

## Ionis reports second quarter 2021 financial results and recent business achievements

August 4, 2021

**Key Phase 3 milestones move tofersen, eplontersen and pelacarsen closer to the market**  
**Exclusive license to Bicycle Therapeutics' technology potentially expands LICA technology capabilities**  
**Webcast today, August 4, 2021, at 11:30 a.m. Eastern Time**

CARLSBAD, Calif., Aug. 4, 2021 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) today reported its financial results for the second quarter of 2021 and recent business achievements.



"Since our last quarterly update, we continued to execute on our strategic objectives to prepare for multiple Ionis commercial launches, expand our drug delivery capabilities and advance new products towards the market. Biogen completed dosing in the tofersen Phase 3 VALOR study and began offering tofersen to SOD1-ALS patients on an individual compassionate use basis. We achieved full enrollment in the eplontersen Phase 3 NEURO-TTRansform study and 50 percent enrollment in the pelacarsen Phase 3 Lp(a) HORIZON study. Additionally, we licensed Bicycle Therapeutics' technology to expand the capabilities of our LICA technology," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "Looking ahead, we expect data from multiple pipeline programs, including additional data supporting the potential for our IONIS-PKK-L<sub>Rx</sub> program to change the standard of care for patients with hereditary angioedema. And by this fall, we expect data from the Phase 3 VALOR study of tofersen in patients with SOD1-ALS. If results from the VALOR study are positive, we expect tofersen to be our next commercial medicine. These key recent achievements and upcoming catalysts keep us on track for a regular cadence of Phase 3 data and new drug applications, leading to 12 or more products on the market in 2026."

### Second Quarter 2021 and Recent Summary Financial Results

- Second quarter results reflect focus on Ionis' strategic objectives
  - \$126 million in total revenues
  - \$154 million of operating expenses on a non-GAAP basis<sup>(1)</sup> and \$199 million on a GAAP basis
  - Net loss of \$36 million on a non-GAAP basis<sup>(1)</sup> and \$81 million on a GAAP basis
- Well capitalized with cash and investments of \$2.1 billion at the end of the second quarter

"In addition to advancing our pipeline and expanding our drug discovery capabilities, we have taken multiple steps to streamline our operations in support of our wholly owned medicines. We have completed the integration of Akcea, entered distribution arrangements with Sobi and restructured our commercial operations. These steps enabled us to unlock significant resources that we are redirecting towards our highest priority programs," said Elizabeth L. Hougen, chief financial officer of Ionis. "We remain on track to achieve our 2021 revenue guidance of more than \$600 million. We continue to expect increased R&D revenue in the second half of this year. Already in the third quarter, we earned \$25 million from Novartis for the pelacarsen enrollment milestone. We are revising our 2021 operating expense and net loss guidance because of our license of Bicycle's technology. Importantly, we remain well-capitalized with the resources we need to achieve our strategic objectives."

### Revised 2021 Financial Guidance

- Updated operating expense and net loss guidance because of Ionis' license of Bicycle's technology<sup>(1)</sup>

	Prior 2021 Guidance	Revised 2021 Guidance
Revenue	>\$600 million	Unchanged
Operating Expenses <sup>(1)</sup>	\$675 million to \$725 million	\$710 million to \$750 million
Net Loss <sup>(1)</sup>	<\$75 million	<\$110 million

(1) All non-GAAP amounts referred to in this press release exclude non-cash compensation expense related to equity awards and expenses related to the Akcea acquisition and restructured commercial operations and the related tax effects. Please refer to the section below titled "Financial Impacts of Akcea Acquisition and Restructured Commercial Operations" for a summary of the costs specific to these transactions. Additionally, please refer to the detailed reconciliation of non-GAAP and GAAP measures, which is provided later in this release.

## Second Quarter 2021 Marketed Products Highlights

- SPINRAZA<sup>®</sup>: The global market leader for the treatment of spinal muscular atrophy (SMA) patients of all ages
  - \$500 million in worldwide sales in the second quarter
  - More than 11,000 patients worldwide on therapy at the end of the second quarter across commercial, expanded access and clinical trial settings
  - New data presented at CureSMA reinforce the potential for higher-dose SPINRAZA to improve SMA patient outcomes and further support SPINRAZA's potential long-term benefit for SMA patients of all ages
- TEGSEDI<sup>®</sup> and WAYLIVRA<sup>®</sup>: important medicines approved for the treatment of patients with severe rare diseases
  - Successfully completed the transition of North American TEGSEDI operations to Swedish Orphan Biovitrum AB (Sobi)

