UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, DC 20549

Form 10-Q

(Mark One)

☒ QUARTERLY REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the Quarterly Period Ended September 30, 2025

OR

☐ TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF SECURITIES EXCHANGE ACT OF 1934

For the transition period from _____ to _____

Commission file number 000-19125

Ionis Pharmaceuticals, Inc.
(Exact name of Registrant as specified in its charter)

Delaware	**33-0336973**
(State or other jurisdiction of incorporation or organization)	(IRS Employer Identification No.)
2855 Gazelle Court, Carlsbad, California	**92010**
(Address of Principal Executive Offices)	(Zip Code)

760-931-9200
(Registrant's telephone number, including area code)

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading symbol	Name of each exchange on which registered
Common Stock, $.001 Par Value	"IONS"	The Nasdaq Stock Market LLC

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes ☒ No ☐

Indicate by check mark whether the registrant has submitted electronically every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit such files). Yes ☒ No ☐

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, a non-accelerated filer, smaller reporting company, or an emerging growth company. See the definitions of "large accelerated filer," "accelerated filer," "smaller reporting company," and "emerging growth company" in Rule 12b-2 of the Exchange Act.

Large Accelerated Filer ☒	Accelerated Filer ☐
Non-accelerated Filer ☐	Smaller Reporting Company ☐ Emerging Growth Company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12(b)-2 of the Securities Exchange Act of 1934). Yes ☐ No ☒

The number of shares of voting common stock outstanding as of October 23, 2025 was 161,974,393.

Index

IONIS PHARMACEUTICALS, INC.
FORM 10-Q
INDEX

PART I	**FINANCIAL INFORMATION**	
ITEM 1:	Financial Statements:	
	Condensed Consolidated Balance Sheets as of September 30, 2025 (unaudited) and December 31, 2024	3
	Condensed Consolidated Statements of Operations for the three and nine months ended September 30, 2025 and 2024 (unaudited)	4

	Condensed Consolidated Statements of Comprehensive Loss for the three and nine months ended September 30, 2025 and 2024 (unaudited)	5
	Condensed Consolidated Statements of Stockholders' Equity for the three and nine months ended September 30, 2025 and 2024 (unaudited)	6
	Condensed Consolidated Statements of Cash Flows for the nine months ended September 30, 2025 and 2024 (unaudited)	8
	Notes to Condensed Consolidated Financial Statements (unaudited)	9
ITEM 2:	Management's Discussion and Analysis of Financial Condition and Results of Operations:	
	Overview	23
	Critical Accounting Estimates	25
	Results of Operations	26
	Liquidity and Capital Resources	31
ITEM 3:	Quantitative and Qualitative Disclosures about Market Risk	33
ITEM 4:	Controls and Procedures	33
PART II	OTHER INFORMATION	34
ITEM 1:	Legal Proceedings	34
ITEM 1A:	Risk Factors	34
ITEM 2:	Unregistered Sales of Equity Securities and Use of Proceeds	52
ITEM 3:	Default upon Senior Securities	52
ITEM 4:	Mine Safety Disclosures	52
ITEM 5:	Other Information	52
ITEM 6:	Exhibits	53
SIGNATURES		54

TRADEMARKS

"Ionis," the Ionis logo, and other trademarks or service marks of Ionis Pharmaceuticals, Inc. appearing in this report are the property of Ionis Pharmaceuticals, Inc. "Akcea," the Akcea logo, and other trademarks or service marks of Akcea Therapeutics, Inc. appearing in this report are the property of Akcea Therapeutics, Inc., Ionis' wholly owned subsidiary. This report contains additional trade names, trademarks and service marks of others, which are the property of their respective owners. Solely for convenience, trademarks and trade names referred to in this report may appear without the ® or TM symbols.

Index

PART I — FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
(in thousands, except share data)

	September 30, 2025 (unaudited)	December 31, 2024
ASSETS		
Current assets:		
Cash and cash equivalents	$ 338,341	$ 242,077
Short-term investments	1,901,830	2,055,579
Contracts receivable	24,608	92,188
Inventories	10,470	12,512
Other current assets	243,744	217,934
Total current assets	2,518,993	2,620,290
Property, plant and equipment, net	106,117	94,251
Right-of-use assets	241,993	161,856
Deposits and other assets	165,988	127,278
Total assets	$ 3,033,091	$ 3,003,675
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable	$ 14,326	$ 42,964
Accrued compensation	57,019	69,614

Accrued liabilities	99,310	108,438
Income taxes payable	101	34
0 percent convertible senior notes, net	630,911	-
Current portion of deferred contract revenue	76,986	78,989
Other current liabilities	24,803	9,279
Total current liabilities	903,456	309,318
Long-term deferred contract revenue	107,906	156,504
1.75 percent convertible senior notes, net	567,123	565,026
0 percent convertible senior notes, net	-	628,535
Liability related to sale of future royalties, net	545,182	542,212
Long-term lease liabilities	262,672	161,805
Long-term obligations	28,785	51,924
Total liabilities	2,415,124	2,415,324
Stockholders' equity:		
Common stock, $0.001 par value; 300,000,000 shares authorized, 161,137,930 and 157,908,815 shares issued and outstanding at September 30, 2025 and December 31, 2024, respectively	161	158
Additional paid-in capital	3,045,585	2,868,812
Accumulated other comprehensive income	(25,978)	(30,811)
Accumulated deficit	(2,401,801)	(2,249,808)
Total stockholders' equity	617,967	588,351
Total liabilities and stockholders' equity	$ 3,033,091	$ 3,003,675

See accompanying notes.

Index

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except per share amounts)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Revenue:				
Commercial revenue:				
Product sales, net	$ 31,792	$ -	$ 57,353	$ -
Royalty revenue	75,694	66,807	209,811	180,036
Other commercial revenue	8,112	8,924	27,359	27,324
Total commercial revenue	115,598	75,731	294,523	207,360
Research and development revenue:				
Collaborative agreement revenue	31,436	44,883	413,387	235,753
WAINUA joint development revenue	9,685	13,200	32,471	35,449
Total research and development revenue	41,121	58,083	445,858	271,202
Total revenue	156,719	133,814	740,381	478,562
Expenses:				
Cost of sales	2,338	1,071	7,952	7,385
Research, development and patent	217,754	219,761	635,973	656,040
Selling, general and administrative	96,809	61,638	263,681	179,395
Total operating expenses	316,901	282,470	907,606	842,820
Loss from operations	(160,182)	(148,656)	(167,225)	(364,258)
Other income (expense):				
Investment income	23,682	26,228	73,035	78,112
Interest expense	(4,212)	(4,161)	(12,434)	(12,803)
Interest expense related to sale of future royalties	(17,952)	(18,533)	(55,422)	(54,788)
Gain (loss) on investments, net	29,908	879	9,432	(321)
Other income, net	363	142	929	1,029
Loss before income tax benefit (expense)	(128,393)	(144,101)	(151,685)	(353,029)
Income tax benefit (expense)	(213)	3,621	(308)	3,481
Net loss	$ (128,606)	$ (140,480)	$ (151,993)	$ (349,548)
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	159,765	148,593	159,216	146,703

See accompanying notes.

Index

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(in thousands)
(Unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Net loss	$ (128,606)	$ (140,480)	$ (151,993)	$ (349,548)
Unrealized gains on debt securities, net of tax	2,091	10,315	4,088	8,259
Currency translation adjustment	(82)	350	745	213
Comprehensive loss	$ (126,597)	$ (129,815)	$ (147,160)	$ (341,076)

See accompanying notes.

Index

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)
(Unaudited)

Description	Common Stock Shares	Common Stock Amount	Additional Paid in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at June 30, 2024	146,025	$ 146	$ 2,303,369	$ (34,838)	$ (2,004,979)	$ 263,698
Net loss	-	-	-	-	(140,480)	(140,480)
Change in unrealized gains, net of tax	-	-	-	10,315	-	10,315
Foreign currency translation	-	-	-	350	-	350
Issuance of common stock in connection with employee stock plans, net	288	-	7,002	-	-	7,002
Issuance of public common stock, net	11,500	12	489,081	-	-	489,093
Stock-based compensation expense	-	-	32,490	-	-	32,490
Balance at September 30, 2024	157,813	$ 158	$ 2,831,942	$ (24,173)	$ (2,145,459)	$ 662,468
Balance at June 30, 2025	159,197	$ 159	$ 2,932,747	$ (27,987)	$ (2,273,195)	$ 631,724
Net loss	-	-	-	-	(128,606)	(128,606)
Change in unrealized gains, net of tax	-	-	-	2,091	-	2,091
Foreign currency translation	-	-	-	(82)	-	(82)
Issuance of common stock in connection with employee stock plans, net	1,941	2	81,257	-	-	81,259
Stock-based compensation expense	-	-	31,581	-	-	31,581
Balance at September 30, 2025	161,138	$ 161	$ 3,045,585	$ (25,978)	$ (2,401,801)	$ 617,967

See accompanying notes.

Index

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
(in thousands)
(Unaudited)

Description	Common Stock Shares	Common Stock Amount	Additional Paid in Capital	Accumulated Other Comprehensive Loss	Accumulated Deficit	Total Stockholders' Equity
Balance at December 31, 2023	144,341	$ 144	$ 2,215,098	$ (32,645)	$ (1,795,911)	$ 386,686
Net loss	-	-	-	-	(349,548)	(349,548)
Change in unrealized gains, net of tax	-	-	-	8,259	-	8,259
Foreign currency translation	-	-	-	213	-	213
Issuance of common stock in connection with employee stock plans, net	1,972	2	33,205	-	-	33,207
Issuance of public common stock, net	11,500	12	489,081	-	-	489,093
Stock-based compensation expense	-	-	94,558	-	-	94,558
Balance at September 30, 2024	157,813	$ 158	$ 2,831,942	$ (24,173)	$ (2,145,459)	$ 662,468
Balance at December 31, 2024	157,909	$ 158	$ 2,868,812	$ (30,811)	$ (2,249,808)	$ 588,351
Net loss	-	-	-	-	(151,993)	(151,993)
Change in unrealized gains, net of tax	-	-	-	4,088	-	4,088
Foreign currency translation	-	-	-	745	-	745
Issuance of common stock in connection with employee stock plans, net	3,229	3	84,784	-	-	84,787
Stock-based compensation expense	-	-	91,989	-	-	91,989
Balance at September 30, 2025	161,138	$ 161	$ 3,045,585	$ (25,978)	$ (2,401,801)	$ 617,967

See accompanying notes.

