



Q1 2019 Financial Results and Highlights



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, which is on file with the SEC. Copies of this and other documents are available at www.ionispharma.com.

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IONIS™

IONIS: A FORCE FOR LIFE

Positioned for continued growth

Q1 2019:

**Financial results significantly
outperformed Q1 2018**

**Growth in commercial revenue
from SPINRAZA royalties and
TEGSEDI product sales**

**Continued financial strength
while investing aggressively in all
elements of the business**



Q1 2019 Financial Performance

Beth Hougen
Chief Financial Officer

Q1 2019 Financial Results at a Glance

**On Track to Meet
2019 Financial
Guidance**

**\$297 million in
revenue**

More than doubled
over Q1 2018

\$167 million
of operating income*

\$126 million
of net income*



\$60 million

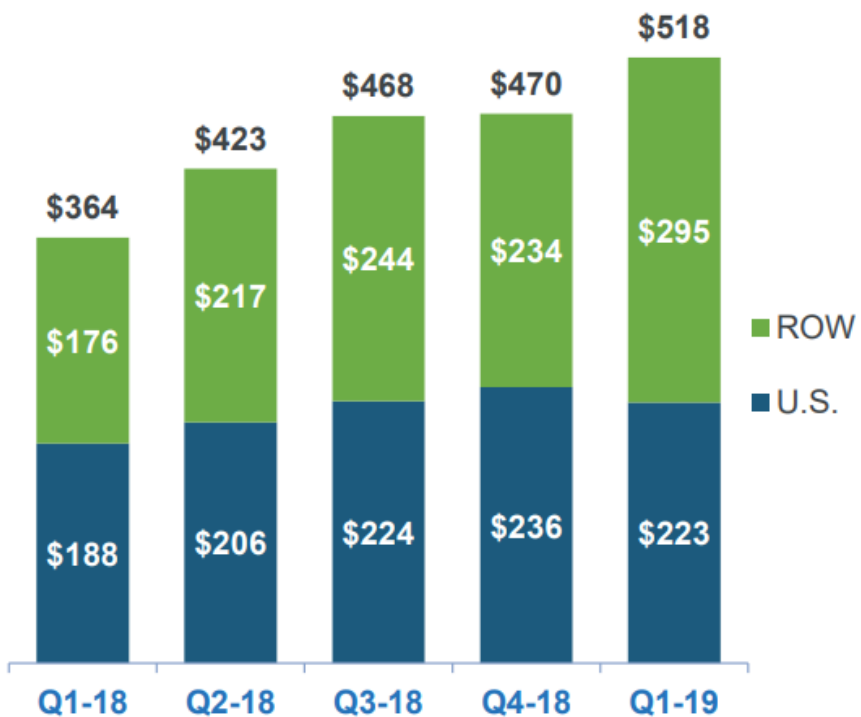
SPINRAZA royalties increased
by 46% over Q1 2018

\$2.3 billion of cash

Enabling investment in
commercial products and pipeline

Continued Blockbuster Performance with \$518 Million in Global Sales

\$60M in Royalties to Ionis in Q1 2019



- SPINRAZA **approved** in over **40** countries*
- **> 7,500 patients** now on therapy worldwide**
- Biogen continues to **increase** the number of **SMA patients on therapy**
 - ✓ In Q1 2019, ~50% of new starts were adult (18+) SMA patients, the largest patient segment in the U.S
 - ✓ 24% increase in patients on SPINRAZA outside the U.S.

