Ionis reports second quarter 2025 financial results and highlights progress on key programs

July 30, 2025

- TRYNGOLZA™ delivers $19 million in net product sales in the second quarter 2025 -

- Donidalorsen approval in hereditary angioedema (HAE) anticipated next month; Ionis' second independent launch -

- Phase 3 data from the pivotal CORE and CORE2 studies in severe hypertriglyceridemia (sHTG) expected in September 2025 -

- Increasing 2025 financial guidance based on strong performance and improved outlook -

CARLSBAD, Calif.--(BUSINESS WIRE)--Jul. 30, 2025-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the "Company") today reported financial results and provided key updates for the second quarter ended June 30, 2025.

"During the second quarter, we continued to build momentum across our business," said Brett P. Monia, Ph.D., chief executive officer of Ionis. "Our strong performance included excellent commercial execution, resulting in a substantial increase in TRYNGOLZA revenues, our first independently launched medicine. We expect additional advancements in the second half, including Ionis' second independent launch with donidalorsen for hereditary angioedema, anticipated next month, and important Phase 3 results for olezarsen in severe hypertriglyceridemia and zilganersen in Alexander disease. We believe these four programs collectively represent multi-billion-dollar revenue potential and a transformational opportunity for Ionis and for patients."

Second Quarter 2025 Summary Financial Results(1):

	Three months ended June 30,		Six months ended June 30,	
	2025	2024	2025	2024
	(amounts in millions)			
Total revenue	$452	$225	$584	$345
Operating expenses	$312	$291	$591	$560
Operating expenses on a non-GAAP basis	$282	$260	$532	$498
Income (loss) from operations	$140	($66)	($7)	($215)
Income (loss) from operations on a non-GAAP basis	$170	($35)	$52	($153)

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

Recent Financial Highlights

- Revenue doubled in the second quarter of 2025 and increased nearly 70% in the first half compared to the same period last year, driven by the continued successful launch of TRYNGOLZA and increased royalty and R&D revenues
- Operating expenses increased by single digits in the second quarter and first half of 2025, compared to the same periods last year, primarily due to investments related to commercialization efforts for TRYNGOLZA, donidalorsen and WAINUA
- Increased 2025 financial guidance reflects an improved outlook for the full year, strong overall revenue performance experienced year-to-date, including the early strength in TRYNGOLZA revenues:

Full Year 2025 Guidance	Previous Guidance	New Guidance
Total Revenue	$725-750 million	$825-850 million
TRYNGOLZA product sales, net	Not provided	$75-80 million
Operating loss on a non-GAAP basis	<$375 million	$300-325 million
Cash, cash equivalents and short-term investments	~$1.9 billion	~$2.0 billion

Second Quarter 2025 Financial Results

"For the second time this year, we are significantly raising our 2025 financial guidance — this time driven by an improved outlook

for the year and strong revenue performance to date, which includes the early launch excellence with TRYNGOLZA. In addition to strong commercial performance, our second quarter results included the substantial revenue we earned from licensing sapablursen, a medicine outside our core areas of focus. We are in a strong financial position, with a commitment to drive operating leverage as we continue executing on our strategic priorities," said Elizabeth L. Hougen, chief financial officer, Ionis. "Moving forward, the three additional independent launches anticipated over the next eighteen months, including donidalorsen for hereditary angioedema, olezarsen in severe hypertriglyceridemia and zilganersen in Alexander disease, position Ionis to deliver substantial and growing product revenue. This product revenue, coupled with anticipated increasing royalty revenue from multiple partner launches, along with disciplined investment, position Ionis to achieve sustained growth and positive cash flow in the next few years."

