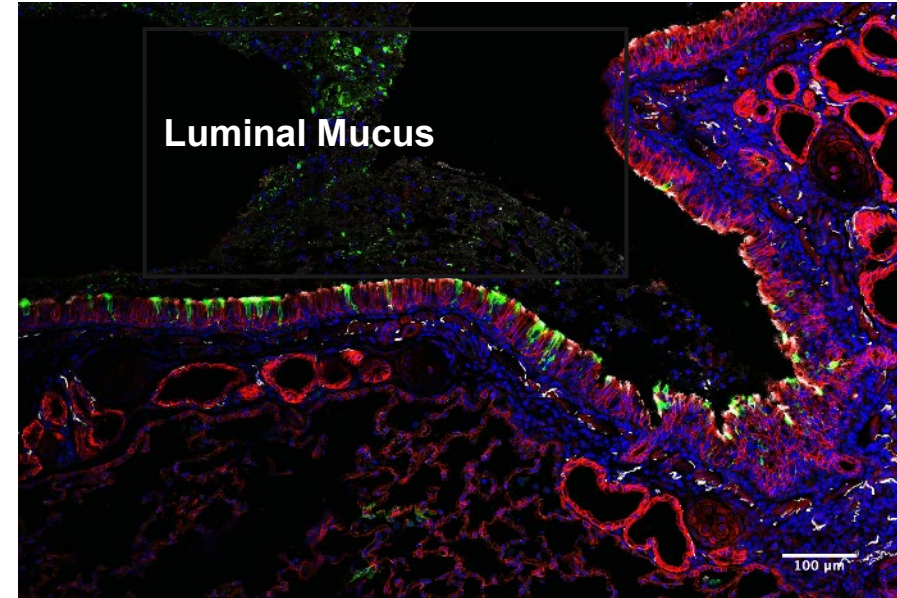
Successfully Transduces Epithelium in the Presence of CF Mucus



Trachea



Bronchus



Green denotes functional expression of protein (Cre)

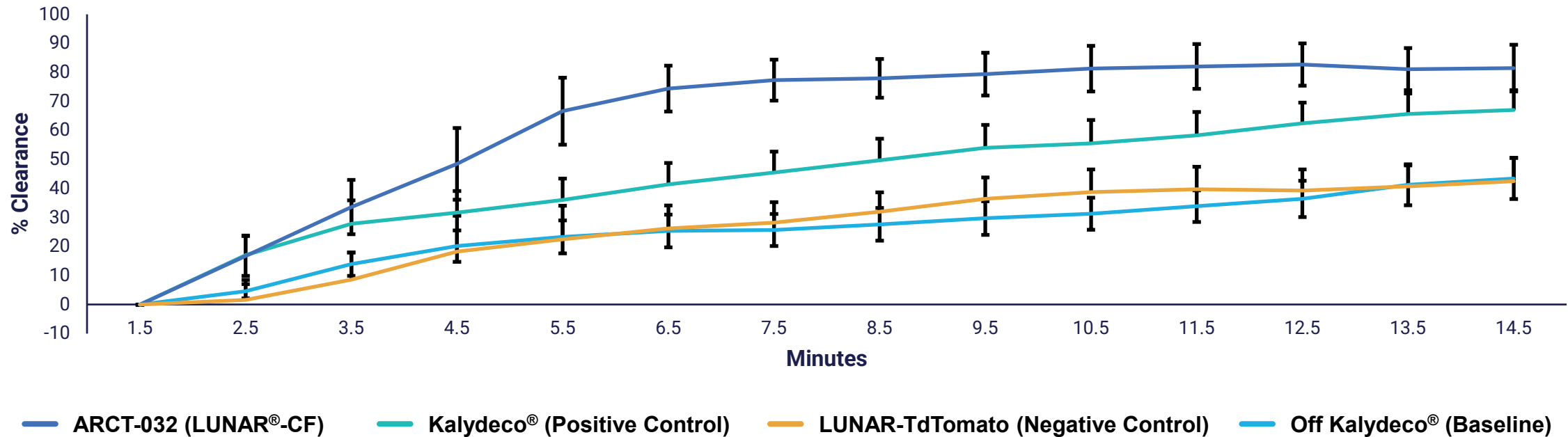
LUNAR[®] Effectively Delivers mRNA Expressing Cre in a Ferret CF Model (G551D)