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



- **\$7 million** in sales in Q1 2019; **\$9 million** in sales since Q4 2018 launch
- **Multi-country launch** going well
- **Positive recommendation** from NICE in England
- Preparing to **expand into new countries**



- **Approved in the EU** for the treatment of FCS
- **EU launch** planned for Q3 2019 in Germany
- Additional **EU country launches** planned for 2020
- Discussions continue with regulators in the **U.S. and Canada**



*Commercialization through affiliate, Akcea Therapeutics



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

**R&D Revenue
Funds a Large
Portion of R&D
Expenses***

1

Amortization of upfront fees

2

Milestone payments

3

License fees

4

Services provided to partners

2019 Financial Guidance: Positioned for Continued Strength

**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	<ul style="list-style-type: none"> Achieved non-GAAP operating income of \$167M and net income of \$126M* Revenue more than doubled to \$297M compared to Q1 2018 Commercial revenue from SPINRAZA royalties increased by 46% to \$60M compared to Q1 2018 R&D revenue included \$150M license fee from Novartis and \$35M milestone payment from Roche Ended Q1 2019 with cash and investments of \$2.3B
SPINRAZA	<ul style="list-style-type: none"> Global SPINRAZA revenues increased by 42% to \$518M compared to Q1 2018 Over 7,500 patients on SPINRAZA treatment across commercial, clinical trial and expanded access program settings U.S. adult SMA patients on treatment increased to >1,000 patients, accounting for 50% of new patient starts Recent approvals in Latin America and Asia Pacific represent potential for global growth
TEGSEDI	<ul style="list-style-type: none"> Earned revenue of \$7M from TEGSEDI product sales in Q1 2019 and \$9M since launch NICE authorized pricing and reimbursement of TEGSEDI in England
WAYLIVRA	<ul style="list-style-type: none"> WAYLIVRA approved in the EU; earned \$6M milestone from PTC Therapeutics for EU approval EU launch preparations are underway, beginning in Germany in Q3 2019
Pipeline	<ul style="list-style-type: none"> Biogen reported tofersen (IONIS-SOD1_{Rx}) treatment led to clinical benefit in measures of disease in SOD-1 ALS patients Roche reported sustained mHTT lowering observed through 9 months of treatment in the OLE study of IONIS-HTT_{Rx} (RG6042) Novartis licensed AKCEA-APO(a)-L_{Rx}; planning is underway for Phase 3 cardiovascular outcomes study initiation AKCEA-TTR-L_{Rx} continued to progress towards pivotal program in 2H 2019

What's Next: Numerous Potential Near-term Commercial and Pipeline Catalysts

Commercial Milestones

- ✓ **SPINRAZA:** Continued growth in sales and approval in additional markets
- **TEGSEDI:** Successful global launch and access in additional markets
- ✓ **WAYLIVRA:** Approval in the EU
- **WAYLIVRA:** Successful EU launch

Pivotal Study Initiations

- ✓ **IONIS-HTT_{Rx} (RG6042):** for Huntington's disease
- ✓ **Tofersen (IONIS-SOD1_{Rx}):** for SOD1-related ALS*
- **AKCEA-APO(a)-L_{Rx} (TQJ23):** for high Lp(a) levels with established risk of CVD
- **AKCEA-TTR-L_{Rx}:** for ATTR

Phase 2 Data Readouts

- **AKCEA-TTR-L_{Rx}:** for hATTR-PN (healthy subjects & patients)
- ✓ **Tofersen (IONIS-SOD1_{Rx}):** for SOD1-related ALS (Phase 1/2 data)
- **Danvatirsen:** for head & neck cancer (additional data)
- **IONIS-FXI_{Rx}:** for end-stage renal disease
- **IONIS-HBV_{Rx}:** for HBV
- ✓ **IONIS-DGAT2_{Rx}:** for fatty liver in T2D patients



2019 and Beyond

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

Ionis: Delivering Sustained Growth Driven by a Pipeline of Potentially Transformative Medicines

Pioneer of
RNA technology
Novel business model
Culture of **YES**

30 years advancing
technology
Ever-**better**
performance
Greater commercial
opportunities

3 commercial
medicines
40+ in development
10+ Phase 3 studies
potentially by YE **2020**
4+ Phase 3 studies
planned by YE **2019**

Q&A



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