Ionis reports second quarter 2024 financial results

August 1, 2024

WAINUA™ U.S. launch progressing well; approved in Canada; EU approval decision expected this year

Olezarsen PDUFA December 19, 2024 for FCS

Positive Phase 3 donidalorsen data for HAE; preparing U.S. and EU regulatory submissions

On track to achieve 2024 financial guidance

CARLSBAD, Calif., Aug. 1, 2024 /PRNewswire/ -- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company"), today reported financial results for the second quarter of 2024.

"Over the first half of this year, we continued to deliver on our goal to bring a steady cadence of medicines to people with serious diseases. The WAINUA launch for hereditary ATTR polyneuropathy (ATTRv-PN) continues to progress well with AstraZeneca. QALSODY is now approved in the EU, expanding the number of patients who can benefit from the first approved treatment for a genetic form of ALS. And we are well positioned for our first independent launch with olezarsen, which was accepted for Priority Review with a December FDA action date for people with familial chylomicronemia syndrome (FCS), a serious and rare disease with no approved treatments in the U.S. Additionally, we completed enrollment in our Phase 3 olezarsen program for the much larger severe hypertriglyceridemia (sHTG) patient population, keeping us on track for data in the second half of next year. And based on recent positive Phase 3 results, we believe donidalorsen, our second planned independent U.S. launch, is positioned to be a preferred choice for people with hereditary angioedema (HAE)," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "We also advanced our next wave of potentially transformational medicines, including announcing plans to independently advance ION582 into a Phase 3 study next year, based on positive data in Angelman syndrome; this program is poised to become the cornerstone of our robust wholly owned neurology pipeline. Our recent achievements, together with multiple upcoming catalysts, position Ionis to deliver next-level value for all stakeholders."

Second Quarter 2024 Summary Financial Results[(1)]:

	Three months ended June 30,		Six months ended June 30,	
	2024	2023	2024	2023
	(amounts in millions)			
Total revenue	$225	$188	$345	$319
Operating expenses	$291	$279	$560	$523
Operating expenses on a non-GAAP basis	$260	$252	$498	$469
Loss from operations	($66)	($91)	($215)	($204)
Loss from operations on a non-GAAP basis	($35)	($64)	($153)	($150)

(1) Reconciliation of GAAP to non-GAAP basis contained later in this release.

Financial Highlights

- Revenue increased for the second quarter and first half of 2024 by 20% and 8% compared to the same periods last year, respectively, primarily driven by an increase in R&D revenue reflecting the value Ionis' pipeline and technology continues to generate
- Operating expenses increased in the second quarter and first half of 2024 compared to the same periods last year, reflecting continued strategic investments in late-stage development, including WAINUA for ATTR cardiomyopathy and olezarsen for sHTG, and commercialization efforts for WAINUA, olezarsen and donidalorsen
- Reaffirmed 2024 financial guidance

Recent Marketed Medicines Highlights

- WAINUA for the treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTRv-PN) generated sales of $16 million and $21 million resulting in royalty revenue of $4 million and $5 million in the second quarter and first half of 2024, respectively

- WAINUA for the treatment of adults with ATTRv-PN approved in Canada
- SPINRAZA for the treatment of spinal muscular atrophy (SMA) generated global sales of $429 million and $770 million resulting in royalty revenue of $57 million and $95 million in the second quarter and first half of 2024, respectively
- QALSODY for the treatment of SOD1-ALS granted marketing approval in the EU

