Ionis reports third quarter 2023 financial results

November 2, 2023

Olezarsen Phase 3 data showed significant triglyceride lowering, substantial reductions in acute pancreatitis attacks and favorable safety and tolerability in patients with FCS; on track for regulatory filings in early 2024

Eplontersen marketing applications accepted for review in the EU and Canada; potential U.S. approval in December 2023

On track to achieve 2023 financial guidance

CARLSBAD, Calif., Nov. 2, 2023 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company"), today reported financial results for the third quarter of 2023.

"We continue to successfully execute on our strategy to deliver a steady cadence of potentially transformational medicines to patients," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "Eplontersen is on track for its first potential approval in the U.S. and is under regulatory review in the EU and Canada. We believe the positive efficacy and safety data coupled with an attractive self-administration dosing profile positions eplontersen to be the preferred therapy in the largely underserved hereditary ATTR polyneuropathy population. We reported positive data from the olezarsen Phase 3 Balance study in patients with familial chylomicronemia syndrome, showing statistically significant triglyceride lowering, substantial reductions in acute pancreatitis attacks and favorable safety and tolerability, positioning olezarsen to be our first independent commercial launch. We also made additional progress across our wholly owned and partnered pipeline, and further expanded our rich Phase 3 pipeline with the advance of zilganersen for patients with Alexander disease into Phase 3 development. Looking ahead, we expect to continue our positive momentum with the potential approval and launch of eplontersen and the Phase 3 data readout of donidalorsen in hereditary angioedema."

Third Quarter 2023 Summary Financial Results:

	Three months ended September 30,		Nine months ended September 30,	
	2023	2022	2023	2022
	(amounts in millions)			
Total revenue	$144	$160	$463	$435
Operating expenses	$287	$219	$811	$637
Operating expenses on a non-GAAP basis	$261	$195	$732	$562
Loss from operations	($143)	($59)	($348)	($202)
Loss from operations on a non-GAAP basis	($117)	($35)	($269)	($127)

Financial Highlights

- Revenue continued to be substantial and sustained, with revenues of $144 million and $463 million in the three and nine months ended September 30, 2023, reflecting a 10% decrease and 6% increase compared to the same periods last year, respectively, driven by the timing of certain partner payments
- Operating expenses increased in the three and nine months ended September 30, 2023 compared to the same periods last year, primarily due to strategic investments to bring eplontersen, olezarsen and donidalorsen to patients
- Cash and short-term investments of $2.2 billion as of September 30, 2023 enables continued investments to drive increasing value
- Reaffirmed 2023 financial guidance

Near-Term Commercial Opportunities and Late-Stage Pipeline Highlights

- Achieved multiple milestones with eplontersen:
  - Eplontersen is under regulatory review by the European Medicines Agency (EMA) and Health Canada for the treatment of hereditary ATTR polyneuropathy (ATTRv-PN)
  - The EMA granted orphan drug designation to eplontersen for the treatment of ATTR in the EU
  - Published positive data from the Phase 3 NEURO-TTRansform study in patients with ATTRv-PN in the *Journal of the American Medical Association (JAMA)* showing eplontersen halted measures of disease progression and continuously improved quality of life at 35-, 66- and 85-weeks
  - Presented positive new data showing continued benefit in secondary endpoints from the Phase 3 NEURO-TTRansform study in patients with ATTRv-PN at the European ATTR Amyloidosis (EU-ATTR) meeting
  - Presented positive exploratory data from a pre-defined cardiac sub-population of patients in NEURO-TTRansform showing improvement in cardiac function and structure compared to external placebo at the Heart Failure Society of America (HFSA) Annual Scientific Meeting
  - Completed enrollment of the Phase 3 CARDIO-TTRansform study of eplontersen in patients with ATTR cardiomyopathy (ATTR-CM), the largest study ever conducted in ATTR-CM; on track for data readout as early as H1:2025
- Reported positive data from the Phase 3 Balance study of olezarsen in patients with familial chylomicronemia syndrome

