

**IONIS**<sup>®</sup>

 **Tryngolza**<sup>™</sup>  
(olezarsen) 80 mg  
injection

# TRYNGOLZA FDA Approval

December 19, 2024

Nasdaq: IONS

# Agenda

## Topic

## Speaker

Entering a New Era as a Fully Integrated Commercial-Stage Biotechnology Company

Brett Monia, Ph.D. *CEO*

Familial Chylomicronemia Syndrome: A Rare, Genetic, Potentially Fatal Disease

Sam Tsimikas, M.D. *SVP, Global CV Development*

Delivering TRYNGOLZA™ (olezarsen) to Adults with FCS

Kyle Jenne, *EVP, Chief Global Product Strategy Officer*

Transforming Innovation into Commercial Success

Brett Monia, Ph.D. *CEO*

Q&A

# Forward-Looking Statements

This presentation includes forward-looking statements regarding the therapeutic and commercial potential of TRYNGOLZA™ (olezarsen), Ionis' technologies, and Ionis' other products in development. Any statement describing Ionis' goals, expectations, financial or other projections, intentions or beliefs is a forward-looking statement and should be considered an at-risk statement. Such statements are subject to certain risks and uncertainties including but not limited to those related to our commercial products and the medicines in our pipeline, and particularly those inherent in the process of discovering, developing and commercializing medicines that are safe and effective for use as human therapeutics, and in the endeavor of building a business around such medicines. Ionis' forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause its results to differ materially from those expressed or implied by such forward-looking statements. Although Ionis' forward-looking statements reflect the good faith judgment of its management, these statements are based only on facts and factors currently known by Ionis. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. As a result, you are cautioned not to rely on these forward-looking statements. These and other risks concerning Ionis' programs are described in additional detail in Ionis' annual report on our Form 10-K for the year ended December 31, 2023, and our most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available at [www.ionis.com](http://www.ionis.com).

In this presentation, unless the context requires otherwise, “Ionis,” “Company,” “we,” “our,” and “us” refers to Ionis Pharmaceuticals and its subsidiaries.

Ionis Pharmaceuticals® is a registered trademark of Ionis Pharmaceuticals, Inc. TRYNGOLZA™ is a trademark of Ionis Pharmaceuticals, Inc. WAINUA™ is a registered trademark of the AstraZeneca group of companies. SPINRAZA® is a registered trademark of Biogen.

# Entering a New Era as a Fully Integrated Commercial-Stage Biotechnology Company

Brett Monia, Ph.D.  
Chief Executive Officer

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injection





The first FDA-approved therapy for adults with FCS

**NOW APPROVED**

To reduce triglycerides in adults with FCS as an adjunct to diet

# Ionis Today: Fully Integrated, Commercial-Stage Biotechnology Company



 **Tryngolza™**  
(olezarsen) 80 mg injection

 **WAINUA™**  
(eplontersen)

## First Independent Ionis Launch

First FDA-approved treatment for adults with familial chylomicronemia syndrome (FCS), adjunct to diet<sup>2</sup>

## First Ionis-branded Medicine

Co-commercializing with AstraZeneca<sup>1</sup>

## More to Come ...

- › 3 additional independent launches in 3 years<sup>3,4,5</sup>
- › Rare and prevalent disease opportunities
- › Multi-billion-dollar revenue potential<sup>3,4</sup>

## Rich History

Discovery & development of transformational medicines

 **SPINRAZA®**  
(nusinersen) injection 12 mg/5 mL

 **QALSODY®**  
(tofersen) 100 mg/15 mL injection

# TRYNGOLZA: First FDA-Approved Treatment for Familial Chylomicronemia Syndrome<sup>1</sup>



## Compelling Clinical Results:

- › Significant and sustained triglyceride reductions
- › Consistent reductions in apoC-III
- › Substantial reduction in acute pancreatitis events
- › Favorable safety and tolerability profile



## First Mover Advantage



## U.S. Launch Before Year End



## Prepared for Commercial Success

# Familial Chylomicronemia Syndrome: A Rare, Genetic, Potentially Fatal Disease

Sam Tsimikas, M.D.