Recent Highlights - Wholly Owned Medicines

- TRYNGOLZA™ (olezarsen), the first and only FDA approved treatment for adults living with familial chylomicronemia syndrome (FCS) as an adjunct to diet
  - Generated net product sales of $19 million in the second quarter of 2025, its second full quarter on the market, and $26 million in the first half of 2025
  - Received a positive opinion from the Committee for Medicinal Products for Human Use (CHMP), paving the way to bring TRYNGOLZA to patients across Europe
- Olezarsen on track for topline Phase 3 data from pivotal CORE and CORE2 studies in patients with sHTG in September 2025, positioning olezarsen to potentially treat this second, more prevalent patient population with high unmet need
  - Announced positive topline results from the Essence study in people with moderately elevated triglycerides; achieved primary and all key secondary endpoints for 80 mg and 50 mg monthly doses with favorable safety and tolerability
- Donidalorsen on track to launch this year, assuming approval, with a U.S. PDUFA date of August 21, 2025
  - Poised to transform the treatment paradigm for individuals with hereditary angioedema (HAE) as the first and only RNA-targeted prophylactic therapy that has the potential to offer durable efficacy, a favorable safety and tolerability profile, and the longest available dosing interval, with self-administration via autoinjector monthly or every other month
  - Donidalorsen is currently under regulatory review in the EU
- First patient dosed in the Phase 3 REVEAL study of ION582, an investigational medicine for the treatment of people living with Angelman syndrome (AS), a serious and rare neurodevelopmental disorder

Recent Highlights – Partnered Medicines

- WAINUA™ (eplontersen) (WAINZUA in EU) for the treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTRv-PN) continues to perform well, achieving several important commercial milestones:
  - Generated sales of $44 million and $84 million resulting in royalty revenue of $10 million and $20 million in the second quarter and first half of 2025, respectively
  - New launches underway in numerous regions, including the EU; additional submissions in progress to expand WAINUA access globally
- SPINRAZA® (nusinersen) for the treatment of spinal muscular atrophy (SMA) generated global sales of $393 million and $817 million resulting in royalty revenue of $54 million and $102 million in the second quarter and first half of 2025, respectively
  - Higher dose nusinersen under review for marketing approval in the U.S. (PDUFA date of September 22, 2025) and in the EU
- Biogen to advance salanersen (formerly ION306/BIIB115), an investigational medicine for SMA into registrational studies based on positive interim Phase 1 results; developed using novel Ionis antisense chemistry with the potential to achieve high efficacy and annual dosing
  - Phase 1 data with salanersen in SMA patients showed substantial slowing of neurodegeneration and clinically meaningful improvements in patients previously treated with gene therapy
- AstraZeneca initiated the Phase 2b study of opemalirsen (formerly ION532/AZD2373), an investigational medicine designed to reduce the production of apolipoprotein L1 (APOL1) for the treatment of APOL1-mediated kidney disease (AMKD) triggering a $30 million milestone payment to Ionis

Corporate Updates

- In June 2025, Ionis announced that Richard Geary, Ph.D., executive vice president and chief development officer, will retire effective January 2026 and that Holly Kordasiewicz, Ph.D., currently senior vice president, neurology, will succeed him in the role

Revenue

Ionis' revenue was comprised of the following:

	Three months ended June 30,	Six months ended June 30,

	2025	2024	2025	2024
Revenue:		(amounts in millions)		
Commercial revenue:				
Product sales, net:				
TRYNGOLZA sales, net	$19	$-	$26	$-
Total product sales, net	19	-	26	-
Royalty revenue:				
SPINRAZA royalties	54	57	102	95
WAINUA royalties	10	4	20	5
Other royalties	6	3	12	13
Total royalty revenue	70	64	134	113
Other commercial revenue:				
TEGSEDI and WAYLIVRA revenue, net	14	8	19	17
Other revenue	-	-	-	2
Total commercial revenue	**103**	**72**	**179**	**132**
Research and development revenue:				
Collaborative agreement revenue	337	141	382	191
WAINUA joint development revenue	12	12	23	22
Total research and development revenue	**349**	**153**	**405**	**213**
Total revenue	**$452**	**$225**	**$584**	**$345**

Commercial revenue for the second quarter and first half of 2025 increased 43% and 36% respectively, compared to the same periods in 2024. This increase was driven by TRYNGOLZA product sales. Higher royalty revenue also contributed to the year over year increase.

The remainder of the Company's revenue came from programs under its R&D collaborations, including a $280 million upfront payment for the global license of sapablursen to Ono Pharmaceutical Co., Ltd., reflecting the value that Ionis' pipeline and technology continues to generate.