In collaboration with Univ. of Iowa; presented at North American CF Conference Nov 2023

ARCT-032 in a Kalydeco®-responsive CF Ferret Model (G551D)



Proof of Activity: Mucociliary clearance improves after single administration of ARCT-032



ARCT-032 Functionally Restores Mucociliary Clearance to Normal Levels in CF Ferrets

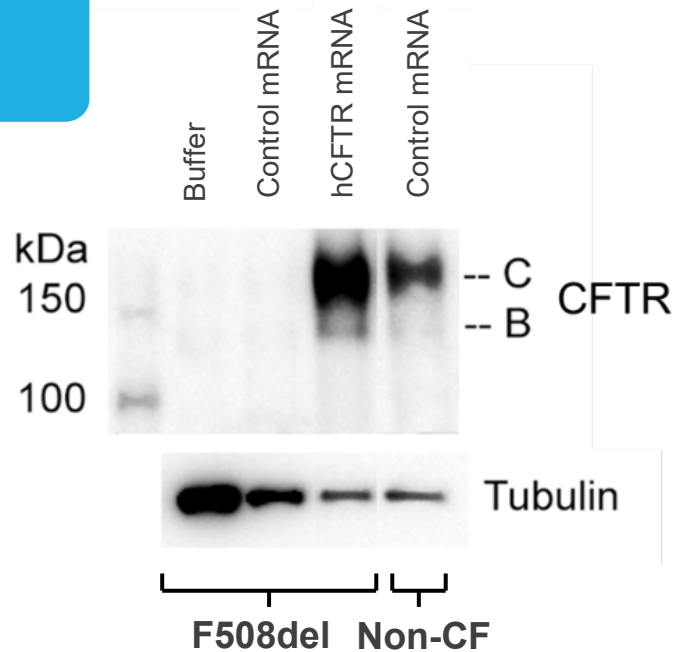
In collaboration with Univ. of Iowa; presented at North American CF Conference Nov 2023

ARCT-032 Restores CFTR Expression & Function

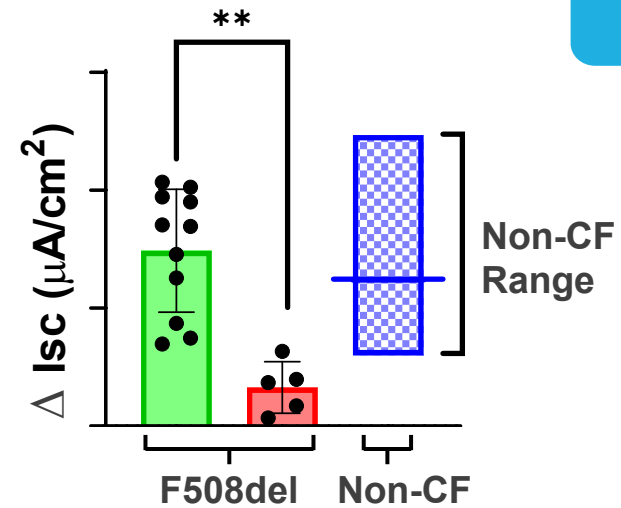
Restoration of CFTR Expression and Function in CF Human Bronchial Epithelial Cells

High Expression Levels of CFTR Protein

In collaboration with UAB CFRC and Javier Campos-Gomez



Restored Chloride Activity (Chloride Gradient)



** $P < 0.01$; Data from two F508del donors; Using chamber studies performed with chloride secretory gradient

■ hCFTR mRNA
■ Control mRNA

In collaboration with Univ. of Alabama-Birmingham; presented at North American CF Conference Nov 2022

ARCT-032 Clinical Update

ARCT-032 Phase 2
Interim Data Expected
H1 2025

➤ Phase 1 Study in Healthy Volunteers

- Completed dosing across 4 ascending single-dose cohorts (8 subject per cohort)
- Total number of subjects N = 32
- Safety, tolerability and PK data supported transition to Phase 1b study

➤ Phase 1b Study in Adults with Cystic Fibrosis

- CF Participants received two administrations of ARCT-032
- Total number of CF participants N = 7
- Safety, tolerability and PK data supported transition to Phase 2 study