Recent Late-Stage Pipeline Highlights

- Olezarsen achieved multiple clinical and regulatory milestones that support pursuit of two patient populations with urgent unmet need, familial chylomicronemia syndrome (FCS) and severe hypertriglyceridemia (sHTG):
    - FDA accepted the NDA for patients with FCS for Priority Review with a PDUFA date of December 19, 2024
    - Presented positive Phase 3 Balance study data in patients with FCS with a simultaneous publication in the *New England Journal of Medicine*
    - Opened Expanded Access Program (EAP) for FCS in the U.S.
    - Completed enrollment for all Phase 3 sHTG studies: CORE pivotal study, CORE2 confirmatory pivotal study and ESSENCE supportive exposure study; on track for data across all three studies in H2:2025
    - Presented positive Phase 2b Bridge study data in patients with HTG and sHTG with a simultaneous publication in the *New England Journal of Medicine*
- Donidalorsen achieved multiple clinical milestones positioning it to become the first RNA-targeted prophylactic treatment for people with hereditary angioedema (HAE):
    - Preparing to submit NDA
    - Otsuka preparing to submit MAA; expanded Otsuka EU commercial licensing agreement to include Asia Pacific
    - Presented positive Phase 3 OASIS-HAE study data in patients treated every four weeks or every eight weeks with a simultaneous publication in the *New England Journal of Medicine*
    - Presented positive Phase 3 OASISplus open-label extension study data in patients treated every four weeks or every eight weeks
    - Presented positive Phase 3 OASISplus switch study data in patients previously treated with other prophylactic therapies
- Zilganersen (GFAP) Phase 3 study for the treatment of patients with Alexander disease fully enrolled; on track for data in 2025
- Bepirovirsen Phase 3 studies for the treatment of patients with chronic hepatitis B (CHB) fully enrolled; on track for data in 2026

Recent Other Pipeline Updates

- Presented positive Phase 2 data for ION582 (UBE3A), our wholly owned medicine, in patients with Angelman syndrome; preparing for meetings with global regulators ahead of planned Phase 3 study start in H1:2025
- Presented positive Phase 2 data for ION224 (DGAT2) in patients with metabolic dysfunction-associated steatohepatitis (MASH)
- Initiated the Phase 1/2 Orbit study of ION356 (PLP1) in patients with Pelizaeus-Merzbacher disease (PMD)
- Discontinued development of IONIS-FB-L_{Rx} for geographic atrophy (GA) and ION541 for amyotrophic lateral sclerosis (ALS) following completion of Phase 2 studies showing favorable safety profiles and good target engagement, but insufficient efficacy to advance into Phase 3 development

Second Quarter 2024 Financial Results

"Ionis is at a critical inflection point. We have achieved important development and regulatory milestones for WAINUA, olezarsen and donidalorsen, all of which have significant potential to help patients in need. In parallel, we continue to advance our next wave of potentially transformational medicines," said Elizabeth L. Hougen, chief financial officer of Ionis. "To drive next-level of value creation for all stakeholders, we remain focused on strategically investing our capital to fully unlock the potential of our promising near-and longer-term portfolio. Our investments are focused on go-to-market preparations for our upcoming planned olezarsen and donidalorsen launches. And with our increased confidence in the potential of WAINUA and olezarsen to address broader patient populations, we are planning additional investments to scale our capabilities in line with the significant potential that these important medicines represent. Additionally, we are investing in our next wave of medicines, including pre-commercialization activities and Phase 3 development for ION582 for Angelman syndrome, which we plan to start in the first half of next year. We expect our investments today and in the years ahead will position Ionis for sustainable growth for years to come."

Revenue

Ionis' revenue was comprised of the following:

	Three months ended June 30,		Six months ended June 30,	
	2024	2023	2024	2023
Revenue:	(amounts in millions)			
Commercial revenue:				
SPINRAZA royalties	$57	$61	$95	$111

WAINUA royalties	4	-	5	-
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	8	11	17	17
Licensing and other royalty revenue	3	6	15	18
Total commercial revenue	72	78	132	146
Research and development revenue:				
Amortization from upfront payments	35	15	77	29
Milestone payments	53	51	60	74
License fees	38	20	38	20
Other services	15	4	16	6
Collaborative agreement revenue	141	90	191	129
WAINUA joint development revenue	12	20	22	44
Total research and development revenue	153	110	213	173
Total revenue	$225	$188	$345	$319

Commercial revenue in the second quarter and first half of 2024 included a new source of royalty revenue with the launch of WAINUA in the U.S. in late January 2024. Ionis' commercial revenue in the second quarter and first half of 2024 also included royalties from the net sales of QALSODY, which Biogen launched in the U.S. in the second quarter of 2023 and in the EU in the second quarter of 2024.

