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

October 29, 2025

- TRYNGOLZA® generated $32 million in net product sales in the third quarter 2025 -

- DAWNZERA™ (donidalorsen) launch off to encouraging start -

- Olezarsen significantly reduced triglycerides and acute pancreatitis events in severe hypertriglyceridemia (sHTG) in landmark Phase 3 studies; sNDA submission on track by year-end –

- Positive pivotal zilganersen results in Alexander disease position Ionis for first independent neurology launch in 2026 -

- Increasing 2025 financial guidance driven by continued strength across the business –

CARLSBAD, Calif.--(BUSINESS WIRE)--Oct. 29, 2025-- Ionis Pharmaceuticals, Inc. (Nasdaq: IONS) (the “Company”) today reported financial results and provided key updates for the third quarter ended September 30, 2025.

"The third quarter was a watershed moment for Ionis, as we made important progress advancing our Ionis-owned medicines. With two independent launches now underway, and two more anticipated in 2026, we are delivering on our goal to bring a steady cadence of new medicines to people in need,” said Brett P. Monia, Ph.D., chief executive officer of Ionis. “Last month, we announced groundbreaking, positive topline Phase 3 results for olezarsen in severe hypertriglyceridemia and for zilganersen in Alexander disease, with regulatory filings planned in the coming months. Our approved and late-stage portfolio continues to deliver — positioning Ionis for substantial growth while, most importantly, offering the opportunity to profoundly improve the lives of people with serious diseases."

Third Quarter 2025 Summary Financial Results(1):

	Three months ended September 30,		Nine months ended September 30,	
	2025	2024	2025	2024
	(amounts in millions)			
Total revenue	$ 157	$ 134	$ 740	$ 479
Operating expenses	$ 317	$ 282	$ 907	$ 843
Operating expenses on a non-GAAP basis	$ 286	$ 250	$ 816	$ 749
Loss from operations	($ 160)	($ 148)	($ 167)	($ 364)
Loss from operations on a non-GAAP basis	($ 129)	($ 116)	($ 76)	($ 270)

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

Recent Financial Highlights

- Revenue increased 17% in the third quarter of 2025 and increased 55% in the nine months ended September 30, 2025, compared to the same periods last year, driven by the continued successful launch of TRYNGOLZA and increased royalty revenues. Contributing to the year-to-date increase, Ionis earned a $280 million upfront payment for the global license of sapablursen to Ono Pharmaceutical Co., Ltd. in the second quarter of 2025
- Operating expenses on a non-GAAP basis increased 14% in the third quarter of 2025 and increased 9% in the nine months ended September 30, 2025, compared to the same periods last year, primarily due to investments related to commercialization efforts for TRYNGOLZA, DAWNZERA and WAINUA
- Increasing 2025 financial guidance reflects strong overall revenue performance experienced year-to-date and fourth quarter outlook, including strong momentum seen with TRYNGOLZA revenues:

Full Year 2025 Guidance	Previous Guidance	New Guidance
Total Revenue	$825-850 million	$875-900 million
TRYNGOLZA product sales, net	$75-80 million	$85-95 million

Operating loss on a non-GAAP basis	$300-325 million	$275-300 million
Cash, cash equivalents and short-term investments	~$2.0 billion	>$2.1 billion

Third Quarter 2025 Financial Results

"In the third quarter of 2025, we delivered strong revenue performance, highlighted by TRYNGOLZA's nearly 70% increase over the prior quarter. As a result of this strength and our fourth quarter outlook, we are increasing our financial guidance again for 2025," said Elizabeth L. Hougen, chief financial officer of Ionis. "Looking ahead, we expect the 2026 independent launches of olezarsen in severe hypertriglyceridemia and zilganersen in Alexander disease to further strengthen our commercial portfolio. We anticipate that growth in our product revenues coupled with additional partner revenues will position Ionis to achieve cash flow breakeven in 2028 and generate substantial and sustainable positive cash flow for years to come."