## Second Quarter 2021 and Recent Events

- Phase 3 Pipeline: Six Phase 3 studies on track for a regular cadence of data readouts beginning this year
  - Completed dosing in the Phase 3 VALOR study of tofersen in patients with SOD1-ALS, with data expected by this fall
    - Opened individual compassionate use access for SOD1-ALS patients with the most rapidly progressive disease
  - Achieved full enrollment in the Phase 3 NEURO-TTRansform study of eplontersen in patients with TTR polyneuropathy, with data expected by mid-2022
  - Achieved 50 percent enrollment in the Phase 3 Lp(a) HORIZON study of pelacarsen for patients at risk for Lp(a)-driven cardiovascular disease, resulting in a \$25 million payment from Novartis
  - Advanced ION363 into a Phase 3 study in patients with FUS-ALS
- Mid-stage Pipeline: multiple medicines with potential to change the standard of care for patients with severe diseases
  - Continued to advance the Phase 2b RE-THINc ESRD study of IONIS-FXI-L<sub>Rx</sub>, with data expected in the first half of 2022
  - Reported data from the Phase 1/2 study of IONIS-MAPT<sub>Rx</sub> in patients with Alzheimer's disease, demonstrating durable, time and dose-dependent reductions in CSF tau protein; IONIS-MAPT<sub>Rx</sub> was generally well tolerated
  - Advanced the ongoing Phase 2 study of ION541 in patients with ALS regardless of family history, resulting in a \$10 million payment from Biogen
  - Advanced ION224 into a Phase 2b study in patients with non-alcoholic steatohepatitis (NASH)
  - Advanced ION373 into the Phase 2 portion of a pivotal study in patients with Alexander disease
- Strategic and Business Events
  - Entered a license agreement with Bicycle Therapeutics for exclusive rights to Bicycle's peptide technology to expand the capabilities of Ionis' LICA technology
  - Announced changes to the Ionis board of directors
    - Joseph Loscalzo, M.D., Ph.D., appointed as chairman and Allene M. Diaz as a member of the board
    - Joseph Wender appointed as lead independent director
    - Ionis founder and executive chairman, Stanley T. Crooke M.D., Ph.D. and Breaux B. Castleman retired from the board

## Upcoming 2021 Pipeline Catalysts<sup>(2)</sup>

### Anticipated Key 2021 Data Readouts

Program	Phase	Anticipated Indication	H1	H2
IONIS-PKK-L <sub>Rx</sub>	2	Hereditary angioedema (top-line data)	√	
IONIS-AGT-L <sub>Rx</sub>	2	Hypertension	√	
Tominersen	3	Huntington's disease	√	

IONIS-ENAC-2.5Rx	2	Cystic fibrosis	√	
IONIS-MAPT <sub>Rx</sub>	1/2	Alzheimer's disease		√
Tofersen	3 (VALOR)	SOD1-ALS		•
Vupanorsen	2b	sHTG/CVD risk reduction		•
IONIS-PKK-LRx	2	Hereditary angioedema (full data)		•
IONIS-GHR-LRx	2 + OLE	Acromegaly		•

#### Anticipated Key 2021 Study Initiations

Program	Phase	Anticipated Indication	H1	H2
SPINRAZA	4 (RESPOND)	SMA, suboptimal gene therapy response	√	
Tofersen	3 (ATLAS)	Presymptomatic SOD1-ALS	√	
ION363	3	FUS-ALS	√	
IONIS-AGT-LRx	2b	Resistant hypertension	√	
IONIS-AGT-LRx	2	Heart failure with reduced ejection fraction	√	
ION373	2/3	Alexander disease	√	
ION224	2b	NASH	√	
IONIS-APOCIII-LRx	3	Second TG indication (sHTG)		•
ION582	2	Angelman Syndrome		•

(2) Timing of partnered program catalysts based on partners' most recent publicly available disclosures

#### Second Quarter 2021 Financial Results

##### Revenue

Ionis' revenue was comprised of the following (amounts in millions):

	Three months ended,		Six months ended	
	June 30, 2021	2020	June 30, 2021	2020
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$72	\$72	\$132	\$138
TEGSEDI and WAYLIVRA revenue, net	12	16	31	32
Licensing and royalty revenue	2	2	7	4
Total commercial revenue	86	90	170	174
R&D Revenue:				
Amortization from upfront payments	20	28	40	49
Milestone payments	15	7	20	30
License fees	-	15	-	15
Other services	5	6	7	11
Total R&D revenue	40	56	67	105
Total revenue	\$126	\$146	\$237	\$279

In the second quarter of 2021, the Company successfully completed the transition of its TEGSEDI operations in North America to Sobi. As a result, the Company's commercial revenue from product sales shifted to distribution fees based on net sales generated by Sobi.