Operating Expenses

SG&A expenses increased as anticipated for the second quarter and first half of 2025, compared to the same periods in 2024, primarily due to the launches of TRYNGOLZA and WAINUA, and advancing launch preparation activities for donidalorsen. This increase was partially offset by a decrease in R&D expenses as several late-stage studies ended. Overall, this led to a modest year-over-year increase in total operating expenses.

Balance Sheet

As of June 30, 2025, Ionis' cash, cash equivalents and short-term investments were $2.3 billion, consistent with December 31, 2024. Ionis received $280 million from the global license of sapablursen in the second quarter of 2025. Ionis' working capital decreased over the same period primarily due to the reclassification of the Company's 0% convertible notes as a current liability.

Webcast and Other Updates

Management will host a conference call and webcast to discuss Ionis' second quarter 2025 results at 11:30 a.m. Eastern time on Wednesday, July 30, 2025. 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 2025 earnings slides click here.

Ionis will be initiating a quiet period starting July 31, 2025, as the Company plans to announce the topline results from both the CORE and CORE2 studies simultaneously. The quiet period will be lifted upon the data announcement, expected in September.

Ionis' Marketed Medicines

INDICATION for TRYNGOLZA™ (olezarsen)

TRYNGOLZA™ (olezarsen) was approved by theU.S. Food and Drug Administration as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome (FCS).

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

TRYNGOLZA is contraindicated in patients with a history of serious hypersensitivity to TRYNGOLZA or any of the excipients in

TRYNGOLZA. Hypersensitivity reactions requiring medical treatment have occurred.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions (including symptoms of bronchospasm, diffuse erythema, facial swelling, urticaria, chills and myalgias) have been reported in patients treated with TRYNGOLZA. Advise patients on the signs and symptoms of hypersensitivity reactions and instruct patients to promptly seek medical attention and discontinue use of TRYNGOLZA if hypersensitivity reactions occur.

ADVERSE REACTIONS

The most common adverse reactions (incidence >5% of TRYNGOLZA-treated patients and >3% higher frequency than placebo) were injection site reactions, decreased platelet count and arthralgia.

Please see full Prescribing Information for TRYNGOLZA.

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.

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).

About Ionis Pharmaceuticals, Inc.

For three decades, Ionis has invented medicines that bring better futures to people with serious diseases. Ionis currently has 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), LinkedIn and Instagram.

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, 2024, 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.

Inc. AKCEA™ is a trademark of Akcea Therapeutics, Inc. TEGSEDI™ is a trademark of Akcea Therapeutics, Inc. WAYLIVRA™ is a trademark of Akcea Therapeutics, Inc. SPINRAZA® and QALSODY® are registered trademarks of Biogen. WAINUA® is a registered trademark of the AstraZeneca group of companies.

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,	
	2025	2024	2025	2024
	(unaudited)			
Revenue:				
Commercial revenue:				
Product sales, net	$19	$-	$26	$-
Royalty revenue	70	64	134	113
Other commercial revenue	14	8	19	19
Total commercial revenue	103	72	179	132
Research and development revenue:				
Collaborative agreement revenue	337	141	382	191
WAINUA joint development revenue	12	12	23	22
Total research and development revenue	349	153	405	213
Total revenue	452	225	584	345
Expenses:				
Cost of sales	4	4	6	6
Research, development and patent	217	222	418	436
Selling, general and administrative	91	65	167	118
Total operating expenses	312	291	591	560
Income (loss) from operations	140	(66)	(7)	(215)
Other income (expense):				
Interest expense related to the sale of future royalties	(19)	(18)	(37)	(36)
Other income, net	3	18	21	42
Income (loss) before income tax benefit (expense)	124	(66)	(23)	(209)
Income tax benefit (expense)	-	-	-	-
Net income (loss)	$124	($66)	($23)	($209)
Basic net income (loss) per share	$0.78	($0.45)	($0.15)	($1.43)
Diluted net income (loss) per share	$0.70	($0.45)	($0.15)	($1.43)
Shares used in computing basic net income (loss) per share	159	146	159	146
Shares used in computing diluted net income (loss) per share	182	146	159	146

IONIS PHARMACEUTICALS, INC.