R&D revenue in the second quarter and first half of 2024 increased compared to the same periods last year primarily due to the amortization of upfront payments from the new collaborations with Roche and Novartis that Ionis entered into during the second half of last year. In addition, license fees increased year over year as a result of new collaborations Ionis entered into during the second quarter of 2024, including the expanded donidalorsen licensing agreement with Otsuka, which now includes the Asia-Pacific region in addition to Europe. These increases were partially offset by the decrease in WAINUA joint development revenue, which decreased as development activities relating to ATTRv-PN wound down with the launch of WAINUA for this indication.

Operating Expenses

Ionis' operating expenses increased in the second quarter and first half of 2024 compared to the same periods in 2023, consistent with expectations. SG&A expenses increased year over year primarily due to the launch of WAINUA in the U.S. and launch preparation activities for olezarsen and donidalorsen, including establishing the field team for olezarsen. R&D expenses decreased in the second quarter and were essentially flat in the first half of 2024 compared to the same periods last year as several late-stage studies have ended.

Balance Sheet

As of June 30, 2024, Ionis' cash, cash equivalents and short-term investments decreased to $2.1 billion compared to $2.3 billion at December 31, 2023. The Company plans to continue deploying its capital resources toward growth opportunities, and as previously guided, projects to end 2024 with $1.7 billion in cash, cash equivalents and short-term investments. Ionis' working capital also decreased over the same period primarily due to the Company's lower cash and short-term investments balance. We expect to make increased strategic investments in the years ahead, with a focus on late-stage programs, wholly owned assets, and our next wave of innovative medicines.

Webcast

Management will host a conference call and webcast to discuss Ionis' second quarter 2024 results at 11:30 a.m. Eastern time on Thursday, August 1, 2024. 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 second quarter 2024 earnings slides click here.

For more information about SPINRAZA and QALSODY, visit https://www.spinraza.com/ and https://www.qalsody.com/, respectively. QALSODY is approved under accelerated approval based on reduction in plasma neurofilament light chain (NfL) observed in patients treated with QALSODY. Continued approval may be contingent upon verification of clinical benefit in confirmatory trial(s).

INDICATION for WAINUA™ (eplontersen)
WAINUA injection, for subcutaneous use, 45 mg is indicated for the treatment of the polyneuropathy of hereditary transthyretin-mediated amyloidosis in adults.

IMPORTANT SAFETY INFORMATION for WAINUA™(eplontersen)

WARNINGS AND PRECAUTIONS
Reduced Serum Vitamin A Levels and Recommended Supplementation WAINUA leads to a decrease in serum vitamin A levels. Supplement with recommended daily allowance of vitamin A. Refer patient to an ophthalmologist if ocular symptoms suggestive of vitamin A deficiency occur.

ADVERSE REACTIONS
Most common adverse reactions (≥9% in WAINUA-treated patients) were vitamin A decreased (15%) and vomiting (9%).

Please see link to U.S. Full Prescribing Information for WAINUA.

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has five marketed medicines and a leading pipeline in neurology, cardiology, and other areas of high patient need. As the pioneer in RNA-targeted medicines, Ionis continues to drive innovation in RNA therapies in addition to advancing new approaches in gene editing. A deep understanding of disease biology and industry-

leading technology propels our work, coupled with a passion and urgency to deliver life-changing advances for patients. To learn more about Ionis, visit Ionis.com and follow us on X (Twitter) and LinkedIn.

Ionis' Forward-looking Statement

This press release includes forward-looking statements regarding Ionis' business, financial guidance and the therapeutic and commercial potential of our commercial medicines, additional medicines in development and technologies. 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. Except as required by law, we undertake no obligation to update any forward-looking statements for any reason. 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, 2023, 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.

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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,	
	2024	2023	2024	2023
	(unaudited)			
Revenue:				
Commercial revenue:				
SPINRAZA royalties	$57	$61	$95	$111
WAINUA royalties	4	-	5	-
Other commercial revenue	11	17	32	35
Total commercial revenue	72	78	132	146
Research and development revenue:				
Collaborative agreement revenue	141	90	191	129
WAINUA joint development revenue	12	20	22	44
Total research and development revenue	153	110	213	173
Total revenue	225	188	345	319
Expenses:				
Cost of sales	4	3	6	4
Research, development and patent	222	230	436	428
Selling, general and administrative	65	46	118	91
Total operating expenses	291	279	560	523
Loss from operations	(66)	(91)	(215)	(204)
Other income (expense):				
Interest expense related to the sale of future royalties	(18)	(18)	(36)	(33)
Other income, net	18	32	42	47
Loss before income tax expense	(66)	(77)	(209)	(190)

