



Q4 and FY 2019 Financial Results and Highlights

February 26, 2020



On Today's Earnings Call



Brett Monia, Ph.D.
Chief Executive Officer



Onaiza Cadoret-Manier
*Chief Corp. Development &
Commercial Officer*



Beth Hougen
Chief Financial Officer



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*Senior Vice President,
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*Senior Vice President,
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Forward Looking Language Statement

This presentation includes forward-looking statements regarding our business, financial guidance and the therapeutic and commercial potential of SPINRAZA® (nusinersen), TEGSEDI® (inotersen), WAYLIVRA® (volanesorsen) and Ionis' technologies and products in development, including the business of Akcea Therapeutics, Inc., Ionis' majority owned affiliate. 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, 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. 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 Form 10-K for the year ended December 31, 2018 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.ionispharma.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 trademark of Ionis Pharmaceuticals, Inc. Akcea Therapeutics® is a registered trademark of Akcea Therapeutics, Inc. TEGSEDI® is a trademark of Akcea Therapeutics, Inc. WAYLIVRA® is a registered trademark of Akcea Therapeutics, Inc. SPINRAZA® is a registered trademark of Biogen.

Introduction

Brett Monia, Ph.D.

Chief Executive Officer

2019 In Review

Exceptional Performance Across the Business

- ✓ Delivered **exceptional financial results**
- ✓ Advanced **four medicines** into **Phase 3** development
- ✓ Achieved positive clinical **proof-of-concept results** from **5 medicines**
- ✓ Advanced 5 **medicines** into Phase 1
- ✓ Advanced 6 new **Ionis-owned medicines** into development
- ✓ Advanced and broadened the **scope** of our **technology**

**Well positioned to achieve goal of 10 or more
NDA filings through 2025**

Commercial Strategy

Onaiza Cadoret-Manier

***Chief Corporate Development &
Commercial Officer***

Developing our Commercial Strategy

- Identify **optimal commercial pathway** and **organization** for each medicine while preserving Ionis' culture of innovation
- Develop capabilities to bring medicines to patients from our **growing Ionis-owned pipeline**
- Continue establishing **strategic partnerships** for medicines addressing broad indications
- Support **Akcea** in pursuing its **strategic goals**

Goal:
**Maximize the
value of every
medicine in our
pipeline**

2019 Financial Performance

Beth Hougen

Chief Financial Officer

Achieved Exceptional 2019 Financial Results While Returning Value to Shareholders

\$1.1 billion in revenue

Nearly doubled over 2018



\$293 million

>20% increase over 2018

\$513 million
of operating income*

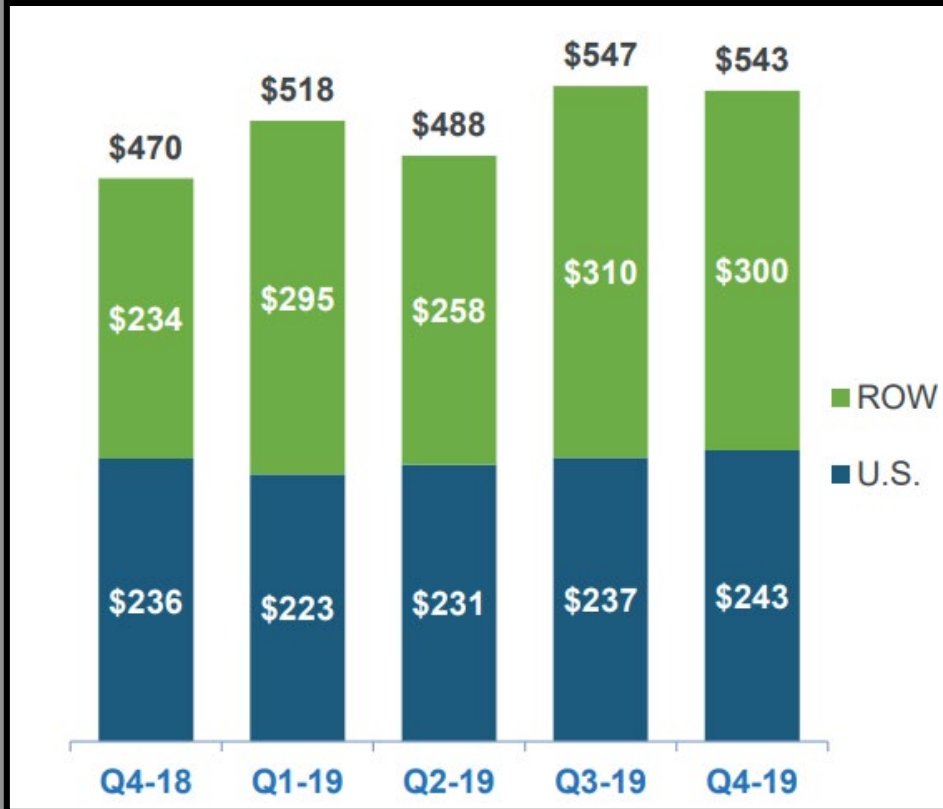
\$402 million
of net income*

\$2.5 billion of cash

Enabling investment across the business to drive value creation

Continued Blockbuster Performance with over \$2 Billion in Global Sales in 2019

\$293M in Royalties to Ionis



Source: Biogen Q4 2019 Financial Results and Business Update; *Includes patients from commercial, clinical and EAP settings; **Adult SMA patients are the largest SMA patient segment