Senior Vice President, Global Cardiovascular Development

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# FCS: Rare, Genetic, Potentially Fatal Disease



Genetic form of sHTG caused by loss of LPL activity<sup>1,2</sup>



Triglyceride levels 10-100x greater than normal<sup>1,2</sup>



Increased potentially fatal acute pancreatitis risk, debilitating daily symptoms, frequent hospitalizations<sup>3,4</sup>



High disease burden also results in psychological stress and reduced quality of life<sup>5</sup>

## Clinical Manifestations of FCS<sup>3,6</sup>

**Lipemia Retinalis**  
(fatty deposits in the retina)

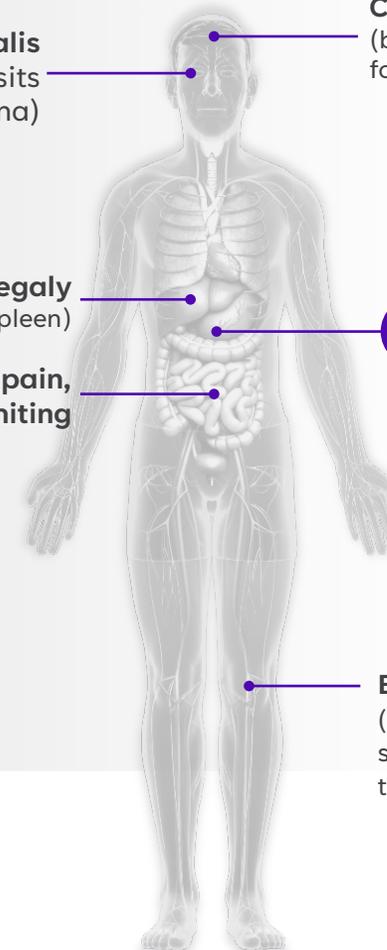
**Cognitive symptoms**  
(brain fog, fatigue, lack of focus, memory loss)