(FCS)
    - Olezarsen demonstrated robust, dose-dependent reductions in APOCIII, statistically significant reductions in triglycerides, substantial reductions in acute pancreatitis attacks and a favorable safety and tolerability profile
    - On track to file for regulatory approval in the U.S. and EU in early 2024
- The FDA granted orphan drug designation to donidalorsen for the treatment of patients with hereditary angioedema (HAE); on track for data readout in the Phase 3 OASIS-HAE study in H1:2024
- Advanced zilganersen (GFAP) into Phase 3 development for the treatment of patients with Alexander disease
- The FDA granted orphan drug designation to ulefnersen (FUS) for the treatment of patients with FUS-ALS

Partnered Program Highlights

- GSK reported positive data from the Phase 2b B-Together study of bepirovirsen followed by pegylated interferon in patients with chronic hepatitis B virus (HBV)
- Reported positive interim data from the ongoing Phase 2 study of IONIS-FB-L_{Rx} in patients with immunoglobulin A nephropathy (IgAN)
- Biogen reported positive data from the Phase 1/2 study of IONIS-$MAPT_{Rx}$ (BIIB080) in patients with Alzheimer's disease
- Completed enrollment in the Phase 1/2 HALOS study of ION582 (BIIB121) in patients with Angelman syndrome
- Entered a new agreement with Roche to advance two novel RNA-targeted programs for Alzheimer's disease and Huntington's disease

Third Quarter 2023 Financial Results

"Our year-to-date financial results keep us on track to achieve our 2023 guidance as we execute on a strategy to unlock next-level value," said Elizabeth L. Hougen, chief financial officer of Ionis. "Our strong financial foundation includes more than $2B in cash, significant royalty revenue with SPINRAZA, and substantial and sustained R&D revenue from multiple partners. We are well positioned to continue investing in our key priorities to drive future positive cash flow, including advancing our go-to-market activities, growing our wholly owned pipeline and optimizing new cutting-edge technologies for future medicines. We look forward to the potential U.S. eplontersen ATTRv-PN approval next month followed closely by launch. Together with our partner, AstraZeneca, we believe we are well positioned to identify new patients to further grow the market and become the treatment of choice for this population that remains largely underserved by current therapies."

Revenue

Ionis' revenue was comprised of the following:

	Three months ended September 30,		Nine months ended September 30,	
	2023	2022	2023	2022
Revenue:	(amounts in millions)			
Commercial revenue:				
SPINRAZA royalties	$67	$62	$179	$175
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	8	6	25	23
Licensing and royalty revenue	9	5	26	25
Total commercial revenue	84	73	230	223
Research and development revenue:				
Amortization from upfront payments	18	18	47	54
Milestone payments	16	15	90	60
License fees	5	35	25	37
Other services	5	1	11	6
Collaborative agreement revenue	44	69	173	157
Eplontersen joint development revenue	16	18	60	55
Total research and development revenue	60	87	233	212
Total revenue	$144	$160	$463	$435

Commercial revenue for the three and nine months ended September 30, 2023 included $67 million and $179 million from SPINRAZA royalties, respectively, which were essentially flat compared to the same periods last year reflecting SPINRAZA's resilience against emerging competition. Ionis' commercial revenue in the three and nine months ended September 30, 2023 also included royalties from the U.S. launch of QALSODY.

R&D revenue decreased for the three months ended September 30, 2023 and increased for the nine months ended September 30, 2023 compared to the same periods last year due to the timing of certain partner payments, including the $35 million license fee for IONIS-FB-L_{Rx} that Ionis earned from Roche in the three months ended September 30, 2022.

Operating Expenses

Ionis' operating expenses increased in the three and nine months ended September 30, 2023 compared to the same periods in 2022, consistent with expectations. As Ionis advanced its robust pipeline, study costs increased compared to the same periods in 2022 as most of the Company's Phase 3 studies are either fully enrolled or approaching full enrollment, resulting in higher R&D expenses year over year. Ionis' SG&A expenses also increased

year over year primarily due to launch preparation activities for eplontersen, olezarsen and donidalorsen.