The Company's R&D revenue decreased in the second quarter of 2021 compared to the same period last year primarily because the Company earned more milestone payments in the second quarter of 2020 than the same period this year. The Company expects its R&D revenue to increase in the second half of 2021 compared to the first half as its partnered programs advance. Already in the third quarter of 2021, the Company earned a \$25 million milestone payment from Novartis when Novartis achieved 50 percent enrollment in the Phase 3 Lp(a) HORIZON study of pelacarsen.

#### Financial Impacts of Akcea Acquisition and Restructured Commercial Operations

In the second quarter of 2021, the Company incurred \$15 million of costs in conjunction with the Akcea acquisition and restructuring of the Company's commercial operations. The Company excluded these costs from its non-GAAP amounts for the period. Refer to the detailed reconciliation of non-GAAP and GAAP measures that is provided later in this release.

#### Operating Expenses

Ionis' operating expenses for the second quarter of 2021 increased slightly compared to the same period last year driven by an increase in R&D expenses, partially offset by a decrease in SG&A expenses. Ionis' increased R&D expenses were primarily driven by the Company's investments in advancing its late-stage wholly owned pipeline. Ionis' decreased SG&A expenses were primarily from operating efficiencies achieved from integrating Akcea and restructuring the Company's commercial operations.

#### Net Loss Attributable to Ionis Common Stockholders

Ionis' net loss attributable to Ionis' common stockholders for the second quarter of 2021 increased compared to the same period in the prior year for the reasons discussed above. Additionally, the Company recognized an \$8.6 million non-cash loss from the early retirement of a significant portion of its 1 percent senior convertible notes.

## Balance Sheet

Ionis ended June 2021 with cash, cash equivalents and short-term investments of \$2.1 billion, compared to \$1.9 billion at December 31, 2020. In April 2021, Ionis issued \$632.5 million of 0 percent senior convertible notes due in April 2026 and repurchased \$247.9 million of its 1 percent senior convertible notes. The Company's remaining \$62 million of 1 percent senior convertible notes mature in November 2021.

The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

## Webcast

Today, at 11:30 a.m. Eastern Time, Ionis will conduct a live webcast to discuss this earnings release and related activities. Interested parties may access the webcast [here](#). A webcast replay will be available for a limited time at the same address.

## About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been the leader in RNA-targeted therapy, pioneering new markets and changing the standards of care with its novel antisense technology. Ionis currently has three marketed medicines and a premier late-stage pipeline highlighted by industry leading neurological and cardiometabolic franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision of becoming one of the most successful biotechnology companies.

To learn more about Ionis visit [www.ionispharma.com](http://www.ionispharma.com) or follow us on Twitter @ionispharma.

## Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of SPINRAZA (nusinersen), TEGSEDI (inotersen) and WAYLIVRA (volanesorsen) and Ionis' technologies and 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 those related to the impact COVID-19 could have on our business, and including 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, 2020, and the most recent Form 10-Q quarterly filing, which are on file with the SEC. Copies of these and other documents are available from the Company.

In this press release, 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 registered trademark of Akcea Therapeutics, Inc. WAYLIVRA® is a registered trademark of Akcea Therapeutics, Inc. SPINRAZA® is a registered trademark of Biogen.

### IONIS PHARMACEUTICALS, INC. SELECTED FINANCIAL INFORMATION Condensed Consolidated Statements of Operations (In Millions, Except Per Share Data)

	Three months ended, June 30,		Six months ended, June 30,	
	2021	2020	2021	2020
	(as revised*)		(as revised*)	
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	\$72	\$72	\$132	\$138
TEGSEDI and WAYLIVRA revenue, net	12	16	31	32
Licensing and royalty revenue	2	2	7	4
Total commercial revenue	86	90	170	174
Research and development revenue under collaborative agreements	40	56	67	105
Total revenue	126	146	237	279
Expenses:				
Cost of sales	3	3	6	6
Research, development and patent	139	122	279	239
Selling, general and administrative	57	73	117	147
Total operating expenses	199	198	402	392
Loss from operations	(73)	(52)	(165)	(113)
Other income (expense):				
Loss on early retirement of debt	(8)	-	(8)	-
Other income, net	-	17	3	25
Loss before income tax (expense) benefit	(81)	(35)	(170)	(88)

Income tax (expense) benefit	-	(3)	(1)	1
Net loss	(\$81)	(\$38)	(\$171)	(\$87)
Net loss attributable to noncontrolling interest in Akcea Therapeutics, Inc.	-	12	-	22
Net loss attributable to Ionis Pharmaceuticals, Inc. common stockholders	(\$81)	(\$26)	(\$171)	(\$65)
Basic and diluted net loss per share	(\$0.57)	(\$0.18)	(\$1.21)	(\$0.47)
Shares used in computing basic and diluted net loss per share	141	139	141	139