**Hepatosplenomegaly**  
(enlarged liver and spleen)

**Acute pancreatitis**

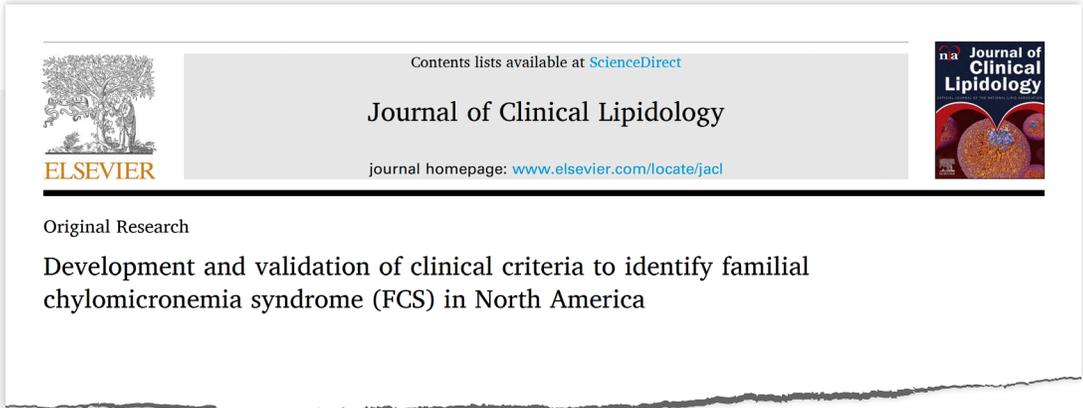
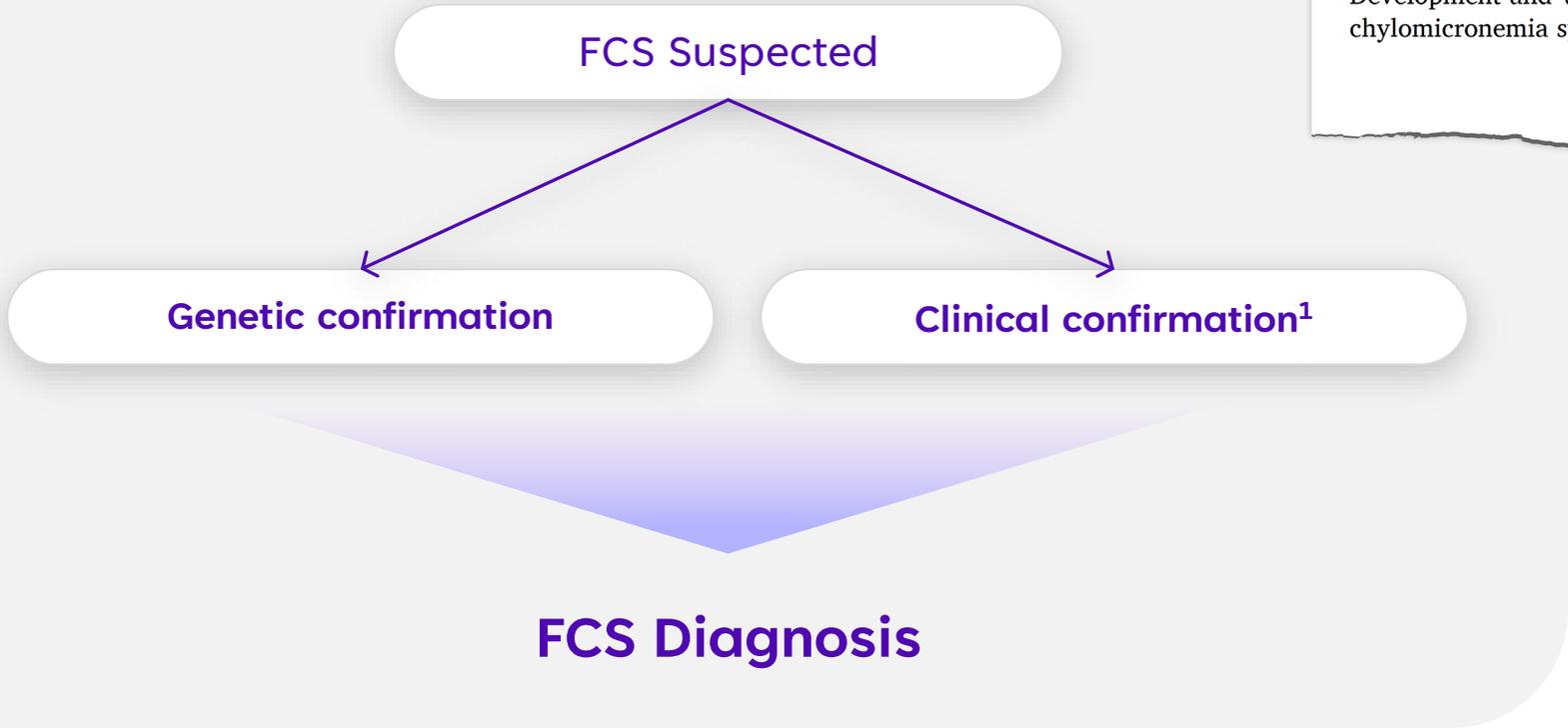
**Severe abdominal pain, nausea & vomiting**

**Eruptive xanthomas**  
(fatty deposits under the skin, usually on buttocks, trunk, knees, and elbows)



1. Moulin P, et al. *Atherosclerosis* 2018;275:265-72. 2. Brown EE, et al. *J Clin Lipidol* 2020;14(4):398-413. 3. Davidson M, et al. *J Clin Lipidol*. 2018;12(4):898-907. 4. Nawaz H, et al. *Am J Gastroenterol* 2015; 110:1497-1503. 5. Gaudet D, et al. *Lipids Health Dis*. 2020;19(1):120. 6. Brunzell JD, Bierman EL. *Med Clin North Am*. 1982;66(2):455-68.