Balance Sheet

As of September 30, 2023, Ionis' cash, cash equivalents and short-term investments increased to $2.2 billion compared to $2.0 billion at December 31, 2022 primarily due to the $500 million Ionis received from Royalty Pharma in January 2023. Ionis' working capital also increased over the same period primarily due to the Company's higher cash and short-term investments balance. In the first quarter of 2023, the Company recorded a long-term liability for future royalties due to Royalty Pharma. In June 2023, Ionis issued $575 million of senior convertible notes due in June 2028 with an interest rate of 1.75%. The Company used the majority of the proceeds to repurchase $504 million of its 0.125% convertible notes.

Webcast

Management will host a conference call and webcast to discuss Ionis' third quarter 2023 results at 11:30 a.m. Eastern time on Thursday, November 2, 2023. Interested parties may access the webcast here. A webcast replay will be available for a limited time at the same address. To access the Company's third quarter 2023 earnings slides click here.

About Ionis Pharmaceuticals, Inc.

For more than 30 years, Ionis has been a leader in RNA-targeted therapy, pioneering new markets and changing standards of care. Ionis currently has four marketed medicines and a promising late-stage pipeline highlighted by cardiovascular and neurological franchises. Our scientific innovation began and continues with the knowledge that sick people depend on us, which fuels our vision to become the leader in genetic medicine, utilizing a multi-platform approach to discover, develop and deliver life-transforming therapies.

To learn more about Ionis visit 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 QALSODY (tofersen), SPINRAZA (nusinersen), TEGSEDI (inotersen), WAYLIVRA (volanesorsen), eplontersen, olezarsen, donidalorsen, zilganersen, ulefnersen, pelacarsen, bepirovirsen, IONIS-FB-L_{Rx}, Ionis' technologies and Ionis' other 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 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, 2022, and most recent Form 10-Q, which are on file with the Securities and Exchange Commission. 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" all refer to Ionis Pharmaceuticals and its subsidiaries.

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

	Three months ended September 30,		Nine months ended September 30,	
	2023	2022	2023	2022
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$67	$62	$179	$175
Other commercial revenue	17	11	51	48
Total commercial revenue	84	73	230	223
Research and development revenue:				
Collaborative agreement revenue	44	69	173	157
Eplontersen joint development revenue	16	18	60	55
Total research and development revenue	60	87	233	212
Total revenue	144	160	463	435
Expenses:				
Cost of sales	2	2	6	10
Research, development and patent	215	183	643	525

Selling, general and administrative	70	34	162	102
Total operating expenses	287	219	811	637
Loss from operations	(143)	(59)	(348)	(202)
Other income (expense):				
Interest expense related to the sale of future royalties:	(18)	-	(51)	-
Other income (expense), net	20	12	68	(12)
Loss before income tax expense	(141)	(47)	(331)	(214)
Income tax expense	(6)	-	(26)	(3)
Net loss	($147)	($47)	($357)	($217)
Basic and diluted net loss per share	($1.03)	($0.33)	($2.50)	($1.53)
Shares used in computing basic and diluted net loss per share	143	142	143	142

IONIS PHARMACEUTICALS, INC.
Reconciliation of GAAP to Non-GAAP Basis:
Condensed Consolidated Operating Expenses, Loss From Operations, and Net Loss
(In Millions)

