



H1 2019 Financial Results and Highlights

August 7, 2019



On Today's Earnings Call



Stanley Crooke, M.D., Ph.D.
*Chief Executive Officer
and Chairman*



Brett Monia, Ph.D.
Chief Operating Officer



Beth Hougen
Chief Financial Officer



Damien McDevitt, Ph.D.
Chief Business Officer

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 the 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.

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Introduction



Stanley Crooke, M.D., Ph.D.
Chief Executive Officer and Chairman

Delivering Value Today and in the Future

Sustained Profitability While Investing in Value-Focused Innovation

POSITIONED FOR CONTINUED GROWTH

DRIVEN BY...

TODAY

- ✓ SPINRAZA
- ✓ TEGSEDI
- ✓ WAYLIVRA

1 - 2 Years

- **4 medicines** planned to be in Phase 3 studies by YE19
- **Growing pipeline** of mid-stage medicines approaching value-driving catalysts

5 Years

- **Additional** commercial medicines
- **Advancing** technology
 - More tissues, routes of administration & mechanisms

— G R O W I N G R & D R E V E N U E —

H1 2019 Financial Performance



Beth Hougen
Chief Financial Officer

Strong Financial Performance

H1 2019 Financial Results at a Glance

**On Track
for Third Year of
Net Income***

**\$461 million in
revenue**

>75% increase
over H1 2018

\$190 million
of operating income*

\$162 million
of net income*



\$130 million

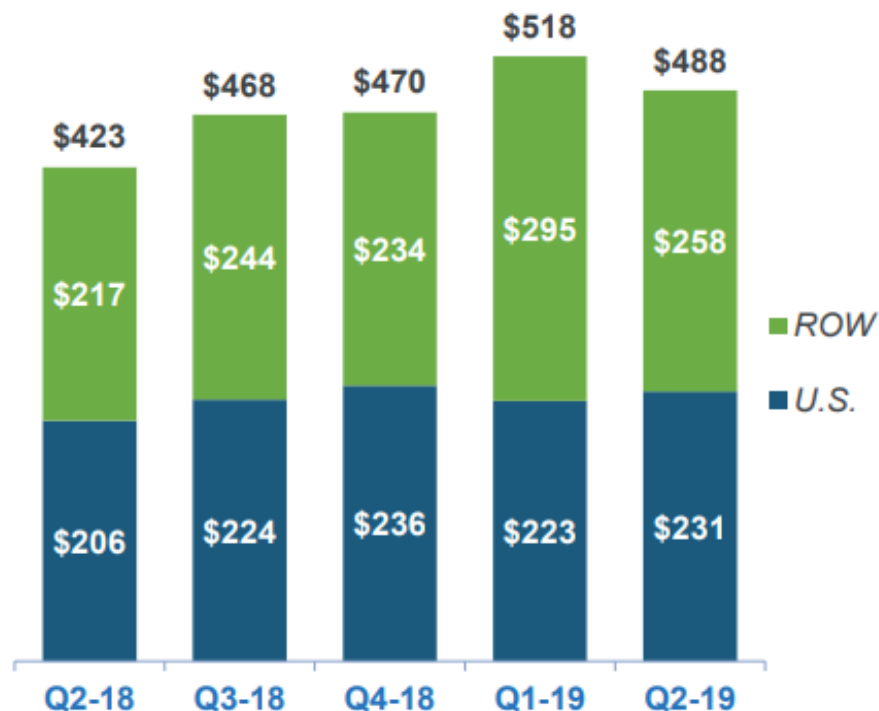
>30% increase
over H1 2018

\$2.3 billion of cash

Enabling investment in
commercial products and pipeline

Continued Blockbuster Performance with \$1 Billion in Global Sales in H1 2019

>\$130M in Royalties to Ionis



- SPINRAZA **approved** in over **40** countries, with formal **reimbursement** in over **35** countries
- Continued **global growth** in new patients on SPINRAZA
- **~8,400 patients** now on SPINRAZA therapy worldwide*
 - ~12% increase in patients on commercial therapy worldwide
 - ~50% of new patient starts in the U.S. were adult (18+) SMA patients, the largest patient segment.