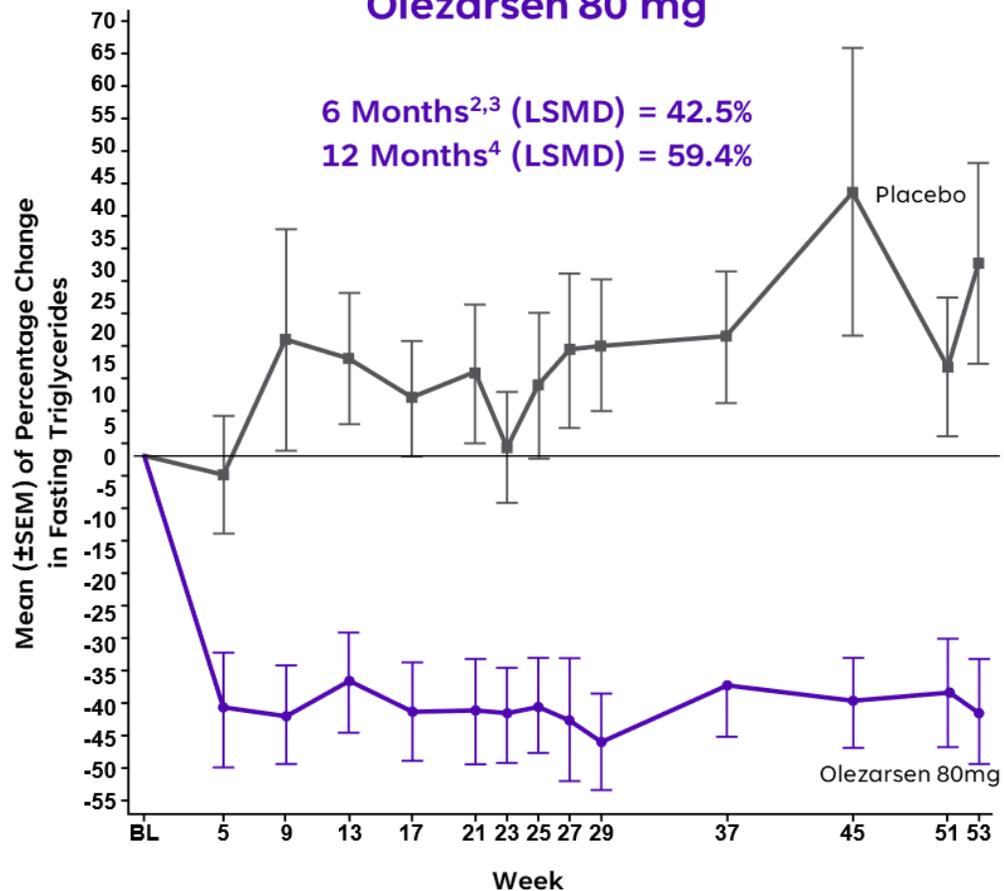
# Adults Diagnosed with FCS are Eligible for TRYNGOLZA



1. Hegele RA, et al. *J Clin Lipidology* 2024.

# Robust Efficacy and Safety Profile Highlighted in *NEJM*<sup>1</sup>

## Mean Change (%) in TGs Olezarsen 80 mg



The NEW ENGLAND  
JOURNAL of MEDICINE

ORIGINAL ARTICLE

## Olezarsen, Acute Pancreatitis, and Familial Chylomicronemia Syndrome

- › Significant triglyceride reductions at 6 months compared to placebo in FCS patients
- › Triglyceride reductions further improved through 12 months of treatment compared to placebo
- › Clinically meaningful reductions in acute pancreatitis and substantially longer time to first event compared to placebo
- › 84% reduction in all cause hospitalizations and substantial reduction in days spent in hospital compared to placebo<sup>5</sup>
- › Favorable safety and tolerability profile

LSMD, Least squares mean difference. 1. [Stroes E, et al. N Engl J Med. 2024](#). 2. Average of weeks 23, 25, and 27. 3. Olezarsen 80 mg at 6 months ( $p < 0.001$ ). 4. Average of weeks 51 and 53. 5. Exploratory endpoint.