Index

IONIS PHARMACEUTICALS, INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

(Unaudited)

	Nine Months Ended September 30,	
	2025	2024
Operating activities:		
Net loss	$ (151,993)	$ (349,548)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation	6,749	7,374
Amortization of right-of-use operating lease assets	6,803	7,472
Amortization of other assets	1,801	1,877
Amortization of discount on investments, net	(18,063)	(28,283)
Amortization of debt issuance costs	4,940	5,016
Non-cash royalty revenue related to sale of royalties	(38,478)	(30,422)
Non-cash interest related to sale of future royalties	54,964	54,330
Stock-based compensation expense	90,554	94,052
Loss (gain) on investments, net	(9,437)	320
Non-cash losses related to other assets	(3,643)	1,009
Changes in operating assets and liabilities:		
Contracts receivable	67,580	79,850
Inventories	(14,600)	(27)
Other current and long-term assets	(123,489)	(8,155)
Accounts payable	(29,116)	(19,215)
Income taxes	67	(2,110)
Accrued compensation	(12,595)	(27,169)
Accrued liabilities and other liabilities	87,683	(28,661)
Deferred contract revenue	(50,601)	(142,518)
Net cash used in operating activities	(130,874)	(384,808)
Investing activities:		
Purchases of short-term investments	(1,126,595)	(1,519,227)
Proceeds from sale of short-term investments	1,302,751	1,339,284
Purchases of property, plant and equipment	(30,152)	(19,783)
Acquisition of licenses and other assets, net	(4,275)	(2,514)
Net cash provided by (used in) investing activities	141,729	(202,240)
Financing activities:		
Proceeds from issuance of common stock through equity plans, net	84,787	33,207
Proceeds from issuance of common stock in public offering, net	-	489,093
Principal payments on mortgage debt	(123)	(126)
Net cash provided by financing activities	84,664	522,174
Effects of exchange rates on cash	745	213
Net increase (decrease) in cash and cash equivalents	96,264	(64,661)
Cash and cash equivalents at beginning of period	242,077	399,266
Cash and cash equivalents at end of period	$ 338,341	$ 334,605
Supplemental disclosures of cash flow information:		
Interest paid	$ 5,399	$ 5,714
Income taxes paid (refunds received), net	$ (661)	$ 2,072
Supplemental disclosures of non-cash investing and financing activities:		
Right-of-use assets obtained in exchange for lease obligations	$ 86,939	$ -
Amounts accrued for capital and patent expenditures	$ 478	$ 2,240

See accompanying notes.

Index

IONIS PHARMACEUTICALS, INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
September 30, 2025
(Unaudited)

1. Organization and Basis of Presentation

Organization and Business Activity

We incorporated in California on January 10, 1989. In conjunction with our initial public offering, we reorganized as a Delaware corporation in April 1991. We are a fully integrated commercial-stage biotechnology company and a leader in the discovery and development of RNA-targeted therapeutics.

Basis of Presentation

We prepared the unaudited interim condensed consolidated financial statements for the three and nine months ended September 30, 2025 and 2024 on the same basis as the audited financial statements for the year ended December 31, 2024. We included all normal recurring adjustments in the financial statements, which we considered necessary for a fair presentation of our financial position at such dates and our operating results and cash flows for those periods. Our operating results for the interim periods may not be indicative of what our operating results will be for the entire year. For more complete financial information, these financial statements, and notes thereto, should be read in conjunction with the audited financial statements for the year ended December 31, 2024 included in our Annual Report on Form 10-K filed with the Securities and Exchange Commission, or SEC.

In our condensed consolidated financial statements, we included the accounts of Ionis Pharmaceuticals, Inc. and the consolidated results of our wholly owned subsidiary, Akcea Therapeutics, Inc. and its wholly owned subsidiaries ("we", "us" or "our").

We operate as a single segment, Ionis operations, because our chief operating decision maker, or CODM, reviews operating results on an aggregate basis and manages our operations as a single operating segment. Refer to Note 15, *Segment Information*, for further details on our segment information.

Use of Estimates

We prepare our condensed consolidated financial statements in conformity with accounting principles generally accepted in the United States, or U.S., that require us to make estimates and assumptions that affect the amounts reported in our condensed consolidated financial statements and accompanying notes. Actual results could differ from our estimates.

2. Significant Accounting Policies

Below, we have included our accounting policies for revenue recognition related to product sales, net and cost of sales as a result of our launch of TRYNGOLZA and DAWNZERA in the U.S. Our other significant accounting policies have not changed substantially from those included in our Annual Report on Form 10-K for the year ended December 31, 2024.

Revenue Recognition

Product Sales, Net

We recognize revenue from product sales when the customer obtains control of our product in the amount of the transaction price, which is the amount that reflects the consideration which we expect to receive. We estimate reserves for variable consideration related to applicable discounts, rebates, chargebacks and other allowances included in our agreements with customers, payors and other third parties. We include the amount of variable consideration in the transaction price to the extent that it is probable that a significant reversal in the amount of the cumulative revenue recognized will not occur in a future period. If actual results vary significantly from our estimates, we adjust our estimates in the period that we become aware of such variances.

Index

Cost of Sales

Our cost of sales is comprised of costs related to our commercial revenue, including manufacturing costs, transportation and freight costs and indirect overhead costs associated with the manufacturing and distribution of our products. We also may include certain period costs related to manufacturing services and inventory adjustments in cost of sales.

Cost of sales for a newly launched product, such as TRYNGOLZA or DAWNZERA, does not include the full cost of manufacturing until we manufacture and sell additional inventory after exhausting pre-launch inventory, which we previously recorded as research and development, or R&D, expense.

Recent Accounting Standards

In November 2023, the Financial Accounting Standards Board, or FASB, issued Accounting Standard Update, or ASU, 2023-07, which provides updated guidance on segment reporting. The guidance requires public companies to disclose significant expenses that are regularly provided to the CODM, other segment items for each reportable segment and measures of segment profit or loss used by the CODM for allocating resources. In addition, the updated guidance requires public companies with a single reportable segment to provide all disclosures required under Accounting Standards Codification, or ASC, Topic 280, *Segment Reporting*, and public companies to include in interim reports all disclosures related to a reportable segment's profit or loss and assets that are currently required in annual reports. We adopted the reporting requirements in our 2024 Annual Report on Form 10-K and began providing the interim reporting requirements in our Quarterly Report on Form 10-Q for the first quarter of 2025. Refer to Note 15, *Segment Information*, for further details on our segment information.

In July 2025, the FASB issued ASU 2025-05, which amended the guidance in ASC 326 to simplify the estimation of credit losses on accounts receivable and contract assets from revenue transactions. The amended guidance allows companies to elect a practical expedient to assume that conditions as of the balance sheet date will remain unchanged for the remaining life of the asset when estimating the expected credit losses of the asset. This update is effective for annual periods beginning after December 15, 2025 and interim periods within those annual periods. Early adoption of this guidance is permitted. Companies that elect the practical expedient are required to apply the amendments prospectively. We are currently assessing the impact and timing of adopting this update.

In September 2025, the FASB issued ASU 2025-06, which amended and simplified the existing guidance for software costs. The amended guidance removes references to software development stages and allows companies to begin capitalizing software costs when management has authorized and committed to funding the software project and it is probable that the project will be completed with the software performing the intended function. This update is effective for annual periods beginning after December 15, 2027 and interim periods within those annual periods. Early adoption of this guidance is permitted at the beginning of an annual reporting period. The guidance may be applied on a prospective or retrospective basis. We expect to early adopt this update on January 1, 2026 on a prospective basis.

In September 2025, the FASB issued ASU 2025-07, which clarifies that share-based non-cash consideration received from a customer in exchange for goods or services under a revenue contract is subject to the guidance on non-cash consideration under ASC 606. This update is effective for annual periods beginning after December 15, 2026 and interim periods within those annual periods. Early adoption of this guidance is permitted. The guidance may be applied on a prospective or modified retrospective basis. We are currently assessing the impact and timing of adopting this update.

We do not expect any recently issued accounting standards other than the standards mentioned above and those included in our Annual Report on Form 10-K for the year ended December 31, 2024 to have a material impact to our financial results.

3. Supplemental Financial Data

Inventories

Our inventories consisted of the following (in thousands):

	September 30, 2025	December 31, 2024
Raw materials	$ 424	$ 5,557
Work in process	26,139	6,679
Finished goods	549	$ 276
Total	$ 27,112	12,512
Reported as:		

Inventories	$ 10,470	$ 12,512
Deposits and other assets	16,642	-
Total	$ 27,112	$ 12,512

We classify inventories as non-current assets when we expect the inventories to remain on hand beyond one year. We include non-current inventories in deposits and other assets in our condensed consolidated balance sheets. The amount reported as deposits and other assets as of September 30, 2025 consists of work in process inventory.

Accrued Liabilities

Our accrued liabilities consisted of the following (in thousands):

	September 30, 2025	December 31, 2024
Clinical expenses	$ 54,842	$ 77,436
In-licensing expenses	7,770	7,951
Commercial expenses	15,017	3,589
Other miscellaneous expenses	21,681	19,462
Total accrued liabilities	$ 99,310	$ 108,438

Index

4. Revenues

During the three and nine months ended September 30, 2025 and 2024, our revenues consisted of the following (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Revenue:				
Commercial revenue:				
Product sales, net:				
TRYNGOLZA sales, net	$ 31,792	$ -	$ 57,353	$ -
Total product sales, net	31,792	-	57,353	-
Royalty revenue:				
SPINRAZA royalties	55,896	57,208	158,243	152,406
WAINUA royalties	13,320	5,371	33,107	10,278
Other royalties	6,478	4,228	18,461	17,352
Total royalty revenue	75,694	66,807	209,811	180,036
Other commercial revenue	8,112	8,924	27,359	27,324
Total commercial revenue	115,598	75,731	294,523	207,360
Research and development revenue:				
Collaborative agreement revenue	31,436	44,883	413,387	235,753
WAINUA joint development revenue	9,685	13,200	32,471	35,449
Total research and development revenue	41,121	58,083	445,858	271,202
Total revenue	$ 156,719	$ 133,814	$ 740,381	$ 478,562

Revenue Sources

The following are sources of revenue and when we typically recognize revenue.

Commercial Revenue

In December 2024, the U.S. Food and Drug Administration, or FDA, approved TRYNGOLZA (olezarsen) for the treatment of familial chylomicronemia syndrome, or FCS. Following the approval, we launched TRYNGOLZA and began earning revenue from TRYNGOLZA sales.

In August 2025, the FDA approved DAWNZERA (donidalorsen) for prophylaxis to prevent attacks of hereditary angioedema, or HAE, in adult and pediatric patients 12 years of age and older. Our launch of DAWNZERA is currently underway.

We earn royalty payments primarily on net sales of SPINRAZA, WAINUA and QALSODY.

We earn commercial revenue from TEGSEDI and WAYLIVRA sales under our distribution agreements with Swedish Orphan Biovitrum AB, or Sobi. In addition, we receive royalties from PTC Therapeutics International Limited, or PTC, for TEGSEDI and WAYLIVRA sales. Refer to Part IV, Item 15, Note 4, *Collaborative Arrangements and Licensing Agreements*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024 for details on our commercialization partnerships with Sobi and PTC.

