



**Q1 2020
Financial Results and
Highlights**

May 6, 2020



On Today's Earnings Call



Brett Monia, Ph.D.
Chief Executive Officer



Beth Hougen
Chief Financial Officer



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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, including those related to the impact COVID-19 could have on our business, and 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. 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, 2019, which is 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.

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Introduction



Brett Monia, Ph.D.

Chief Executive Officer

Q1 2020:

On track to achieve 2020 guidance
while fully investing in strategic priorities

Strong commercial + pipeline performance
SPINRAZA, TEGSEDI and WAYLIVRA growth
plus successes achieved across the pipeline

Effectively managing COVID-19 challenges
strategies in place to protect people,
data integrity and timelines

**Well positioned
to achieve our
2020 goals**

Q1 2020 Financial Performance

Beth Hougen

Chief Financial Officer

Q1 2020 Financial Performance

On track to achieve 2020 financial guidance

\$130 million in revenue

Driven by 25% increase in
commercial revenue



\$66 million**

>10% increase over Q1 2019

Nearing breakeven

net loss \$15 million*

\$2.4 billion of cash

Enabling investment across the
business to drive value creation



Substantial Financial Strength

Enabling investment in strategic priorities

Strong, sustainable balance sheet

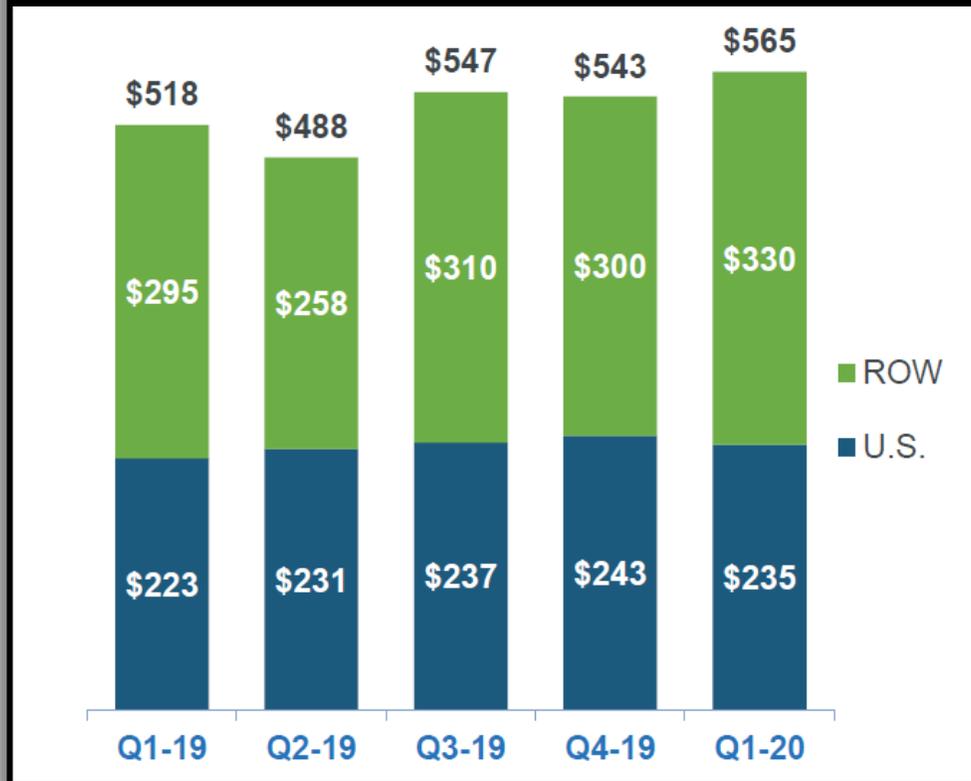
Well capitalized, with cash balance of \$2.4 billion

**Strengthened balance sheet by refinancing
debt in late 2019**

**Maintaining financial strength while effectively
managing COVID-19 challenges**

Continued Blockbuster Performance with \$565 Million in Q1 2020 Global Sales

\$66M in Royalties to Ionis¹



- **~10,800 patients** on SPINRAZA therapy worldwide^{2,3}
 - U.S. growth driven primarily by adult patients⁴
 - Growth across all major regions outside the U.S.
- Continued **opportunity** for **growth**
 - Significant number of untreated patients in established and emerging markets
- Initiated **DEVOTE Phase 2/3** study
 - Potential to achieve greater efficacy with higher dose