# Delivering TRYNGOLZA to Adults with FCS

Kyle Jenne

EVP, Chief Global Product Strategy Officer

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# Ionis is Poised for Launch Success with TRYNGOLZA<sup>1</sup>

## Compelling Product Profile



- › Robust efficacy and safety
- › Convenience of once-monthly self-administration with an autoinjector

## Launch Ready



- › Seasoned team with extensive rare disease experience
- › Product in channel before year end

## First Mover Advantage



- › First FDA-approved treatment for FCS

# TRYNGOLZA Label Enables Treatment of Adults with Genetically or Clinically Confirmed FCS<sup>1</sup>



Indicated as an adjunct to diet to reduce triglycerides in adults with FCS

Statistically significant and sustained triglyceride reductions

Substantial reductions in AP events

Favorable safety and tolerability profile

Once-monthly self-administration with an autoinjector

1. TRYNGOLZA is approved in the U.S. for Familial Chylomicronemia Syndrome in adults; see [Full Prescribing Information](#).

# TRYNGOLZA Uptake to be Driven by Increasing FCS Awareness<sup>1-5</sup>

Potential for up to  
**~3,000**  
people to be diagnosed  
with FCS in the U.S.

The **majority**  
of U.S. FCS patients  
remain undiagnosed

With the approval of TRYNGOLZA,  
we expect new patient diagnoses to increase

1. Dron JS, et al. *BMC Med Genomics* 2020;13(1):23. 2. Hegele RA. *Nat Rev Genet* 2009;10(2):109-21. 3. Pallazola VA, et al. *Eur J Prev Cardiol* 2020;27(19):2276-8. 4. Tripathi M, et al. *Endocr Pract* 2021;27(1):71-6.  
5. Warden BA, et al. *J Clin Lipidol* 2020;14(2):201-6.

# TRYNGOLZA Launch Strategy Designed for Success



## Education & Awareness

Education to support patient identification



HCP engagement, evidence generation, patient advocacy



## Commercial Execution

Efficient and targeted U.S. commercial team



Now deployed in preparation for U.S. launch before year-end



## Comprehensive Support Program

Services designed for patients and HCPs



Patient assistance, authorization support, financial support for eligible patients



## Coverage & Reimbursement

Market access team engaging with payers



To ensure access for people who may benefit from TRYNGOLZA



## Omnichannel Engagement

Targeted HCP and patient engagement



Innovative capabilities to identify patients, extend commercial team reach

# Ionis Every Step™ Designed to Meet the Unique Needs of the FCS Community



Suite of services offering personal support for patients and HCPs



Disease & nutrition education, injection training & other resources through dedicated patient education managers



Authorization and reauthorization assistance, delivery coordination and refill reminders to support adherence



Financial support programs to help appropriate patients afford TRYNGOLZA; commercially insured patients may pay as little as \$0 out of pocket



The first FDA-approved therapy for adults with FCS

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# Transforming Innovation into Commercial Success

Brett Monia, Ph.D.  
Chief Executive Officer

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# Delivering on our Promise to Become a Fully Integrated Commercial-Stage Biotechnology Company<sup>1</sup>

**TRYNGOLZA Launch  
Before Year End**

**Four Independent  
Launches in Three Years<sup>2,3</sup>**

**Rich and Growing  
Wholly Owned Pipeline**

**Multi-Billion Dollar Opportunity  
from Wholly Owned Medicines**

# Q&A

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