Under our distribution agreements with Sobi, we concluded that our performance obligation is to provide services to Sobi over the term of the agreement, which includes supplying finished goods inventory to Sobi. We are also responsible for maintaining the marketing authorization for TEGSEDI and WAYLIVRA in major markets and for leading the global commercial strategy for each medicine. We view this performance obligation as a series of distinct activities that are substantially the same. Therefore, we recognize as revenue the price Sobi pays us for the inventory when we deliver the finished goods inventory to Sobi. We also recognize distribution fee revenue based on Sobi's net sales of TEGSEDI and WAYLIVRA. Under our agreements with Sobi, Sobi does not generally have a right of return.

Research and development revenue under collaboration agreements

We enter into collaboration agreements to license and sell our technology on an exclusive or non-exclusive basis. Our collaboration agreements typically contain multiple elements, or performance obligations, including technology licenses or options to obtain technology licenses, R&D services and manufacturing services.

Index

For R&D services that we recognize over time, we measure our progress using an input method. The input methods we use are based on the effort we expend or costs we incur toward the satisfaction of our performance obligation. We estimate the amount of effort we expend, including the time we estimate it will take us to complete the activities, or costs we incur in a given period, relative to the estimated total effort or costs to satisfy the performance obligation. This results in a percentage that we multiply by the transaction price to determine the amount of revenue we recognize each period. This approach requires us to make numerous estimates that may involve judgement. If our estimates or judgements change over the course of the collaboration, they may affect the timing and amount of revenue that we recognize in the current and future periods.

Upfront payments: When we enter into a collaboration agreement and receive an upfront payment, we record the entire upfront payment as deferred revenue if our only performance obligation is for R&D services we will provide in the future. We amortize the upfront payment into revenue as we perform the R&D services. If part or all of the upfront payment is a license fee, we recognize as revenue the portion related to the license when we deliver the license to our partner because our partner has full use of the license and we do not have any additional performance obligations related to the license after delivery.

Milestone payments: We consider milestone payments to be variable consideration and include them in the transaction price when it is probable. We typically include milestone payments for R&D services in the transaction price when they are achieved. We include these milestone payments when they are achieved because there is considerable uncertainty in the research and development processes that trigger these payments. Similarly, we include regulatory milestone payments in the transaction price once the medicine is approved by the applicable regulatory agency. We will recognize sales-based milestone payments in the period in which we achieve the milestone under the sales-based royalty exception allowed under accounting rules.

We recognize milestone payments that relate to an ongoing performance obligation over our period of performance. For example, when we achieve a milestone payment from a partner for advancing a clinical study under a collaboration agreement, we add the milestone payment to the transaction price if the milestone relates to an ongoing R&D services performance obligation and recognize revenue related to the milestone payment over our estimated period of performance. If we have partially completed our performance obligation, then we record a cumulative-effect adjustment in the period we add the milestone payment to the transaction price.

Conversely, we recognize in full those milestone payments that we earn based on our partners' activities when our partner achieves the milestone event and we do not have a remaining performance obligation.

License fees: We recognize as revenue the total amount we determine to be the relative stand-alone selling price of a license when we deliver the license to our partner because our partner has full use of the license and we do not have any additional performance obligations related to the license after delivery.

WAINUA (Eplontersen) Collaboration with AstraZeneca

In 2021, we entered into a joint development and commercialization agreement with AstraZeneca to develop and commercialize WAINUA for the treatment of transthyretin amyloidosis, or ATTR. Under the terms of the agreement, we received a $200 million upfront payment in 2021.

We evaluated our WAINUA collaboration under ASC Topic 808, *Collaborative Arrangements*, or ASC 808, and identified four material components: (i) the license we granted to AstraZeneca in 2021, (ii) the co-development activities that we and AstraZeneca are performing, (iii) the co-commercialization activities that we and AstraZeneca are performing and (iv) the co-medical affairs activities that we and AstraZeneca are performing.

We determined that we had a vendor-customer relationship within the scope of ASC Topic 606, *Revenue from Contracts with Customers*, or ASC 606, for the license we granted to AstraZeneca and as a result we had one performance obligation. For our sole performance obligation, we determined the transaction price was the $200 million upfront payment we received. We recognized the upfront payment in full in 2021 because we did not have any remaining performance obligations after we delivered the license to AstraZeneca.

Index

We also concluded that the co-development activities, the co-commercialization activities and the co-medical affairs activities are within the scope of ASC 808 because we and AstraZeneca are active participants exposed to the risks and benefits of the activities under the collaboration and therefore do not have a vendor-customer relationship. AstraZeneca is currently responsible for 55 percent of the costs associated with the ongoing global Phase 3 development program. Because we are leading the Phase 3 development program, we made an accounting policy election to recognize as non-customer revenue the cost-share funding from AstraZeneca, net of our share of AstraZeneca's development expenses, in the same period we incur the related development expenses. As AstraZeneca is responsible for the majority of the commercial and medical affairs costs in the U.S. and all costs associated with bringing WAINUA to market outside the U.S., we made an accounting policy election to recognize cost-share funding we receive from AstraZeneca related to commercial and medical affairs activities as reductions of our selling, general and administrative, or SG&A, expense and R&D expense, respectively.

5. Collaborative Arrangements and Licensing Agreements

Below, we have included our AstraZeneca and Ono collaborations, which were the only collaborations that had either substantive changes or were new from those included in Part IV, Item 15, Note 4, *Collaborative Arrangements and Licensing Agreements*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024.

AstraZeneca

We have two collaborations with AstraZeneca: one focused on the joint development and commercialization of WAINUA and one focused on the treatment of cardiovascular, renal and metabolic diseases. From inception through September 30, 2025, we have received more than $960 million from these collaborations.

In the second quarter of 2025, we earned a $30 million milestone payment under our cardiovascular, renal and metabolic diseases collaboration when AstraZeneca initiated the Phase 2b study of opemalirsen (formerly ION532), an investigational medicine designed to reduce the production of apolipoprotein L1, or APOL1, for the treatment of APOL1-mediated kidney disease. We recognized this milestone payment as R&D revenue in full in the second quarter of 2025 because we did not have any remaining performance obligations related to the milestone payment. We will achieve the next payment of $20 million if AstraZeneca advances a medicine under this collaboration.

During the three and nine months ended September 30, 2025 and 2024, we earned the following revenue from our relationship with AstraZeneca (in thousands, except percentage amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Revenue from our relationship with AstraZeneca	$ 27,128	$ 19,461	$ 101,705	$ 47,106
Percentage of total revenue	17%	15%	14%	10%

We did not have any deferred revenue from our relationship with AstraZeneca at September 30, 2025 and December 31, 2024.

Ono

In March 2025, we entered into an agreement with Ono Pharmaceutical Co., Ltd., or Ono, to develop and commercialize sapablursen, an investigational RNA-targeted medicine for the potential treatment of polycythemia vera, or PV, a rare and potentially life-threatening hematologic disease. We are responsible for completing the ongoing Phase 2 IMPRSSION study, while Ono will be solely responsible for subsequent development, regulatory filings and commercialization of sapablursen.

Over the term of this collaboration, we are eligible to receive up to $940 million, which is comprised of a $280 million upfront payment, a $20 million development milestone payment, up to $20 million in regulatory milestone payments and up to $620 million in sales milestone payments. In addition, we are eligible to receive royalties in the mid-teen percentage range on net sales. From inception through September 30, 2025, we received more than $280 million from this collaboration, which includes the upfront payment and reimbursements for additional R&D services. We will achieve the next payment of $20 million if Ono initiates a pivotal clinical trial under this collaboration.

At inception, we identified two performance obligations under this agreement, comprised of our license of sapablursen to Ono and R&D services for sapablursen. We determined the transaction price to be the $280 million upfront payment we received when this transaction received clearance under the Hart-Scott-Rodino Antitrust Improvements Act of 1976, or HSR Act, in the second quarter of 2025. We allocated the transaction price based on the estimated stand-alone selling price of each performance obligation as follows:

- $278 million for the license of sapablursen; and
- $2 million for the R&D services for sapablursen.

We recognized $278 million of R&D revenue for the license of sapablursen in the second quarter of 2025 because we completed the performance obligation when we delivered the license to Ono. We recognized revenue for our R&D services performance obligation as we performed services based on our effort to satisfy our performance obligation relative to our total effort expected to satisfy our performance obligation. In the second quarter of 2025, we completed our R&D services performance obligation and recognized $2 million of R&D revenue.

During the three and nine months ended September 30, 2025 and 2024, we earned the following revenue from our relationship with Ono (in thousands, except percentage amounts):

	Three Months Ended September 30, 2025	Nine Months Ended September 30, 2025
Revenue from our relationship with Ono	$ 2,979	$ 282,979
Percentage of total revenue	2%	38%

Our condensed consolidated balance sheet at September 30, 2025 included deferred revenue of $2.9 million from our relationship with Ono. We did not have any deferred revenue from our relationship with Ono at December 31, 2024.

6. Basic and Diluted Net Loss Per Share

Basic net loss per share

We calculated our basic net loss per share for the three and nine months ended September 30, 2025 and 2024 by dividing our net loss by our weighted-average number of common shares outstanding during the period.

Index

Diluted net loss per share

For the three and nine months ended September 30, 2025 and 2024, we incurred a net loss; therefore, we did not include dilutive common equivalent shares in the computation of diluted net loss per share because the effect would have been anti-dilutive. Common stock from the following would have had an anti-dilutive effect on net loss per share:

- 1.75 percent convertible senior notes, or 1.75% Notes;
- 0 percent convertible senior notes, or 0% Notes;
- Note hedges related to the 0% Notes;
- Dilutive stock options;
- Unvested restricted stock units, or RSUs;
- Unvested performance restricted stock units, or PRSUs; and
- Employee Stock Purchase Plan, or ESPP.

For the three and nine months ended September 30, 2024, common stock underlying the 0.125 percent convertible senior notes, or 0.125% Notes, and note hedges related to the 0.125% Notes would also have had an anti-dilutive effect on net loss per share.

As of September 30, 2025, we had warrants related to our 0% Notes outstanding. As of September 30, 2024, we had warrants related to our 0% and 0.125% Notes outstanding. We will include the shares issuable under these warrants in our calculation of diluted earnings per share when the average market price per share of our common stock for the reporting period exceeds the strike price of the warrants.

7. Investments

The following table summarizes the contract maturity of the available-for-sale securities we held as of September 30, 2025:

One year or less	67%
After one year but within two years	29%
After two years but within three and a half years	4%
Total	100%

As illustrated above, at September 30, 2025, 96 percent of our available-for-sale securities had a maturity of less than two years.

All of our available-for-sale debt securities are available to us for use in our current operations. As a result, we categorize all of these securities as current assets even though the stated maturity of some individual securities may be one year or more beyond the balance sheet date.

We invest in debt securities with strong credit ratings and an investment grade rating at or above A-1, P-1 or F-1 by Standard & Poor's, Moody's or Fitch, respectively.

At September 30, 2025, we had an equity ownership interest of less than 20 percent in seven private companies and three public companies with which we conduct business.