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 $32 million in the third quarter of 2025, its third full quarter on the market, a nearly 70% increase over the prior quarter, and $57 million in the nine months ended September 30, 2025
  - Approved in the European Union (EU) as an adjunct to diet in adult patients for the treatment of genetically confirmed FCS; Sobi anticipates launching in the fourth quarter 2025
- Olezarsen demonstrated positive topline results in the pivotal Phase 3 CORE and CORE2 studies in sHTG
  - Olezarsen demonstrated a highly statistically significant placebo-adjusted mean reduction in fasting triglycerides of up to 72% and a highly statistically significant reduction in acute pancreatitis events of 85% with favorable safety and tolerability
  - sNDA submission on track for the end of 2025 with approval anticipated in the fourth quarter of 2026
  - Detailed data to be presented at the American Heart Association Conference on November 8, 2025, in a late-breaking session
- DAWNZERA™ (donidalorsen) was approved on August 21, 2025, by the FDA for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older
  - 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 every four or eight weeks
  - U.S. launch underway and off to an encouraging start
  - Currently under regulatory review in the EU
- Zilganersen demonstrated positive results in the pivotal study in children and adults with Alexander disease (AxD), a rare, progressive, and often fatal neurological disorder with no approved disease-modifying treatments
  - Zilganersen 50 mg demonstrated statistically significant and clinically meaningful stabilization on the primary endpoint of gait speed as assessed by the 10-Meter Walk Test (10MWT), compared to control at week 61 (mean difference 33.3%) with favorable safety and tolerability
  - Additional data from the pivotal study in children and adults living with Alexander disease were presented at the Child Neurology Society Annual Meeting in October 2025
  - NDA submission planned for the first quarter of 2026 with approval anticipated next year
- ION582 granted Breakthrough Therapy designation from FDA for the treatment of Angelman syndrome
  - Phase 3 REVEAL study expected to be fully enrolled in 2026
  - Phase 2 HALOS study showed continued improvement across multiple functional measures versus natural history through 18 months including expressive communication

Recent Highlights – Partnered Medicines

- WAINUA® (eplontersen) (WAINZUA in EU) for the treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis (ATTRv-PN) generated sales of $59 million and $143 million resulting in royalty revenue of $13 million and $33 million in the third quarter and the nine months ended September 30, 2025, respectively
  - 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 $374 million and $1.2 billion resulting in royalty revenue of $56 million and $158 million in the third quarter and the nine months ended September 30, 2025, respectively

Revenue

Ionis' revenue was comprised of the following:

	Three months ended September 30,		Nine months ended September 30,	
	2025	2024	2025	2024
Revenue:	(amounts in millions)			
Commercial revenue:				

Product sales, net:				
TRYNGOLZA sales, net	$ 32	$ -	$ 57	$ -
Total product sales, net	32	-	57	-
Royalty revenue:				
SPINRAZA royalties	56	57	158	152
WAINUA royalties	13	5	33	10
Other royalties	7	5	19	18
Total royalty revenue	76	67	210	180
Other commercial revenue	8	9	27	27
Total commercial revenue	**116**	**76**	**294**	**207**
Research and development revenue:				
Collaborative agreement revenue	31	45	414	237
WAINUA joint development revenue	10	13	32	35
Total research and development revenue	**41**	**58**	**446**	**272**
Total revenue	**$ 157**	**$ 134**	**$ 740**	**$ 479**

Commercial revenue for the third quarter and the nine months ended September 30, 2025, increased 53% and 42%, respectively, compared to the same periods in 2024. This increase was primarily 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. in the second quarter of 2025, reflecting the value that Ionis' pipeline and technology continues to generate.

Operating Expenses

SG&A expenses increased as anticipated for the third quarter and the nine months ended September 30, 2025, compared to the same periods in 2024, primarily due to the launches of TRYNGOLZA, DAWNZERA and WAINUA. 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, which was in line with expectations.

Balance Sheet

As of September 30, 2025, Ionis' cash, cash equivalents and short-term investments were $2.2 billion, compared to $2.3 billion on December 31, 2024. 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' third quarter 2025 results at 11:30 a.m. Eastern time on Wednesday, October 29, 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 third quarter 2025 earnings slides click here.

Ionis' Marketed Medicines

INDICATION for TRYNGOLZA® (olezarsen)

TRYNGOLZA® (olezarsen) was approved by the U.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 DAWNZERA™ (donidalorsen)

DAWNZERA™ (donidalorsen) was approved by theU.S. Food and Drug Administration for prophylaxis to prevent attacks of hereditary angioedema (HAE) in adult and pediatric patients 12 years of age and older.

IMPORTANT SAFETY INFORMATION

CONTRAINDICATIONS

DAWNZERA is contraindicated in patients with a history of serious hypersensitivity reactions, including anaphylaxis, to donidalorsen or any of the excipients in DAWNZERA.