Source: Biogen Q1 2020 Financial Results and Business Update; 1. SPINRAZA royalty tier resets at the beginning of each year; 2. Includes patients from commercial, clinical and EAP settings; 3. As of March 31, 2020; 4. Adult SMA patients are the largest SMA patient segment

TEGSEDI and WAYLIVRA*

Continued sequential quarterly growth



- **Commercially available** in 12 countries
- Achieved **reimbursement** in Spain and Austria
- **Launching** in new **EU countries** and expanding in **Latin America** with PTC



- **Launched** in **Germany, Austria** and **France****
- On track to refile for **approval** in the **U.S.** this year
- **Launching** in new **EU countries**; plan to file for **approval** in **Brazil** with PTC this year



*Commercialized by Akcea Therapeutics; **Enrolling in ATU, reimbursed expanded access program

Multiple Sources of Revenue: A Key Competitive Advantage

PARTNERS

**More than
10 partners**

MEDICINES

**More than
20 partnered
medicines**

R&D Revenue

**Numerous
Opportunities
for Growth**

Reaffirming our 2020 Financial Guidance

Revenue

>\$700 million

Operating Expenses

~\$650-\$690 million*

Meaningfully profitable*

Pipeline Performance



Richard Geary, Ph.D.

Executive Vice President, Development

Recent Pipeline Successes

Neurological

- Enrollment complete in the tominersen Phase 3 GENERATION HD1 study¹
- First patient treated in Phase 2/3 DEVOTE study of higher dose SPINRAZA²
- Tofersen (SOD1 ALS) and IONIS-MAPT_{Rx} (AD) studies progressing²
- IONIS-C9_{Rx} granted Fast Track Designation in U.S.; Phase 2 study in C9 ALS progressing²
- On track to initiate first-in-human study in patients with sporadic ALS medicine this year²
- Advanced IONIS-DNM2-2.5_{Rx} into Phase 1/2 study for the treatment of centronuclear myopathies³

Cardiometabolic

- AKCEA-APO(a)-L_{Rx} granted Fast Track Designation in U.S.; Phase 3 study progressing on track⁴
- Reported positive topline Phase 2 results for vupanorsen (AKCEA-ANGPTL3-L_{Rx})
- Initiated Phase 1 study of ION532, targeting APOL1 for the treatment of kidney disease⁵

Ionis-owned

- CARDIO-TTRansform and NEURO-TTRansform studies of AKCEA-TTR-L_{Rx} progressing
- Reported positive topline Phase 2 results for AKCEA-APOCIII-L_{Rx}
- Initiated Phase 2 studies of IONIS-PKK-L_{Rx} in HAE and IONIS-TMPRSS6-L_{Rx} in β -thalassemia
- Initiated Phase 1 study of ION224 for the treatment of NASH
- Advanced medicines for the treatment of Alexanders, Prion and Lafora diseases towards the clinic

Key Catalysts for Remainder of 2020

- Initiate **AKCEA-APOCIII-L_{Rx} Phase 3** study in FCS
- Re-file **NDA** for **WAYLIVRA** in U.S.
- Report clinical **POC** results for **≥ 4 more programs***
- Present **AKCEA-APOCIII-L_{Rx}** and **vupanorsen** Phase 2 results
- Initiate **ION541** first-in-human study in patients with **sporadic ALS**
- Add **≥ 5 new medicines** to development pipeline

Conclusion: 2020 and Beyond

Brett Monia, Ph.D.

Chief Executive Officer

Ionis Today: Stronger than Ever

- Reaffirming our 2020 guidance and well-capitalized
- Effectively managing challenges of COVID-19 pandemic
- Dedicated employees committed to serving patients in need
- Executing on our strategic goals

**On track to deliver NDAs for 10 or more
medicines through 2025**

Q&A

Brett Monia, Ph.D.

Chief Executive Officer



IONIS™

IONIS: A FORCE FOR LIFE