Index

The following is a summary of our investments (in thousands):

September 30, 2025	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Available-for-sale debt securities:				
Corporate debt securities (1)	$ 639,937	$ 815	$ (69)	$ 640,683
Debt securities issued by U.S. government agencies	73,905	66	(16)	73,955
Debt securities issued by the U.S. Treasury (1)	562,662	384	(61)	562,985
Debt securities issued by states of the U.S. and political subdivisions of the states	5,151	11	-	5,162
Total debt securities with a maturity of one year or less	1,281,655	1,276	(146)	1,282,785
Corporate debt securities	415,818	1,688	(121)	417,385
Debt securities issued by U.S. government agencies	76,548	147	(60)	76,635
Debt securities issued by the U.S. Treasury	204,656	493	(49)	205,100
Debt securities issued by states of the U.S. and political subdivisions of the states	1,117	5	-	1,122
Other municipal debt securities	698	-	-	698
Total debt securities with a maturity of more than one year	698,837	2,333	(230)	700,940
Total available-for-sale debt securities	$ 1,980,492	$ 3,609	$ (376)	$ 1,983,725
Equity securities:				
Publicly traded equity securities included in other current assets (2)	$ 11,897	$ 40	$ (8,681)	$ 3,256
Privately held equity securities included in deposits and other assets (3)	4,905	54,395	(7,090)	52,210
Total equity securities	16,802	54,435	(15,771)	55,466
Total available-for-sale debt and equity securities	$ 1,997,294	$ 58,044	$ (16,147)	$ 2,039,191

Index

December 31, 2024	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Estimated Fair Value
Available-for-sale debt securities:				
Corporate debt securities (1)	$ 593,810	$ 487	$ (240)	$ 594,057
Debt securities issued by U.S. government agencies	143,647	287	(39)	143,895
Debt securities issued by the U.S. Treasury (1)	657,285	825	(120)	657,990
Debt securities issued by states of the U.S. and political subdivisions of the states	7,516	8	-	7,524
Total debt securities with a maturity of one year or less	1,402,258	1,607	(399)	1,403,466
Corporate debt securities	439,561	723	(2,275)	438,009
Debt securities issued by U.S. government agencies	65,255	137	(289)	65,103
Debt securities issued by the U.S. Treasury	149,086	124	(476)	148,734
Other municipal debt securities	698	-	(2)	696
Total debt securities with a maturity of more than one year	654,600	984	(3,042)	652,542
Total available-for-sale debt securities	$ 2,056,858	$ 2,591	$ (3,441)	$ 2,056,008
Equity securities:				
Publicly traded equity securities included in other current assets (2)	$ 11,897	$ 26	$ (6,660)	$ 5,263
Privately held equity securities included in deposits and other assets (3)	23,115	25,001	(7,093)	41,023
Total equity securities	35,012	25,027	(13,753)	46,286
Total available-for-sale debt and equity securities	$ 2,091,870	$ 27,618	$ (17,194)	$ 2,102,294

(1) Includes investments classified as cash equivalents in our condensed consolidated balance sheets.

(2) Our publicly traded equity securities are included in other current assets. We recognize publicly traded equity securities at fair value. In the nine months ended September 30, 2025, we recorded a $2.0 million net unrealized loss in our condensed consolidated statements of operations related to changes in the fair value of our investments in publicly traded companies.

(3) Our privately held equity securities are included in deposits and other assets. We recognize our privately held equity securities at cost minus impairments, plus or minus changes resulting from observable price changes in orderly transactions for the identical or similar investment of the same issuer, which are Level 3 inputs. In the nine months ended September 30, 2025, the amortized cost of our privately held equity securities increased $11.2 million. In the third quarter of 2025, we recorded a $29.4 million unrealized gain related to our investment in a privately held company due to an observable price change in an orderly transaction for a similar investment of the investee. This increase was partially offset by a loss of $18.2 million related to an impairment of our investment in another privately held company that we recorded in the second quarter of 2025.

The following is a summary of our investments we consider to be temporarily impaired at September 30, 2025 (in thousands, except for number of investments):

	Number of Investments	Less than 12 Months of Temporary Impairment: Estimated Fair Value	Less than 12 Months of Temporary Impairment: Unrealized Losses	More than 12 Months of Temporary Impairment: Estimated Fair Value	More than 12 Months of Temporary Impairment: Unrealized Losses	Total Temporary Impairment: Estimated Fair Value	Total Temporary Impairment: Unrealized Losses
Corporate debt securities	105	$ 179,031	$ (127)	$ 55,955	$ (63)	$ 234,986	$ (190)
Debt securities issued by U.S. government agencies	43	71,369	(60)	17,286	(16)	88,655	(76)
Debt securities issued by the U.S. Treasury	25	141,191	(74)	46,285	(36)	187,476	(110)

Other municipal debt securities	1	698	-	-	-	698	-
Total temporarily impaired debt securities	174	$ 392,289	$ (261)	$ 119,526	$ (115)	$ 511,815	$ (376)

We believe that the decline in value of these securities is temporary and is primarily related to the change in market interest rates since purchase rather than underlying credit deterioration for any of the issuers. We believe it is more likely than not that we will be able to hold our debt securities with declines in value to maturity. Therefore, we intend to hold these securities to maturity and anticipate full recovery of our debt securities' amortized cost basis at maturity.

Index

8. Fair Value Measurements

The following tables present the major security types we held at September 30, 2025 and December 31, 2024 that we regularly measure and carry at fair value. The following tables segregate each security type by the level within the fair value hierarchy of the valuation techniques we utilized to determine the respective security's fair value (in thousands):

	At September 30, 2025	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)
Cash equivalents (1)	$ 167,298	$ 167,298	$ -
Corporate debt securities (2)	1,058,068	-	1,058,068
Debt securities issued by U.S. government agencies (3)	150,590	-	150,590
Debt securities issued by the U.S. Treasury (4)	768,085	768,085	-
Debt securities issued by states of the U.S. and political subdivisions of the states (5)	6,284	-	6,284
Other municipal debt securities (5)	698	-	698
Publicly traded equity securities included in other current assets (6)	3,256	3,256	-
Total	$ 2,154,279	$ 938,639	$ 1,215,640

	At December 31, 2024	Quoted Prices in Active Markets (Level 1)	Significant Other Observable Inputs (Level 2)
Cash equivalents (1)	$ 180,445	$ 180,445	$ -
Corporate debt securities (5)	1,032,066	-	1,032,066
Debt securities issued by U.S. government agencies (5)	208,998	-	208,998
Debt securities issued by the U.S. Treasury (5)	806,724	806,724	-
Debt securities issued by states of the U.S. and political subdivisions of the states (5)	7,524	-	7,524
Other municipal debt securities (5)	696	-	696
Publicly traded equity securities included in other current assets (6)	5,263	5,263	-
Total	$ 2,241,716	$ 992,432	$ 1,249,284

The following footnotes reference lines in our condensed consolidated balance sheets:

(1) Included in cash and cash equivalents.

(2) $39.9 million was included in cash and cash equivalents, with the difference included in short-term investments.

(3) $6.0 million was included in cash and cash equivalents, with the difference included in short-term investments.

(4) $36.0 million was included in cash and cash equivalents, with the difference included in short-term investments.

(5) Included in short-term investments.

(6) Included in other current assets.

Convertible Notes

Our 1.75% Notes and 0% Notes had a fair value of $794.5 million and $777.0 million at September 30, 2025, respectively. Our 1.75% Notes and 0% Notes had a fair value of $569.3 million and $612.8 million at December 31, 2024, respectively. We determine the fair value of our notes based on quoted market prices for these notes, which are Level 2 measurements because the notes do not trade regularly.

Index

9. Stock-based Compensation Expense

The following table summarizes stock-based compensation expense for the three and nine months ended September 30, 2025 and 2024 (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Cost of sales	$ 145	$ 159	$ 855	$ 609
Research, development and patent expense	20,757	22,120	60,597	67,111
Selling, general and administrative expense	10,244	9,705	29,102	26,332
Stock-based compensation expense, net of amounts capitalized	31,146	31,984	90,554	94,052
Capitalized stock-based compensation expense	435	506	1,435	506
Total stock-based compensation expense	$ 31,581	$ 32,490	$ 91,989	$ 94,558

As of September 30, 2025, total unrecognized estimated stock-based compensation expense related to non-vested stock options, RSUs and PRSUs was $37.2 million, $88.1 million and $13.0 million, respectively. Our actual expenses will likely differ from these estimates because we will adjust our unrecognized stock-based compensation expense for future forfeitures, including any PRSUs that do not vest. We expect to recognize the cost of stock-based compensation expense related to our non-vested stock options, RSUs and PRSUs over a weighted average amortization period of 1.2 years, 1.5 years and 1.4 years, respectively.

Refer to Part IV, Item 15, Note 1, *Organization and Significant Accounting Policies*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024 for further details on how we determine the fair value of stock options granted, RSUs, PRSUs and stock purchase rights under the ESPP.

For the nine months ended September 30, 2025 and 2024, we used the following weighted-average assumptions in our Black-Scholes calculations:

Employee Stock Options:

	Nine Months Ended September 30,	
	2025	**2024**
Risk-free interest rate	4.4%	4.1%
Dividend yield	0.0%	0.0%
Volatility	42.1%	43.8%
Expected life	6.3 years	6.3 years

Board of Director Stock Options:

	Nine Months Ended September 30,	
	2025	**2024**
Risk-free interest rate	4.0%	4.5%
Dividend yield	0.0%	0.0%
Volatility	43.0%	49.8%
Expected life	7.4 years	7.5 years

ESPP:

	Nine Months Ended September 30,	
	2025	**2024**
Risk-free interest rate	4.2%	5.2%
Dividend yield	0.0%	0.0%
Volatility	48.2%	37.8%
Expected life	6 months	6 months

Index

Stock Options:

The weighted-average grant date fair value of stock options granted to employees for the nine months ended September 30, 2025 and 2024 was $17.21 and $24.73 per share, respectively. The weighted-average grant date fair value of stock options granted to non-employee directors for the nine months ended September 30, 2025 and 2024 was $20.86 and $27.47 per share, respectively.

RSUs:

The weighted-average grant date fair value of RSUs granted to employees for the nine months ended September 30, 2025 and 2024 was $33.78 and $52.08 per share, respectively.

PRSUs:

Under the terms of the PRSUs we granted in 2025 and 2024, the PRSUs may vest at the end of the three-year performance period based on our relative total shareholder return, or TSR, as compared to a peer group of companies and as measured at the end of the performance period. Under the terms of the grants, no number of PRSUs is guaranteed to vest and the actual number of PRSUs that will vest at the end of each performance period may be anywhere from zero to 200 percent of the target number depending on our relative TSR.

The weighted-average grant date fair value of PRSUs we granted to our executive officers for the nine months ended September 30, 2025 and 2024 was $48.81 and $78.41 per share, respectively.