	Three months ended September 30,		Nine months ended September 30,	
	2023	2022	2023	2022
	(unaudited)			
As reported research, development and patent expenses according to GAAP	$215	$183	$643	$525
Excluding compensation expense related to equity awards	(19)	(18)	(58)	(55)
Non-GAAP research, development and patent expenses	$196	$165	$585	$470
As reported selling, general and administrative expenses according to GAAP	$70	$34	$162	$102
Excluding compensation expense related to equity awards	(7)	(6)	(22)	(19)
Non-GAAP selling, general and administrative expenses	$63	$28	$140	$83
As reported operating expenses according to GAAP	$287	$219	$811	$637
Excluding compensation expense related to equity awards	(26)	(24)	(79)	(75)
Non-GAAP operating expenses	$261	$195	$732	$562
As reported loss from operations according to GAAP	($143)	($59)	($348)	($202)
Excluding compensation expense related to equity awards	(26)	(24)	(79)	(75)
Non-GAAP loss from operations	($117)	($35)	($269)	($127)
As reported net loss according to GAAP	($147)	($47)	($357)	($217)
Excluding compensation expense related to equity awards and related tax effects	(26)	(24)	(79)	(75)
Non-GAAP net loss	($121)	($23)	($278)	($142)

Reconciliation of GAAP to Non-GAAP Basis

As illustrated in the Selected Financial Information in this press release, non-GAAP operating expenses, non-GAAP loss from operations, and non-GAAP net loss were adjusted from GAAP to exclude compensation expense related to equity awards and the related tax effects. Compensation expense related to equity awards are non-cash. 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)

September 30, December 31,

	2023	2022
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$2,236	$1,987
Contracts receivable	142	26
Other current assets	207	190
Property, plant and equipment, net	71	74
Right-of-use assets	174	182
Other assets	104	75
Total assets	2,934	$2,534
Liabilities and stockholders' equity:		
Other current liabilities	$199	$221
Current portion of deferred contract revenue	205	91
1.75% convertible senior notes, net	562	-
0% convertible senior notes, net	625	622
0.125% convertible senior notes, net	44	545
Liability related to sale of future royalties, net	513	-
Long-term lease liabilities	173	178
Long-term obligations, less current portion	49	16
Long-term deferred contract revenue	249	288
Total stockholders' equity	315	573
Total liabilities and stockholders' equity	$2,934	$2,534

Key 2023 Value Driving Events(1)

Regulatory Actions			
Program	**Indication**	**Regulatory Action**	**Achieved**
QALSODY	SOD1-ALS	NDA approval	•
		EU approval[2]	
Eplontersen (TTR)	ATTRv-PN	NDA approval	
		OUS filings	•

Key Clinical Data Events			
Program	**Indication**	**Event**	**Achieved**
Eplontersen (TTR)	ATTRv-PN	Phase 3 data (week 35, 66 & 85)	•
Olezarsen (APOCIII)	FCS	Phase 3 data	•
Donidalorsen (PKK)	HAE	Phase 2, OLE 1-year data	•
Donidalorsen (PKK)	HAE	Phase 2, OLE 2-year data	•
Bepirovirsen	HBV	Phase 2b B-Together data	•
IONIS-FB-L_{Rx}	IgAN	Phase 2 interim data	•

Enrollment Achievements			
Program	**Indication**	**Event**	**Achieved**
Eplontersen (TTR)	ATTR-CM	Phase 3 full enrollment	•
Donidalorsen (PKK)	HAE	Phase 3 full enrollment	•
IONIS-FB-L_{Rx}	GA	Phase 2 full enrollment	•
ION582 (UBE3A)	Angelman syndrome	Phase 1/2 full enrollment	•

Phase 3 Initiations		
Program	**Indication**	**Achieved**
Zilganersen (GFAP)	Alexander disease	•
Bepirovirsen	HBV	•
IONIS-FB-L_{Rx}	IgAN	•

(1) Timing expectations based on current assumptions and subject to change.
(2) CHMP opinion anticipated in Q4:2023.

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SOURCE Ionis Pharmaceuticals, Inc.

Ionis Investor Contact: D. Wade Walke, Ph.D., info@ionisph.com 760-603-2331; Ionis Media Contact: David Polk, J.D., ionis_ca@ionisph.com 760-603-4679