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

	Three months ended June 30,		Six months ended June 30,	
	2025	2024	2025	2024
	(unaudited)			

As reported research, development and patent expenses according to GAAP	$217	$222	$418	$436
Excluding compensation expense related to equity awards	(20)	(23)	(40)	(45)
Non-GAAP research, development and patent expenses	$197	$199	$378	$391
As reported selling, general and administrative expenses according to GAAP	$91	$65	$167	$118
Excluding compensation expense related to equity awards	(10)	(8)	(19)	(17)
Non-GAAP selling, general and administrative expenses	$81	$57	$148	$101
As reported operating expenses according to GAAP	$312	$291	$591	$560
Excluding compensation expense related to equity awards	(30)	(31)	(59)	(62)
Non-GAAP operating expenses	$282	$260	$532	$498
As reported income (loss) from operations according to GAAP	$140	($66)	($7)	($215)
Excluding compensation expense related to equity awards	(30)	(31)	(59)	(62)
Non-GAAP income (loss) from operations	$170	($35)	$52	($153)
As reported net income (loss) according to GAAP	$124	($66)	($23)	($209)
Excluding compensation expense related to equity awards and related tax effects	(30)	(31)	(59)	(62)
Non-GAAP net income (loss)	$154	($35)	$36	($147)

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) 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, 2025	December 31, 2024
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$2,290	$2,298
Contracts receivable	53	92
Other current assets	235	230
Property, plant and equipment, net	112	94
Right-of-use assets	164	162
Other assets	131	127
Total assets	$2,985	$3,003
Liabilities and stockholders' equity:		
Current portion of deferred contract revenue	$76	$79
0% convertible senior notes, net – current	630	-
Other current liabilities	191	229
1.75% convertible senior notes, net	566	565

0% convertible senior notes, net	-	629
Liability related to sale of future royalties, net	541	542
Long-term lease liabilities	164	162
Long-term obligations, less current portion	60	52
Long-term deferred contract revenue	125	157
Total stockholders' equity	632	588
Total liabilities and stockholders' equity	$2,985	$3,003

Key 2025 and 2026 Value Driving Events(1)

New Product Launches

Program	Indication	2025	2026
Donidalorsen (U.S.)	HAE	•	
TRYNGOLZA (U.S.)	FCS	Achieved	
WAINZUA (EU)	ATTRv-PN	Achieved	
Olezarsen (U.S.)	sHTG		•
Zilganersen (U.S.)	Alexander disease		•

Regulatory Actions

Program	Indication	Regulatory Action	2025	2026
Donidalorsen	HAE	U.S. approval decision	•	
		EU approval decision		•
TRYNGOLZA	FCS	EU approval decision	•	
Olezarsen	sHTG	U.S. submission	•	
		U.S. approval decision		•
Zilganersen	Alexander disease	U.S. submission		•
		U.S. approval decision		•
Nusinersen (higher dose)	SMA	U.S. and EU submissions	Achieved	
		U.S. approval decision	•	
WAINZUA	ATTRv-PN	EU approval decision	Achieved	
Pelacarsen	Lp(a)- CVD	U.S. submission		•
Bepirovirsen	HBV	Regulatory submission(s)		•
		Regulatory decision(s)		•

Key Phase 3 Clinical Events

Program	Indication	Event	2025	2026
Olezarsen	sHTG	CORE, CORE2 data	•	
		Essence data	Achieved	
Zilganersen	Alexander disease	Phase 3 data	•	
ION582	Angelman syndrome	Phase 3 study start	Achieved	
		Phase 3 enrollment completion		•
Pelacarsen	Lp(a)-CVD	Lp(a) HORIZON data		•
Bepirovirsen	HBV	B-Well data		•
Eplontersen	ATTR-CM	CARDIO-TTRansform data		•
Sefaxersen	IgAN	IMAGINATION data		•
Ulefnersen	FUS-ALS	FUSION data		•

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

- Indicates that the milestone is anticipated in the respective year.

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