10. Income Taxes

We recorded nominal income tax expense for the three and nine months ended September 30, 2025 compared to income tax benefit of $3.6 million and $3.5 million for the same periods in 2024.

The benefit for the three and nine months ended September 30, 2024 was primarily related to the 2023 tax return position for the royalty purchase agreement with Royalty Pharma that we finalized during the third quarter of 2024.

In July 2025, the One Big Beautiful Bill Act, or OBBBA, was signed into law, introducing significant changes to U.S. federal tax law. The new law restores current expensing of domestic R&D costs and allows us to accelerate the deduction for a significant amount of such costs we capitalized since 2022. The tax law changes from the OBBBA did not have a material effect on our tax expense for the three and nine months ended September 30, 2025.

We continue to maintain a full valuation allowance on all of our net deferred tax assets.

11. Liability Related to Sale of Future Royalties

In 2023, we entered into a royalty purchase agreement with Royalty Pharma Investments, or Royalty Pharma, to monetize a portion of our future SPINRAZA and pelacarsen royalties we are entitled to under our arrangements with Biogen and Novartis, respectively. As a result, we received an upfront payment of $500 million and we are eligible to receive up to $625 million in additional milestone payments. Under the terms of the agreement, Royalty Pharma will receive 25 percent of our

SPINRAZA royalty payments from 2023 through 2027, increasing to 45 percent of royalty payments in 2028, on up to $1.5 billion in annual sales. In addition, Royalty Pharma will receive 25 percent of any future royalty payments on pelacarsen, our medicine in development to treat patients with elevated lipoprotein(a)-driven cardiovascular disease. Royalty Pharma's royalty interest in SPINRAZA will revert to us after total SPINRAZA royalty payments to Royalty Pharma reach either $475 million or $550 million, depending on the timing and occurrence of FDA approval of pelacarsen.

We recorded the upfront payment of $500 million as a liability related to the sale of future royalties, net of transaction costs of $10.4 million, which we are amortizing over the estimated life of the arrangement using the effective interest rate method. We recognize royalty revenue in the period in which the counterparty sells the related product and recognizes the related revenue. We record royalty payments made to Royalty Pharma as a reduction of the liability.

We determine the effective interest rate used to record interest expense under this agreement based on an estimate of future royalty payments to Royalty Pharma. As of September 30, 2025 and 2024, the estimated effective interest rate under the agreement was 12.4 percent and 13.5 percent, respectively.

Index

The following table sets forth information on our liability related to sale of future royalties (in thousands):

Liability related to sale of future royalties, net as of December 31, 2024	$	542,212
Royalty payments to Royalty Pharma		(38,478)
Interest expense related to sale of future royalties		54,964
Amortization of issuance costs related to sale of future royalties		458
Liability related to sale of future royalties, net as of September 30, 2025	$	559,156
Less: Current portion (1)		(13,974)
Liability related to sale of future royalties, net as of September 30, 2025 – Non-current	$	545,182

(1) Included in other current liabilities in our condensed consolidated balance sheet.

There are numerous factors, most of which are not within our control, that could materially impact the amount and timing of royalty payments from Biogen and Novartis, and result in changes to our estimate of future royalty payments to Royalty Pharma. Such factors include, but are not limited to, the commercial sales of SPINRAZA, the regulatory approval and commercial sales of pelacarsen, competing products or other significant events.

12. Convertible Debt

1.75 Percent Convertible Senior Notes

In 2023, we completed a $575.0 million offering of our 1.75% Notes.

At September 30, 2025, we had the following 1.75% Notes outstanding (in millions except interest rate and price per share data):

		1.75% Notes
Outstanding principal balance	$	575.0
Unamortized debt issuance costs	$	7.9
Maturity date		June 2028
Interest rate		1.75%
Effective interest rate	$	2.30%
Conversion price per share		53.73
Total shares of common stock subject to conversion		10.7

0 Percent Convertible Senior Notes and Call Spread

In 2021, we completed a $632.5 million offering of our 0% Notes.

At September 30, 2025, we had the following 0% Notes outstanding (in millions except interest rate and price per share data):

		0% Notes
Outstanding principal balance	$	632.5
Unamortized debt issuance costs	$	1.6
Maturity date		April 2026
Interest rate		0%
Effective interest rate		0.50%
Conversion price per share	$	57.84
Effective conversion price per share with call spread	$	76.39
Total shares of common stock subject to conversion		10.9

Index

In conjunction with the 2021 offering, we entered into a call spread transaction, which was comprised of purchasing note hedges and selling warrants, to minimize the impact of potential economic dilution upon conversion of our 0% Notes by increasing the effective conversion price on our 0% Notes. We increased our effective conversion price to $76.39 with the same number of underlying shares as our 0% Notes. The call spread cost us $46.9 million, of which $136.7 million was for the note hedge purchase, offset by $89.8 million we received for selling the warrants. Similar to our 0% Notes, our note hedges are subject to adjustment. Additionally, our note hedges are exercisable upon conversion of the 0% Notes. The note hedges will expire upon maturity of the 0% Notes, or April 2026. The warrants will expire in July 2026. The note hedges and warrants are separate transactions and are not part of the terms of our 0% Notes. The holders of the 0% Notes do not have any rights with respect to the note hedges and warrants.

We recorded the amount we paid for the note hedges and the amount we received for the warrants in additional paid-in capital in our condensed consolidated balance sheets. Refer to Part IV, Item 15, Note 1, *Organization and Significant Accounting Policies*, of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024 for our Call Spread accounting policy. We reassess our ability to continue to classify the note hedges and warrants in shareholders' equity at each reporting period.

Other Terms of Convertible Senior Notes

The 1.75% and 0% Notes are convertible under certain conditions, at the option of the note holders. We can settle conversions of the notes, at our election, in cash, shares of our common stock or a combination of both. We may not redeem the notes prior to maturity, and we do not have to provide a sinking fund for them. Holders of the notes may require us to purchase some or all of their notes upon the occurrence of certain fundamental changes, as set forth in the indentures governing the notes, at a purchase price equal to 100 percent of the principal amount of the notes to be purchased, plus any accrued and unpaid interest.

13. Operating Leases

In 2022, we concurrently entered into two purchase and sale agreements with a real estate investor. In the same period, we closed the first transaction in which we sold the facilities at our headquarters in Carlsbad, California, which includes our primary R&D facility, for a purchase price of $263.4 million. In connection with this transaction, we leased back our headquarters facilities for an initial lease term of 15 years with options to extend the lease for two additional terms of five years each.

In 2023, we closed the second transaction and transferred legal ownership of two lots of undeveloped land adjacent to our headquarters to the real estate investor for a purchase price of $33.0 million. In connection with this transaction, we entered into a build-to-suit lease agreement with the same real estate investor to lease a new R&D facility. The lessor developed and constructed a new building composed of R&D and office space. We are designing and constructing tenant improvements to customize the facility's interior space.

The lease commenced in September 2025 when the lessor completed constructing the structure of the new facility. The initial lease term for this facility is 15 years with options to extend the lease for 2 additional terms of five years each. We determined at lease inception that it was not reasonably certain that we would exercise any of the options to extend the lease. We estimated our lease payments over the initial term to total approximately $230 million. In addition, we expect to receive reimbursements totaling $41.2 million from the lessor for tenant improvements that we own.

Since the building was under construction and unavailable to lease, we were unable to complete the sale-leaseback evaluation under ASC Topic 842, Leases, in 2023. As a result, the land remained in our consolidated balance sheets and we accounted for the proceeds as a financial liability. In September 2025, we reassessed the transaction under the sale-leaseback accounting guidance when the facility became available for lease commencement. We determined the transaction qualified as a sale-leaseback transaction upon lease commencement. As a result, we de-recognized the land and recorded a net gain of $4.2 million that we reported within operating loss in our condensed consolidated statements of operations. In addition, we recorded a financial liability of $19.6 million, which reflects the difference in the fair value of the land as of the lease commencement date compared to the purchase price of the land in 2023. We reported the current portion of the financial liability in other current liabilities and the non-current portion of the financial liability in long-term obligations in our condensed consolidated balance sheets. We recognize interest expense related to the financial liability based on our incremental borrowing rate at the commencement of the lease. We allocate payments to the lessor between the financial liability and lease expense.

14. Legal Proceedings

From time to time, we are involved in legal proceedings arising in the ordinary course of our business. Periodically, we evaluate the status of each legal matter and assess our potential financial exposure. If we consider the potential loss from any legal proceeding to be probable and we can reasonably estimate the amount, we accrue a liability for the estimated loss. The outcome of any proceeding is not determinable in advance. Therefore, we are required to use significant judgment to determine the probability of a loss and whether the amount of the loss is reasonably estimable. Our assessment of a potential liability and the amount of accruals we recorded are based only on the information available to us at the time. As additional information becomes available, we reassess the potential liability related to the legal proceeding and may revise our estimates.

On September 10, 2025, Arrowhead Pharmaceuticals, Inc., or Arrowhead, filed a lawsuit in the District of Delaware seeking a declaratory judgment that our patent US9,593,333 is invalid or not infringed by use of Arrowhead's ApoCIII inhibitor plozasiran. On September 11, 2025, we filed suit in the Central District of California asserting infringement of that same patent by Arrowhead's announced intention to commercialize plozasiran in November 2025. On October 8, 2025, we filed a motion to dismiss, or in the alternative, transfer Arrowhead's Delaware suit in favor of the case we brought in the Central District of California. At present, both lawsuits remain pending.

15. Segment Information

We operate as a single operating segment, Ionis operations, focused on the research, development and commercialization of our RNA-targeted medicines to bring better futures to people with serious diseases. The CODM, our Chief Executive Officer, manages our company, reviews operating results, assesses performance and allocates resources on an aggregate basis using consolidated net income or loss as the key measure of segment profit or loss. As such, results of our operations are reported on a consolidated basis for purposes of management and segment reporting.

Ionis operations derives its revenues from commercial and R&D revenue sources. Refer to Note 4, *Revenues*, for further details on our sources of revenue.

Index

The following table sets forth information on segment profit or loss, including significant segment expenses (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Revenue	$ 156,719	$ 133,814	$ 740,381	$ 478,562
Less:				
Cost of sales	2,193	912	7,097	6,815
Drug discovery	28,412	25,790	85,656	80,652
Drug development	120,828	132,201	351,463	392,151
Medical affairs	8,874	5,511	22,342	17,279
Manufacturing and development chemistry	15,790	14,087	51,616	39,723
R&D support	23,092	20,052	64,252	59,065
Selling, general and administrative	86,565	51,933	234,626	153,083
Other segment items (1)	(429)	23,808	75,322	79,342
Consolidated net loss	$ (128,606)	$ (140,480)	$ (151,993)	$ (349,548)

(1) Other segment items include stock-based compensation expense, investment income, interest expense, gain or loss on investments, other income or expense and income tax expense or benefit.