➤ Phase 2 Study in CF Participants – Initiated December 2024

- Multiple ascending dose open-label study
- Evaluating safety, tolerability and efficacy – including FEV improvements in lung function
- Each participant is expected to receive daily treatments of ARCT-032 over a period of 28 days
- Recruiting individuals that do not qualify or benefit from CFTR modulator therapy

➤ The Cystic Fibrosis Foundation has committed ~\$25 Million to advance 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)

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./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



LUNAR-OTC

Exceeds Target of 5% Enzyme Replacement in OTC-Deficient Mouse Model



OTC deficiency impacts ureagenesis (ammonia detoxification)



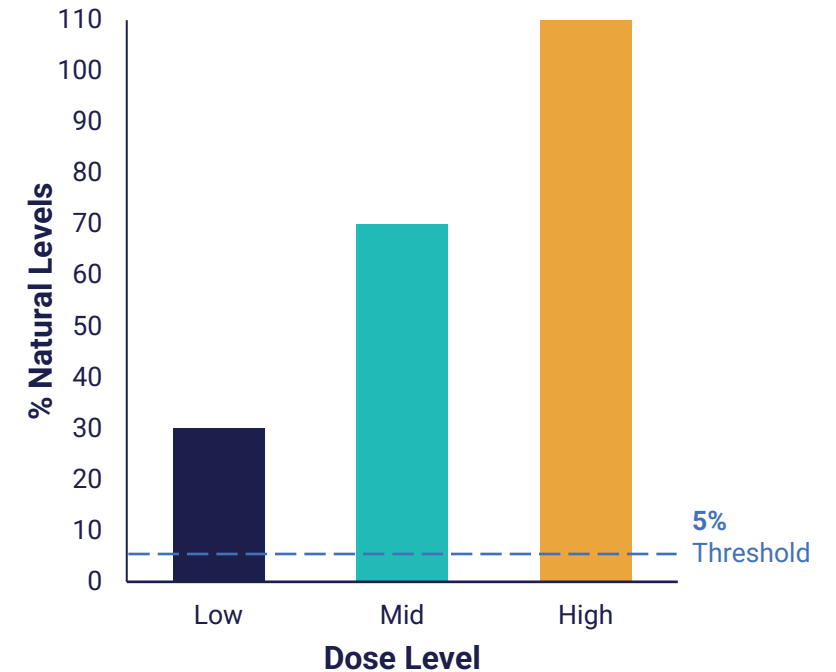
The main site of ureagenesis is the **periportal** region of the liver*



The critical threshold of **5%** residual enzymatic OTC activity helps avoid severe manifestations of the disease (neonatal coma, mortality)*

LUNAR-OTC Treatment Increases OTC Expression in Mouse Periportal Hepatocytes (Main Site of Ureagenesis)

Periportal Expression of OTC Protein in Mouse Liver



* Li, L. et al. PGC-1 α Promotes Ureagenesis in Mouse Periportal Hepatocytes through SIRT3 and SIRT5 in Response to Glucagon. *Scientific Reports*. 6:24156 | DOI: 10.1038/srep24156, April 2016

* Lamers, W.H., Hakvoort, T.B.M., and Köhler, E.S. 'Molecular Pathology of Liver Diseases' in Monga S.P.S. (ed.), *MOLECULAR PATHOLOGY LIBRARY SERIES*, Springer Publishing, New York, pp. 125-132 | DOI: 10.1007/978-1-4419-7107-4

* Scharre, Svenja. "In vitro enzyme activity predicts phenotypic severity in male individuals with ornithine transcarbamylase deficiency." SSIEM Annual Symposium 2022, Freiburg, Germany. 30 August – 2 September 2022. Poster Presentation.

ARCT-810 Clinical Update

ARCT-810 Phase 2 (EU & U.S.)
Interim Data Expected H1 2025

➤ Phase 1 Study in Healthy Volunteers

- Completed dosing up to 0.4 mg/kg, total number of subjects 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 subjects 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 Expansion Study (U.S.)

- Enrolling patients with more severe disease
- Multiple dose levels to be evaluated
- Each participant is expected to receive five intravenous infusions administered over two months
- First participant dosed at 0.5 mg/kg in December 2024

➤ 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)



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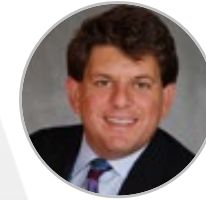
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