\*The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

**IONIS PHARMACEUTICALS, INC.**  
**Reconciliation of GAAP to Non-GAAP Basis:**

**Condensed Consolidated Operating Expenses, Loss From Operations, and Net Income (Loss)**  
**(In Millions)**

	Three months ended,		Six months ended,	
	June 30, 2021	June 30, 2020	June 30, 2021	June 30, 2020
	(as revised*)		(as revised*)	
	(unaudited)			
<b>As reported research, development and patent expenses according to GAAP</b>	\$139	\$122	\$279	\$239
Excluding compensation expense related to equity awards	(23)	(26)	(49)	(52)
Excluding Akcea acquisition and restructured commercial operation costs	(4)	-	(6)	-
<b>Non-GAAP research, development and patent expenses</b>	<u>\$112</u>	<u>\$96</u>	<u>\$224</u>	<u>\$187</u>
<b>As reported selling, general and administrative expenses according to GAAP</b>	\$57	\$73	\$117	\$147
Excluding compensation expense related to equity awards	(7)	(22)	(19)	(37)
Excluding Akcea acquisition and restructured commercial operation costs	(11)	-	(16)	-
<b>Non-GAAP selling, general and administrative expenses</b>	<u>\$39</u>	<u>\$51</u>	<u>\$82</u>	<u>\$110</u>
<b>As reported operating expenses according to GAAP</b>	\$199	\$198	\$402	\$392
Excluding compensation expense related to equity awards	(30)	(48)	(68)	(89)
Excluding Akcea acquisition and restructured commercial operation costs	(15)	-	(22)	-
<b>Non-GAAP operating expenses</b>	<u>\$154</u>	<u>\$150</u>	<u>\$312</u>	<u>\$303</u>
<b>As reported loss from operations according to GAAP</b>	\$(73)	\$(52)	\$(165)	\$(113)
Excluding compensation expense related to equity awards	(30)	(48)	(68)	(89)
Excluding Akcea acquisition and restructured commercial operation costs	(15)	-	(22)	-
<b>Non-GAAP loss from operations</b>	<u>\$(28)</u>	<u>\$(4)</u>	<u>\$(75)</u>	<u>\$(24)</u>
<b>As reported net loss attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP</b>	\$(81)	\$(26)	\$(171)	(\$65)
Excluding compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	(30)	(45)	(68)	(84)
Excluding Akcea acquisition and restructured commercial operation costs	(15)	-	(22)	-
Income tax effect related to compensation expense related to equity awards attributable to Ionis Pharmaceuticals, Inc. common stockholders	-	4	-	12
<b>Non-GAAP net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders according to GAAP</b>	<u>\$(36)</u>	<u>\$15</u>	<u>\$(81)</u>	<u>\$7</u>

\*The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

### Reconciliation of GAAP to Non-GAAP Basis

As illustrated in the Selected Financial Information in this press release, non-GAAP operating expenses, non-GAAP income (loss) from operations, and non-GAAP net income (loss) attributable to Ionis Pharmaceuticals, Inc. common stockholders were adjusted from GAAP to exclude compensation expense related to equity awards and costs related to the Akcea acquisition and restructured commercial operations and the related tax effects. Compensation expense related to equity awards are non-cash. Costs related to the Akcea acquisition and restructured commercial operations include: severance costs, retention costs and other costs related to commercial operations. Ionis has regularly reported non-GAAP measures for operating results as non-GAAP results. These measures are provided as supplementary information and are not a substitute for financial measures calculated in accordance with GAAP. Ionis reports these non-GAAP results to better enable financial statement users to assess and compare its historical performance and project its future operating results and cash flows. Further, the presentation of Ionis' non-GAAP results is consistent with how Ionis' management internally evaluates the performance of its operations.

### IONIS PHARMACEUTICALS, INC. Condensed Consolidated Balance Sheets (In Millions)

	June 30, December 31,	
	2021	2020
	(as revised*)	
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	\$2,059	\$1,892
Contracts receivable	24	76
Other current assets	155	162
Property, plant and equipment, net	179	181
Other assets	80	79
Total assets	<u>\$2,497</u>	<u>\$2,390</u>
Liabilities and stockholders' equity:		
Other current liabilities	\$130	\$183
Current portion of 1% convertible senior notes, net	62	309
Current portion of deferred contract revenue	102	108
0% convertible senior notes, net	617	-
0.125% convertible senior notes, net	541	540
Long-term obligations, less current portion	82	83
Long-term deferred contract revenue	380	424
Total stockholders' equity	<u>583</u>	<u>743</u>
Total liabilities and stockholders' equity	<u>\$2,497</u>	<u>\$2,390</u>

\*The Company revised its 2020 amounts to reflect the simplified convertible instruments guidance the Company adopted retrospectively on January 1, 2021.

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SOURCE Ionis Pharmaceuticals, Inc.

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