Index

ITEM 2. MANAGEMENT'S DISCUSSION AND ANALYSIS OF FINANCIAL CONDITION AND RESULTS OF OPERATIONS

In this Report on Form 10-Q, unless the context requires otherwise, "Ionis," the "Company," "we," "our," and "us," means Ionis Pharmaceuticals, Inc.

and its subsidiaries.

Forward-Looking Statements

In addition to historical information contained in this Report on Form 10-Q, the Report includes forward-looking statements regarding our business and the therapeutic and commercial potential of our commercial medicines, additional medicines in development and technologies. Any statement describing our 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 and particularly 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. Our forward-looking statements also involve assumptions that, if they never materialize or prove correct, could cause our results to differ materially from those expressed or implied by such forward-looking statements. Factors that could cause or contribute to such differences include, but are not limited to, those discussed in this report and described in additional detail in our annual report on Form 10-K for the year ended December 31, 2024, which is on file with the U.S. Securities and Exchange Commission and is available from us, and those identified within Part II Item 1A. Risk Factors of this Report. Although our forward-looking statements reflect the good faith judgment of our management, these statements are based only on facts and factors currently known by us. 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.

Overview

For three decades, we have invented medicines that bring better futures to people with serious diseases. As a pioneer in RNA-targeted medicines with a deep understanding of disease biology and an industry-leading drug discovery technology, we are driven to deliver innovative, life-changing advances for patients.

With our commercial launch of TRYNGOLZA (olezarsen) in the United States, or U.S., following its approval by the U.S. Food and Drug Administration, or FDA, we began a new chapter as a fully integrated commercial-stage biotechnology company. In August 2025, we launched DAWNZERA (donidalorsen) in the U.S. after receiving FDA approval for prophylaxis to prevent attacks of hereditary angioedema, or HAE. We currently have seven marketed medicines to treat serious diseases: TRYNGOLZA, DAWNZERA, WAINUA (eplontersen), SPINRAZA (nusinersen), QALSODY (tofersen), TEGSEDI (inotersen) and WAYLIVRA (volanesorsen). In addition, we are positioned to independently launch two medicines, olezarsen for the treatment of severe hypertriglyceridemia, or sHTG, and zilganersen for Alexander disease, or AxD, by the end of 2026, assuming regulatory approval. We also have a rich innovative pipeline across our focus areas of neurology, cardiometabolic diseases and select areas of high patient need. We currently have three wholly owned medicines and six partnered medicines in Phase 3 development, including ION582 for Angelman syndrome, or AS, which we advanced into a Phase 3 study in the second quarter of 2025. We also have additional medicines in early and mid-stage development.

Our multiple sources of revenue and strong financial foundation enable our continued investments to support ongoing and upcoming planned launches and to advance our wholly owned medicines in development. Our key recent achievements, combined with our independent and partnered product launches anticipated by the end of 2027, position us well to help patients with serious diseases and to deliver increasing product and royalty revenue.

Our Marketed Medicines

TRYNGOLZA is a once monthly, self-administered LIgand-Conjugated Antisense, or LICA, medicine approved in the U.S. as an adjunct to diet to reduce triglycerides in adults with familial chylomicronemia syndrome, or FCS. TRYNGOLZA is the first and only FDA-approved treatment that significantly and substantially reduces triglyceride levels in adults with FCS and provides a clinically meaningful reduction in acute pancreatitis, or AP, events. TRYNGOLZA is the first medicine we are commercializing independently in the U.S. In September 2025, TRYNGOLZA was approved in the European Union, or EU, as an adjunct to diet in adult patients for the treatment of genetically confirmed FCS. Sobi has exclusive rights to commercialize TRYNGOLZA in countries outside of the U.S., Canada and China.

DAWNZERA is an RNA-targeted medicine approved in the U.S. for prophylaxis to prevent attacks of HAE in adult and pediatric patients 12 years of age and older. DAWNZERA 80mg is self-administered via subcutaneous autoinjector once every four or eight weeks. DAWNZERA is the first and only FDA-approved RNA-targeted prophylactic therapy. DAWNZERA has the potential to offer durable efficacy, a favorable safety and tolerability profile, and the longest available dosing interval. DAWNZERA is the second medicine we are commercializing independently in the U.S. DAWNZERA is currently under regulatory review in the EU. We licensed commercialization rights for DAWNZERA in Europe and the Asia-Pacific region to Otsuka Pharmaceutical Co., Ltd., or Otsuka.

Index

WAINUA (WAINZUA in Europe) is a once monthly, self-administered subcutaneous LICA medicine that is approved in the U.S., European Union, or EU, and numerous other countries for the treatment of adults with polyneuropathy of hereditary transthyretin-mediated amyloidosis, or ATTRv-PN, a debilitating, progressive, and fatal disease. In January 2024, we and AstraZeneca launched WAINUA in the U.S. for the treatment of adults with ATTRv-PN. The launch of WAINUA is underway in numerous countries, including the countries in the EU, following the approval by the European Commission, or EC, in March 2025. We and AstraZeneca are co-commercializing WAINUA in the U.S. AstraZeneca has exclusive rights to commercialize WAINUA outside of the U.S. From inception through September 30, 2025, we have earned more than $590 million in revenues from our WAINUA collaboration, including more than $50 million in royalties on sales of WAINUA.

SPINRAZA is an antisense medicine for the treatment of patients with spinal muscular atrophy, or SMA, a progressive, debilitating and often fatal genetic disease. Our partner, Biogen, is responsible for commercializing SPINRAZA worldwide. From inception through September 30, 2025, we have earned more than $2.4 billion in revenues from our SPINRAZA collaboration, including more than $2.0 billion in royalties on sales of SPINRAZA.

QALSODY is an antisense medicine that received accelerated approval from the FDA in April 2023 and marketing authorization under exceptional circumstances from the European Medicines Agency, or EMA, in May 2024 for the treatment of adult patients with superoxide dismutase 1 amyotrophic lateral sclerosis, or SOD1-ALS, a rare, neurodegenerative disorder that causes progressive loss of motor neurons leading to death. QALSODY was the first treatment approved to target a genetic cause of ALS. Our partner, Biogen, is responsible for commercializing QALSODY worldwide. Biogen is also evaluating QALSODY as a potential treatment for presymptomatic SOD1-ALS patients in the ongoing ATLAS study. QALSODY was granted Orphan Drug designation by the FDA and EMA.

TEGSEDI is a once weekly, self-administered subcutaneous medicine approved in Europe and Brazil for the treatment of patients with ATTRv-PN. We currently sell TEGSEDI in Europe through our distribution agreement with Swedish Orphan Biovitrum AB, or Sobi. In Latin America, PTC Therapeutics International Limited, or PTC, is commercializing TEGSEDI in Brazil and is pursuing access in additional Latin American countries through its exclusive license agreement with us.

WAYLIVRA is a once weekly, self-administered, subcutaneous medicine approved in Europe and Brazil as an adjunct to diet in adult patients with genetically confirmed FCS and at high risk for pancreatitis. We sell WAYLIVRA in Europe through our distribution agreement with Sobi. In Latin America, PTC is commercializing WAYLIVRA in Brazil for two indications, FCS and familial partial lipodystrophy, or FPL, and is pursuing access in additional Latin American countries through its exclusive license agreement with us.

Our Innovative Late-Stage Pipeline of Ionis-Owned Investigational Medicines

Olezarsen is our medicine in development for sHTG, a second potential indication which has a large patient population. We are developing olezarsen for the treatment of sHTG. In September 2025, we announced positive topline results in the pivotal Phase 3 CORE and CORE2 studies in sHTG. In March 2025, we published the Phase 3 study design and baseline characteristics for the CORE, CORE2 and Essence studies in the *American Heart Journal*. In May 2025, we announced positive

topline results from the Essence study in people with moderate hypertriglyceridemia with or at risk for atherosclerotic cardiovascular disease. In August 2025, we published data from the Phase 3 Essence study evaluating olezarsen in patients with moderate hypertriglyceridemia and elevated cardiovascular risk in *The New England Journal of Medicine*. We licensed commercialization rights for olezarsen in most countries outside of the U.S., Canada and China to Sobi.

Zilganersen is our medicine in development for AxD. In September 2025, we announced positive topline results in the Phase 3 portion of the pivotal study of zilganersen in children and adults living with AxD. We presented additional data from the pivotal study of zilganersen in children and adults living with AxD at the Child Neurology Society Annual Meeting in October 2025. Zilganersen was granted Fast Track designation for the treatment of AxD and Rare Pediatric designation by the FDA. Additionally, zilganersen was granted Orphan Drug designation by the FDA and EMA.

Index

ION582 is our medicine in development for AS. In June 2025, we initiated the Phase 3 study, REVEAL, which we designed to evaluate the efficacy and safety of ION582. In addition, we are continuing to conduct the open label Phase 1/2 study, HALOS, of ION582 in patients with AS designed to assess the safety, tolerability and activity of multiple ascending doses of ION582 administered intrathecally. In 2024, we presented positive results from the completed multiple ascending dose portion of the study in people with AS. The FDA and EMA granted Orphan Drug designation to ION582. Additionally, the FDA granted Fast Track, Rare Pediatric and Breakthrough Therapy designations to ION582.

Our Innovative Late-Stage Pipeline of Partnered Investigational Medicines

Eplontersen is our medicine in development to treat patients with transthyretin amyloidosis cardiomyopathy, or ATTR-CM. We completed enrollment in the Phase 3 CARDIO-TTRansform study in July 2023. The FDA granted Fast Track designation to eplontersen for the treatment of patients with ATTR-CM. Additionally, the FDA and EMA granted Orphan Drug designation to eplontersen for the treatment of ATTR.

Pelacarsen is our medicine in development to treat patients with elevated lipoprotein(a)-driven cardiovascular disease, or Lp(a)-driven CVD. Novartis is developing pelacarsen, including conducting the ongoing Phase 3 Lp(a) HORIZON cardiovascular outcome study in patients with elevated Lp(a)-driven CVD, which achieved full enrollment in July 2022 with more than 8,000 patients. The study design and baseline characteristics of the Phase 3 Lp(a) HORIZON study were published in the *American Heart Journal* in April 2025. The FDA granted Fast Track designation and the Center for Drug Evaluation of China National Medical Products Administration granted Breakthrough Therapy designation to pelacarsen for the treatment of patients with elevated Lp(a) and established CVD.

Bepirovirsen is our medicine in development for chronic hepatitis B virus, or HBV. GSK is developing bepirovirsen, including conducting the ongoing B-Well Phase 3 program in patients with HBV, which achieved full enrollment in June 2024. The FDA granted Fast Track designation and the Japanese Ministry of Health, Labour and Welfare granted SENKU designation to bepirovirsen for the treatment of patients with HBV.

Sefaxersen is our medicine in development for immunoglobulin A, or IgA, nephropathy, or IgAN. In the second quarter of 2023, Roche advanced sefaxersen into Phase 3 development in patients with IgAN based on interim Phase 2 data.