WARNINGS AND PRECAUTIONS

Hypersensitivity Reactions

Hypersensitivity reactions, including anaphylaxis, have been reported in patients treated with DAWNZERA. If signs and symptoms of serious hypersensitivity reactions occur, discontinue DAWNZERA and institute appropriate therapy.

ADVERSE REACTIONS

Most common adverse reactions (incidence ≥ 5%) are injection site reactions, upper respiratory tract infection, urinary tract infection, and abdominal discomfort.

Please see full Prescribing Information for DAWNZERA.

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, cardiometabolic disease and select 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, technologies and our expectations regarding development and regulatory milestones. 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.

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,	
	2025	2024	2025	2024
	(unaudited)			
Revenue:				
Commercial revenue:				
Product sales, net	$ 32	$ -	$ 57	$ -
Royalty revenue	76	67	210	180
Other commercial revenue	8	9	27	27
Total commercial revenue	116	76	294	207
Research and development revenue:				
Collaborative agreement revenue	31	45	414	237
WAINUA joint development revenue	10	13	32	35
Total research and development revenue	41	58	446	272
Total revenue	157	134	740	479
Expenses:				
Cost of sales	2	1	8	7
Research, development and patent	218	220	636	656
Selling, general and administrative	97	61	263	180
Total operating expenses	317	282	907	843
Loss from operations	(160)	(148)	(167)	(364)
Other income (expense):				
Interest expense related to the sale of future royalties	(18)	(19)	(55)	(55)
Other income, net	49	23	70	66
Loss before income tax benefit	(129)	(144)	(152)	(353)
Income tax benefit	-	4	-	3
Net loss	($ 129)	($ 140)	($ 152)	($ 350)
Basic and diluted net loss per share	($ 0.80)	($ 0.95)	($ 0.95)	($ 2.38)
Shares used in computing basic and diluted net loss per share	160	149	159	147

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,	
	2025	2024	2025	2024
	(unaudited)			
As reported research, development and patent expenses according to GAAP	$ 218	$ 220	$ 636	$ 656
Excluding compensation expense related to equity awards	(21)	(22)	(61)	(67)
Non-GAAP research, development and patent expenses	$ 197	$ 198	$ 575	$ 589
As reported selling, general and administrative expenses according to GAAP	$ 97	$ 61	$ 263	$ 180
Excluding compensation expense related to equity awards	(10)	(10)	(29)	(26)
Non-GAAP selling, general and administrative expenses	$ 87	$ 51	$ 234	$ 154
As reported operating expenses according to GAAP	$ 317	$ 282	$ 907	$ 843
Excluding compensation expense related to equity awards	(31)	(32)	(91)	(94)
Non-GAAP operating expenses	$ 286	$ 250	$ 816	$ 749
As reported loss from operations according to GAAP	($ 160)	($ 148)	($ 167)	($ 364)
Excluding compensation expense related to equity awards	(31)	(32)	(91)	(94)
Non-GAAP loss from operations	($ 129)	($ 116)	($ 76)	($ 270)
As reported net loss according to GAAP	($ 129)	($ 140)	($ 152)	($ 350)
Excluding compensation expense related to equity awards and related tax effects	(31)	(32)	(91)	(94)
Non-GAAP net loss	($ 98)	($ 108)	($ 61)	($ 256)

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, 2025	December 31, 2024
	(unaudited)	
Assets:		
Cash, cash equivalents and short-term investments	$ 2,240	$ 2,298
Contracts receivable	25	92
Other current assets	254	230
Property, plant and equipment, net	106	94
Right-of-use assets	242	162

Other assets	166	127
Total assets	$ 3,033	$ 3,003
Liabilities and stockholders' equity:		
Current portion of deferred contract revenue	$ 77	$ 79
0% convertible senior notes, net – current	631	-
Other current liabilities	195	229
1.75% convertible senior notes, net	567	565
0% convertible senior notes, net	-	629
Liability related to sale of future royalties, net	545	542
Long-term lease liabilities	263	162
Long-term obligations, less current portion	29	52
Long-term deferred contract revenue	108	157
Total stockholders' equity	618	588
Total liabilities and stockholders' equity	$ 3,033	$ 3,003

Key 2025 and 2026 Value Driving Events[1]

New Product Launches

Program	Indication	2025	2026
DAWNZERA (U.S.)	HAE	Achieved	
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	Achieved	
		EU approval decision		•
TRYNGOLZA	FCS	EU approval decision	Achieved	
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	Refiling process on track	
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	Achieved	
		Essence data	Achieved	
Zilganersen	Alexander disease	Phase 3 data	Achieved	
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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