TEGSEDI and WAYLIVRA: Two Transformational Medicines Approved for Serious Diseases*



- **\$17 million** in sales in H1 2019; **\$10 million** in sales in Q2 2019
- Launching in **England** this month, additional **EU country** launches planned
- Planned expansion in **Latin America**, beginning in **Brazil**, through **PTC Therapeutics**



- **Launching** in **Germany** this month; additional **EU country** launches planned in 2020
- **Encouraging** discussions with the **FDA** to clarify path forward **in the U.S.**
- In **FPL**, significant **reductions in TGs** and **liver fat**, good safety and tolerability



*Commercialized by Akcea Therapeutics

R&D Revenue Remains a Significant and Sustainable Source of Revenue

- 1** Amortization of upfront fees
- 2** Milestone payments
- 3** License fees
- 4** Services provided to partners

On Track to Meet or Improve Upon 2019 Financial Guidance

**Total
revenue**

>\$725
million

R&D expense
~ \$360-390
million*

SG&A expense
~\$260-290
million*

**Operating
income**

>\$100
million*

**Cash
balance**

~\$2
billion

PROFITABLE AT THE BOTTOM LINE*



Key Pipeline Accomplishments

Brett Monia, Ph.D.
Chief Operating Officer

Key Recent Achievements

Financial	- Achieved operating income of \$190M¹ and net income of \$162M¹ in H1 2019 - Revenue increased >75% to \$461M in H1 2019 compared to H1 2018 - Commercial revenue from SPINRAZA royalties increased by >30% to \$130M in H1 2019 compared to H1 2018 - R&D revenue nearly doubled in H1 2019 compared to H1 2018 - Ended H1 2019 with cash and investments of \$2.3B
	- Global SPINRAZA revenues in H1 2019 increased by nearly 30% to \$1B compared to H1 2018 - Patients on SPINRAZA treatment increased by ~12% to ~8,400 patients³ - Adult SMA patients accounted for ~50% of U.S. new patient starts, with ~20% of adult U.S. patients now on SPINRAZA treatment - Approved in >40 countries; formal reimbursement secured in >35 countries
	- Earned \$17M in revenue from TEGSEDI product sales in H1 2019 and \$10M in revenue in Q2 2019 - Launching in England in August 2019; additional EU country launches planned
	- Launching in the EU beginning in Germany in August 2019; additional EU country launches planned in 2020 - Encouraging discussions continued with the U.S. Food and Drug Administration to clarify a path forward in the U.S. - BROADEN study in FPL achieved statistically significant reductions in TGs and liver fat; good safety and tolerability
	- Phase 3 studies of tofersen (IONIS-SOD1_{Rx}) and IONIS-HTT_{Rx} (RG6042) progressing, both with potential to support registration - Initiation of Phase 3 programs for AKCEA-APO(a)-L_{Rx} and AKCEA-TTR-L_{Rx} on track for H2 2019 - GSK reported positive results achieved the in HBV program; FXI program nearing completion - Initiated Phase 2 study of IONIS-FB-L_{Rx} in complement-mediated diseases and Phase 2 study of IONIS-PKK-L_{Rx} in HAE



¹Non-GAAP – please see reconciliation to GAAP in 2Q 2019 press release; ²As reported by Biogen in 2Q 2019 Financial Results

³Includes commercial patients and patients from the clinical and EAP settings; ⁴Commercialized by Akcea

Delivering Value Today and in the Future

Numerous Upcoming Value Inflection Points

3

Commercial Medicines

✓ SPINRAZA ✓ TEGSEDI ✓ WAYLIVRA

4

Phase 3 Study Starts Planned

✓ IONIS-HTT_{Rx}, ✓ Tofersen

AKCEA-APO(a)-L_{Rx}, AKCEA-TTR-L_{Rx}

6+

Phase 2 Study Readouts Planned

✓ Tofersen ✓ IONIS-HTT_{Rx} ✓ IONIS-DGAT2_{Rx} ✓ HBV_{Rx}/HBV-L_{Rx}

IONIS-FXI_{Rx}, AKCEA-APOCIII-L_{Rx}, AKCEA-ANGPTL3-L_{Rx}
and more



2019 and Beyond

Stanley Crooke, M.D., Ph.D.
Chief Executive Officer and Chairman

Coupling a More Efficient Technology Platform to a Tailored Business Model

Ever-growing competitive advantage

Large and growing commercial opportunities

**Most Direct Route
from Gene to
Patient**

**Higher
Success Rate**

**Efficient
Infrastructure**

**Optimal Approach
for Each Medicine**

Creating growing value for patients and shareholders

Q&A



Stanley Crooke, M.D., Ph.D.
Chief Executive Officer and Chairman

A black and white photograph of a family of four is the background for the lower two-thirds of the image. A man is in the bottom left, smiling broadly with his eyes closed, being embraced from behind by a young girl. Another young girl is in the center, also smiling and looking towards the right. A woman is on the right, smiling and making a peace sign with her right hand. The family is dressed in casual outdoor clothing like jackets. The overall mood is warm and joyful.

IONIS: A FORCE FOR LIFE