Ulefnersen is our medicine in development for amyotrophic lateral sclerosis, or ALS, with mutations in the fused in sarcoma gene, or FUS. We are currently conducting a Phase 3 study of ulefnersen in juvenile and adult patients with FUS-ALS. We licensed global commercialization rights for ulefnersen to Otsuka. The FDA and EMA granted Orphan Drug designation to ulefnersen.

Critical Accounting Estimates

We prepare our condensed consolidated financial statements in conformity with accounting principles generally accepted in the U.S. As such, we make certain estimates, judgments and assumptions that we believe are reasonable, based upon the information available to us. These judgments involve making estimates about the effect of matters that are inherently uncertain and may significantly impact our quarterly or annual results of operations and financial condition. Each quarter, our senior management reviews the development, selection and disclosure of such estimates with the audit committee of our board of directors. The following are our significant accounting estimates, which we believe are the most critical to aid in fully understanding and evaluating our reported financial results:

- Assessing the propriety of revenue recognition and associated deferred revenue;
- Determining the appropriate cost estimates for unbilled preclinical studies and clinical development activities; and
- Assessing the appropriate estimate of anticipated future royalty payments under our royalty purchase agreement

There have been no material changes to our critical accounting estimates from the information provided in Item 7, *Management's Discussion and Analysis of Financial Condition and Results of Operations*, included in our Annual Report on Form 10-K for the year ended December 31, 2024.

Index

Results of Operations

The following is a summary of our financial results (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Total revenue	$ 156.7	$ 133.8	$ 740.4	$ 478.6
Total operating expenses	$ 316.9	$ 282.5	$ 907.6	$ 842.8
Loss from operations	$ (160.2)	$ (148.7)	$ (167.2)	$ (364.3)
Net loss	$ (128.6)	$ (140.5)	$ (152.0)	$ (349.5)

Revenue

Total revenue for the three and nine months ended September 30, 2025 were $156.7 million and $740.4 million, respectively, compared to $133.8 million and $478.6 million for the same periods in 2024 and was comprised of the following (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Revenue:				
Commercial revenue:				
Product sales, net:				
TRYNGOLZA sales, net	$ 31.8	$ -	$ 57.4	$ -

Total product sales, net	31.8	-	57.4	-
Royalty revenue:				
SPINRAZA royalties	55.9	57.2	158.2	152.4
WAINUA royalties	13.3	5.4	33.1	10.3
Other royalties	6.5	4.2	18.5	17.4
Total royalty revenue	75.7	66.8	209.8	180.1
Other commercial revenue	8.1	8.9	27.3	27.3
Total commercial revenue	115.6	75.7	294.5	207.4
Research and development revenue:				
Collaborative agreement revenue	31.4	44.9	413.4	235.8
WAINUA joint development revenue	9.7	13.2	32.5	35.4
Total research and development revenue	41.1	58.1	445.9	271.2
Total revenue	$ 156.7	$ 133.8	$ 740.4	$ 478.6

Commercial revenue for the three and 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 our revenue came from programs under our research and development, or R&D, collaborations, including revenue from the $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 our pipeline and technology continues to generate.

WAINUA (Eplontersen) Collaboration with AstraZeneca

Our financial results for the three and nine months ended September 30, 2025 and 2024 reflected the cost-sharing provisions related to our collaboration with AstraZeneca to develop and commercialize WAINUA for the treatment of ATTR. Under the terms of the collaboration agreement, AstraZeneca is currently paying 55 percent of the costs associated with the ongoing global Phase 3 development program. Because we are leading and conducting the Phase 3 development program, we are recognizing as R&D revenue the 55 percent of cost-share funding AstraZeneca is responsible for, net of our share of AstraZeneca's development expenses, in the same period we incur the related development expenses.

Index

As AstraZeneca is responsible for the majority of the medical affairs and commercial costs in the U.S. and all costs associated with bringing WAINUA to market outside the U.S., we are recognizing cost-share funding we receive from AstraZeneca related to these activities as a reduction of our medical affairs and commercialization expenses, which we classify as R&D and selling, general and administrative, or SG&A expenses, respectively. We expect our medical affairs and commercialization expenses to increase as WAINUA advances toward the market for ATTR-CM under our collaboration with AstraZeneca.

The following table sets forth information on revenue and expenses under this collaboration (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
WAINUA joint development revenue	$ 9.7	$ 13.2	$ 32.5	$ 35.4
Research and development expenses related to Phase 3 development of WAINUA	19.5	28.9	65.8	77.1
Medical affairs expenses for WAINUA	1.7	1.6	5.7	4.8
Commercialization expenses for WAINUA	7.5	6.3	22.0	19.0

Operating Expenses

The following table sets forth information on operating expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Operating expenses, excluding non-cash compensation expense related to equity awards	$ 285.8	$ 250.5	$ 817.0	$ 748.7
Non-cash compensation expense related to equity awards	31.1	32.0	90.6	94.1
Total operating expenses	$ 316.9	$ 282.5	$ 907.6	$ 842.8

Operating expenses, excluding non-cash compensation expense related to equity awards, for the three and nine months ended September 30, 2025 increased compared to the same periods in 2024. SG&A expenses increased as anticipated year over year primarily due to the launches of TRYNGOLZA, DAWNZERA and WAINUA. This increase was partially offset by a decrease in R&D expenses year over year as several late-stage studies ended. We expect our operating expenses, excluding non-cash compensation expense related to equity awards, to continue to increase during the remainder of 2025 as we advance our commercialization activities.

We believe non-cash compensation expense related to equity awards is not indicative of our operating results or cash flows from our operations.

Cost of Sales

Our cost of sales is comprised of costs related to our commercial revenue, which consisted of manufacturing costs, transportation and freight, indirect overhead costs associated with the manufacturing and distribution of TRYNGOLZA, DAWNZERA, TEGSEDI and WAYLIVRA and associated period costs.

Cost of sales for newly launched products, such as TRYNGOLZA and DAWNZERA, does not include the full cost of manufacturing until we manufacture and sell additional inventory after exhausting pre-launch inventory, which we previously recorded as R&D expense.

The following table sets forth information on cost of sales (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Cost of sales, excluding non-cash compensation expense related to equity awards	$ 2.2	$ 0.9	$ 7.1	$ 6.8
Non-cash compensation expense related to equity awards	0.1	0.2	0.9	0.6

Total cost of sales	$ 2.3	$ 1.1	$ 8.0	$ 7.4

Index

Research, Development and Patent Expenses

Our research, development and patent expenses consist of expenses for drug discovery, drug development, medical affairs, manufacturing and development chemistry and R&D support expenses.

The following table sets forth information on research, development and patent expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Research, development and patent expenses, excluding non-cash compensation expense related to equity awards	$ 197.0	$ 197.7	$ 575.4	$ 588.9
Non-cash compensation expense related to equity awards	20.8	22.1	60.6	67.1
Total research, development and patent expenses	$ 217.8	$ 219.8	$ 636.0	$ 656.0

Drug Discovery

We use our proprietary technologies to generate information about the function of genes and to determine the value of genes as drug discovery targets. We use this information to direct our own drug discovery research, and that of our partners. Drug discovery is also the function that is responsible for advancing our core technology. This function is also responsible for making investments in complementary technologies to expand the reach of our technologies.

The following table sets forth information on drug discovery expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Drug discovery expenses, excluding non-cash compensation expense related to equity awards	$ 28.4	$ 25.8	$ 85.7	$ 80.7
Non-cash compensation expense related to equity awards	4.0	4.4	11.7	13.3
Total drug discovery expenses	$ 32.4	$ 30.2	$ 97.4	$ 94.0

Drug discovery expenses, excluding non-cash compensation expense related to equity awards, increased slightly in the three months and nine months ended September 30, 2025 compared to the same periods in 2024 as we continued to advance our technologies discussed above.

Drug Development

The following table sets forth drug development expenses, including expenses for our marketed medicines and those in Phase 3 development for which we have incurred significant costs (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Eplontersen	$ 19.1	$ 28.3	$ 64.5	$ 74.3
Donidalorsen	3.7	3.5	11.8	13.4
Olezarsen	25.6	36.8	68.7	116.3
Zilganersen	2.2	2.5	9.7	6.2
ION582	6.8	2.8	24.3	9.6
Ulefnersen	2.8	3.1	8.0	10.0
Other development projects	23.6	21.0	59.3	65.2
Development overhead expenses	37.0	34.2	105.2	97.2
Total drug development expenses, excluding non-cash compensation expense related to equity awards	120.8	132.2	351.5	392.2
Non-cash compensation expense related to equity awards	9.2	9.7	26.2	30.4
Total drug development expenses	$ 130.0	$ 141.9	$ 377.7	$ 422.6

Our development expenses, excluding non-cash compensation expense related to equity awards, decreased for the three and nine months ended September 30, 2025 compared to the same periods in 2024 as several late-stage studies ended. We expect our development expenses will continue to stabilize as several late-stage studies end and we reallocate resources toward earlier stage programs.

Index

We may conduct multiple clinical trials on a drug candidate, including multiple clinical trials for the various indications we may be studying. Furthermore, as we obtain results from trials, we may elect to discontinue clinical trials for certain drug candidates in certain indications in order to focus our resources on more promising drug candidates or indications. Our Phase 1 and Phase 2 programs are clinical research programs that fuel our Phase 3 pipeline. When our medicines are in Phase 1 or Phase 2 clinical trials, they are in a dynamic state in which we may adjust the development strategy for each medicine. Although we may characterize a medicine as "in Phase 1" or "in Phase 2," it does not mean that we are conducting a single, well-defined study with dedicated resources. Instead, we allocate our internal resources on a shared basis across numerous medicines based on each medicine's particular needs at that time. This means we are constantly shifting resources among medicines. Therefore, what we spend on each medicine during a particular period is usually a function of what is required to keep the medicines progressing in clinical development, not what medicines we think are most important. For example, the number of people required to start a new study is large, the number of people required to keep a study going is modest and the number of people required to finish a study is large. However, such fluctuations are not indicative of a shift in our emphasis from one medicine to another and cannot be used to accurately predict future costs for each medicine. Because we always have numerous medicines in preclinical and varying stages of clinical research, the fluctuations in expenses from medicine to medicine, in large part, offset one another. If we partner a medicine, it may affect the size of a trial, its timing, its total cost and the timing of the related costs.

Medical Affairs

Our medical affairs function is responsible for funding and coordinating investigator-sponsored trials, communicating scientific and clinical information to

healthcare providers, medical professionals and patients, and managing publications.

The following table sets forth information on medical affairs expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Medical affairs expenses, excluding non-cash compensation expense related to equity awards	$ 8.9	$ 5.5	$ 22.3	$ 17.3
Non-cash compensation expense related to equity awards	1.0	1.1	3.8	3.2
Total medical affairs expenses	$ 9.9	$ 6.6	$ 26.1	$ 20.5

Medical affairs expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2025 compared to the same periods in 2024 as we continued advancing our late-stage pipeline.