Income tax expense	-	(8)	-	(20)
Net loss	($66)	($85)	($209)	($210)
Basic and diluted net loss per share	($0.45)	($0.60)	($1.43)	($1.47)
Shares used in computing basic and diluted net loss per share	146	143	146	143

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 June 30,		Six months ended June 30,	
	2024	2023	2024	2023
	(unaudited)			
As reported research, development and patent expenses according to GAAP	$222	$230	$436	$428
Excluding compensation expense related to equity awards	(23)	(19)	(45)	(39)
Non-GAAP research, development and patent expenses	$199	$211	$391	$389
As reported selling, general and administrative expenses according to GAAP	$65	$46	$118	$91
Excluding compensation expense related to equity awards	(8)	(7)	(17)	(14)
Non-GAAP selling, general and administrative expenses	$57	$39	$101	$77
As reported operating expenses according to GAAP	$291	$279	$560	$523
Excluding compensation expense related to equity awards	(31)	(27)	(62)	(54)
Non-GAAP operating expenses	$260	$252	$498	$469
As reported loss from operations according to GAAP	($66)	($91)	($215)	($204)
Excluding compensation expense related to equity awards	(31)	(27)	(62)	(54)
Non-GAAP loss from operations	($35)	($64)	($153)	($150)
As reported net loss according to GAAP	($66)	($85)	($209)	($210)
Excluding compensation expense related to equity awards and related tax effects	(31)	(27)	(62)	(54)
Non-GAAP net loss	($35)	($58)	($147)	($156)

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)

	June 30, 2024	December 31, 2023
	(unaudited)	
Assets:		

Cash, cash equivalents and short-term investments	$2,079	$2,331
Contracts receivable	27	98
Other current assets	223	213
Property, plant and equipment, net	76	71
Right-of-use assets	167	172
Other assets	119	105
Total assets	$2,691	$2,990
Liabilities and stockholders' equity:		
Current portion of deferred contract revenue	$94	$151
0.125% convertible senior notes, net – short-term	44	44
Other current liabilities	168	253
1.75% convertible senior notes, net	564	562
0% convertible senior notes, net	627	625
Liability related to sale of future royalties, net	534	514
Long-term lease liabilities	166	171
Long-term obligations, less current portion	41	42
Long-term deferred contract revenue	189	241
Total stockholders' equity	264	387
Total liabilities and stockholders' equity	$2,691	$2,990

Key 2024 Value Driving Events(1)

New Product Launches		
Program	**Indication**	**Achieved**
WAINUA	ATTRv-PN	•
Olezarsen	FCS	
QALSODY (EU)	SOD1-ALS	•

Regulatory Actions			
Program	**Indication**	**Regulatory Action**	**Achieved**
Eplontersen	ATTRv-PN	Additional OUS filings	•
		EMA approval decision	
		Additional OUS approval decision(s)	•
Olezarsen	FCS	NDA filing	•
		FDA approval decision	
		EU filing	
		Canada filing	
Donidalorsen	HAE	NDA filing	
QALSODY	SOD1-ALS	EMA approval decision	•

Key Phase 3 Clinical Data Events			
Program	**Indication**	**Event**	**Achieved**
Olezarsen	FCS	Balance study full data	•
Donidalorsen	HAE	OASIS-HAE topline data	•
Donidalorsen	HAE	OASIS-HAE full data	•
Donidalorsen	HAE	OASIS-Plus: OLE + Switch data	•
SPINRAZA	SMA	DEVOTE study data (high dose)	

Key Phase 2 Clinical Data Events			
Program	**Indication**	**Event**	**Achieved**
Donidalorsen	HAE	3-year Phase 2 OLE data	
IONIS-FB-L_{Rx}	IgAN	Phase 2 data	
IONIS-FB-L_{Rx}	GA	GOLDEN study data	--
ION224 (DGAT2)	NASH	Phase 2 data	•

ION582 (UBE3A)	Angelman syndrome	HALOS study data	•
ION541 (ATXN2)	ALS	ALSpire study data	--

(1) Timing expectations based on current assumptions and subject to change.

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