- **~10,000 patients** now on SPINRAZA therapy worldwide*
 - >50% of fourth quarter sales driven by markets outside the U.S.
 - U.S. growth driven by pediatric and adult patients
 - ~50% of new U.S. patient starts were adult patients**
- Continued significant **opportunity** for **growth**
- **Approved in over 50 countries**
- Formal **reimbursement** in **40 countries**

TEGSEDI and WAYLIVRA*

Achieved \$42 million in product sales in 2019



- **Commercially available** in over 10 countries; new **country launches** this year
- **Growth in U.S.** new prescribing physicians, patient starts and units shipped to patients
- Broad **payor coverage** achieved in the U.S.
- **Launching in Brazil** with PTC



- **Launched in Germany**; new **country launches** this year
- **ATU enrolling** patients in France
- Potential **approval in Brazil** by the end of this year with PTC
- Goal to refile for **marketing authorization** in the **U.S.** this year



*Commercialized by Akcea Therapeutics

R&D Revenue in 2019 More Than Doubled*

Significant and Sustainable Source of Revenue

\$490M License Fees

\$146M Amortization of Upfront Fees

\$115M Milestone Payments

2020 Guidance

Financial Strength to Achieve our Strategic Goals

Revenue

>\$700 million

Operating Expenses

~\$650-\$690 million*

Meaningfully profitable*

Pipeline Performance: Recent Accomplishments and Upcoming Catalysts

Richard Geary, Ph.D.

Senior Vice President, Development

Recent Pipeline Successes

Neurological

- Phase 3 studies of IONIS-HTT_{Rx}¹ and tofersen² progressing on track
- Completed enrollment in Phase 2 study of IONIS-MAPT_{Rx}, initiated long-term extension study
- Initiated Phase 2 study of ION859 targeting LRRK2 in patients with Parkinson's disease²
- Advanced ION581 for the treatment of Angelman syndrome into development

Cardiometabolic

- Patient enrollment initiated in Phase 3 HORIZON outcome study of AKCEA-APO(a)-L_{Rx}³
- Reported positive topline Phase 2 results for AKCEA-ANGPTL3-L_{Rx}
- Bayer licensed FXI program for the treatment of thrombosis
- Initiated Phase 1 study of ION839 for the treatment of NASH⁴

Ionis-owned

- Initiated Phase 3 studies of AKCEA-TTR-L_{Rx} in TTR polyneuropathy and TTR cardiomyopathy
- Reported positive topline Phase 2 results for AKCEA-APOCIII-L_{Rx}
- Initiated Phase 2 study of IONIS-PKK-L_{Rx} in patients with HAE
- Initiated Phase 2 study of IONIS-ENaC-2.5_{Rx} in patients with cystic fibrosis
- ION373, for the treatment of Alexander disease, granted orphan drug status from the EMA
- Advanced medicines for the treatment of Prion and Lafora diseases into development

Numerous Potential Catalysts in 2020

≥6 Phase 3 studies underway

≥6 POC data readouts*

≥10 Phase 2 starts

≥5 New medicines in development

**Positioned
for up to
10 or more
NDA filings
through 2025**

Conclusion: 2020 and Beyond

Brett Monia, Ph.D.

Chief Executive Officer



RARE DISEASE DAY®

#RareDiseaseDay

rarediseaseday.org

29 FEBRUARY 2020

MORE THAN

90% OF RARE DISEASES

ARE WITHOUT AN

FDA-APPROVED TREATMENT



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ionis-pharmaceuticals

2020 Strategic Priorities

- Grow and advance the **Ionis-owned pipeline**
- Develop our **commercial capabilities** to ensure we **maximize the value** of each of our medicines
- Expand the **reach** of our **technology**
- Identify and invest in **complementary technologies**

**Investing aggressively in areas with the
greatest value-creating potential**

Q&A

Brett Monia, Ph.D.

Chief Executive Officer

A black and white photograph of a family of four is the background for the lower half of the image. A man is in the bottom left, smiling and looking towards the camera. A woman is on the right, smiling and waving her hand. Two young children are in the center, hugging each other and the man. The overall mood is warm and affectionate.

IONIS: A FORCE FOR LIFE