Manufacturing and Development Chemistry

Expenditures in our manufacturing and development chemistry function consist primarily of personnel costs, specialized chemicals for oligonucleotide manufacturing, validation batches to support regulatory approvals, laboratory supplies and outside services. Our manufacturing and development chemistry function is responsible for providing drug supplies to drug development and our collaboration partners. Our manufacturing procedures include testing to satisfy good laboratory and good manufacturing practice requirements.

The following table sets forth information on manufacturing and development chemistry expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Manufacturing and development chemistry expenses, excluding non-cash compensation expense related to equity awards	$ 15.8	$ 14.1	$ 51.6	$ 39.7
Non-cash compensation expense related to equity awards	2.1	2.3	5.8	6.9
Total manufacturing and development chemistry expenses	$ 17.9	$ 16.4	$ 57.4	$ 46.6

Manufacturing and development chemistry expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2025 compared to the same periods in 2024 due to the timing of manufacturing performed by our contract manufacturing organizations for drug product and active pharmaceutical ingredients related to several late-stage programs.

Index

R&D Support

In our research, development and patent expenses, we include support costs such as rent, repair and maintenance for buildings and equipment, utilities, depreciation of laboratory equipment and facilities, amortization of our intellectual property, information technology costs, procurement costs and waste disposal costs. We call these costs R&D support expenses.

The following table sets forth information on R&D support expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Personnel costs	$ 7.6	$ 6.9	$ 21.8	$ 21.9
Occupancy	7.8	7.5	21.6	21.3
Computer software and licenses	3.4	2.4	9.8	5.7
Insurance	0.9	0.7	2.6	2.4
Patent expenses	2.6	1.3	4.1	2.7
Other	0.8	1.3	4.4	5.1
Total R&D support expenses, excluding non-cash compensation expense related to equity awards	23.1	20.1	64.3	59.1
Non-cash compensation expense related to equity awards	4.5	4.6	13.1	13.2
Total R&D support expenses	$ 27.6	$ 24.7	$ 77.4	$ 72.3

R&D support expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2025 compared to the same periods in 2024 primarily due to increased costs relating to computer software and licenses.

Selling, General and Administrative Expenses

SG&A expenses include personnel, information technology systems and outside costs associated with the commercialization and pre-commercialization activities for our medicines and costs to support our company, our employees and our stockholders including, legal, human resources, investor relations and finance. Additionally, we include in SG&A expenses such costs as rent, repair and maintenance of buildings and equipment, depreciation and utilities costs that we need to support the corporate functions listed above. We also include fees we owe under our in-licensing agreements related to SPINRAZA and QALSODY and cost sharing payments associated with co-commercialization activities under our WAINUA collaboration with AstraZeneca.

The following table sets forth information on SG&A expenses (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Selling, general and administrative expenses, excluding non-cash compensation expense related to equity awards	$ 86.6	$ 51.9	$ 234.6	$ 153.1
Non-cash compensation expense related to equity awards	10.2	9.7	29.1	26.3
Total selling, general and administrative expenses	$ 96.8	$ 61.6	$ 263.7	$ 179.4

SG&A expenses, excluding non-cash compensation expense related to equity awards, increased in the three and nine months ended September 30, 2025 compared to the same periods in 2024 primarily due to the launches of TRYNGOLZA, DAWNZERA and WAINUA. We expect SG&A expenses to increase as we continue to invest in our independent commercial launches.

Investment Income

The following table sets forth information on investment income (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Investment income	$ 23.7	$ 26.2	$ 73.0	$ 78.1

Index

Interest Expense

The following table sets forth information on interest expense (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Convertible notes:				
Non-cash amortization of debt issuance costs	$ 1.6	$ 1.5	$ 4.6	$ 4.5
Interest expense payable in cash	2.5	2.6	7.6	8.0
Interest on mortgage for manufacturing facility	0.1	0.1	0.2	0.3
Total interest expense	$ 4.2	$ 4.2	$ 12.4	$ 12.8

Interest Expense Related to Sale of Future Royalties

We recorded $18.0 million and $55.4 million of interest expense related to the sale of future royalties in the three and nine months ended September 30, 2025, respectively, compared to $18.5 million and $54.8 million in the same periods in 2024, respectively. These amounts are related to the Royalty Pharma Investments, or Royalty Pharma, transaction, in which we sold a minority interest in our future SPINRAZA and pelacarsen royalties to Royalty Pharma for a $500 million upfront payment and $625 million of potential future payments. Refer to Part I, Item 1, Note 11, *Liability Related to Sale of Future Royalties*, in the Notes to Condensed Consolidated Financial Statements for further details.

Gain (Loss) on Investments

The following table sets forth information on gain (loss) on investments (in millions):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Gain (loss) on investments	$ 29.9	$ 0.9	$ 9.4	$ (0.3)

Gain on investments increased in the three and nine months ended September 30, 2025 compared to the same periods in 2024 primarily due to a $29.4 million gain related to our investment in a privately held company resulting from an observable price change in an orderly transaction for a similar investment of the issuer that we recorded in the third quarter of 2025. This gain was partially offset by an $18.2 million impairment of our investment in a privately held company that we recorded in the second quarter of 2025.

Income Tax Benefit (Expense)

We recorded nominal income tax expense for the three and nine months ended September 30, 2025 compared to income tax benefit of $3.6 million and $3.5 million for the same periods in 2024.

The benefit for the three and nine months ended September 30, 2024 was primarily related to the 2023 tax return position for the royalty purchase agreement with Royalty Pharma that we finalized during the third quarter of 2024.

In July 2025, the One Big Beautiful Bill Act, or OBBBA, was signed into law, introducing significant changes to U.S. federal tax law. The new law restores current expensing of domestic R&D costs and allows us to accelerate the deduction for a significant amount of such costs we capitalized since 2022. The tax law changes from the OBBBA did not have a material effect on our tax expense for the three and nine months ended September 30, 2025.

We continue to maintain a full valuation allowance on all of our net deferred tax assets.

Net Loss and Net Loss per Share

The following table sets forth information on net loss and net loss per share (in millions, except per share amounts):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2025	2024	2025	2024
Net loss	$ (128.6)	$ (140.5)	$ (152.0)	$ (349.5)
Basic and diluted net loss per share	$ (0.80)	$ (0.95)	$ (0.95)	$ (2.38)

The period-over-period fluctuations in our net loss were driven by factors discussed in the sections above.

Liquidity and Capital Resources

We have financed our operations primarily from research and development collaborative agreements. We also financed our operations from commercial revenue from SPINRAZA, WAINUA and QALSODY royalties and TEGSEDI and WAYLIVRA commercial revenue. In addition, we began earning commercial revenue from TRYNGOLZA product sales in late December 2024 and DAWNZERA product sales in late August 2025. From our inception through September 30, 2025, we have earned approximately $8.7 billion in revenue. We have also financed our operations through the sale of our equity securities, the issuance of long-term debt and the sale of future royalties. From the time we were founded through September 30, 2025, we have raised net proceeds of approximately $2.7 billion from the sale of our equity securities. Additionally, from our inception through September 30, 2025, we have borrowed approximately $2.7 billion under long-term debt arrangements and

received proceeds of $0.5 billion from the sale of future royalties to finance a portion of our operations.

Index

From December 31, 2024 to September 30, 2025, our working capital and long-term obligations decreased as we reclassified our 0% Notes from non-current liabilities to current liabilities in the second quarter of 2025 because the notes are due in April 2026.

The following table summarizes our contractual obligations, excluding our liability related to the sale of future royalties, as of September 30, 2025. The table provides a breakdown of when obligations become due.

	Payments Due by Period (in millions)		
(selected balances described below)	Total	Less than 1 year	More than 1 year
1.75% Notes (principal and interest payable)	$ 605.2	$ 10.1	$ 595.1
0% Notes (principal payable)	632.5	632.5	-
Operating leases	487.3	33.8	453.5
Building mortgage payments (principal and interest payable)	9.2	0.5	8.7
Other obligations (principal and interest payable)	0.7	0.1	0.6
Total	$ 1,734.9	$ 677.0	$ 1,057.9

Our contractual obligations consist primarily of our convertible debt. In addition, we also have a facility mortgage, facility leases, equipment financing arrangements and other obligations. In the third quarter of 2025, our build-to-suit lease in Carlsbad, California commenced, resulting in an increase to our contractual obligations related to operating leases. We believe our cash, cash equivalents and short-term investments, as well as plans for cash in the future, will be sufficient to fund our planned operations and these obligations. We have not entered into, nor do we currently have, any off-balance sheet arrangements (as defined under SEC rules).

Convertible Debt and Call Spread

Refer to Part I, Item 1, Note 12, *Convertible Debt*, in the Notes to Condensed Consolidated Financial Statements for the significant terms of each convertible debt instrument.

Operating Facilities

Refer to Part IV, Item 15, Note 7 of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024 for further details on our operating facilities.

Operating Leases

Refer to Part I, Item 1, Note 13, *Operating Leases*, in the Notes to Condensed Consolidated Financial Statements and Part IV, Item 15, Note 7 of our audited financial statements included in our Annual Report on Form 10-K for the year ended December 31, 2024 for further details on our operating leases.

Liability Related to Sale of Future Royalties

Refer to Part I, Item 1, Note 11, *Liability Related to Sale of Future Royalties,* in the Notes to Condensed Consolidated Financial Statements for further details on our royalty purchase agreement with Royalty Pharma.

Other Obligations

In addition to contractual obligations, we had outstanding purchase orders as of September 30, 2025 for the purchase of services, capital equipment and materials as part of our normal course of business.

We may enter into additional collaborations with partners which could provide for additional revenue to us and we may incur additional cash expenditures related to our obligations under any of the new agreements we may enter into. We currently intend to use our cash, cash equivalents and short-term investments to finance our activities. However, we may also pursue other financing alternatives, like issuing additional shares of our common stock, issuing debt instruments, refinancing our existing debt, securing lines of credit or executing royalty monetization agreements. Whether we use our existing capital resources or choose to obtain financing will depend on various factors, including the future success of our business, the prevailing interest rate environment and the condition of financial markets generally.

Index

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to changes in interest rates primarily from our investments in certain short-term investments. We primarily invest our excess cash in highly liquid short-term investments of the U.S. Treasury and reputable financial institutions, corporations, and U.S. government agencies with strong credit ratings. We typically hold our investments for the duration of the term of the respective instrument. We do not utilize derivative financial instruments, derivative commodity instruments or other market risk sensitive instruments, positions or transactions to manage exposure to interest rate changes. Accordingly, we believe that, while the securities we hold are subject to changes in the financial standing of the issuer of such securities, we are not subject to any material risks arising from changes in interest rates, foreign currency exchange rates, commodity prices, equity prices or other market changes that affect market risk sensitive instruments.

We are also exposed to changes in foreign currency exchange rates as we have foreign subsidiaries with functional currencies other than the U.S. dollar. We translate our subsidiaries' functional currencies into our reporting currency, the U.S. dollar. As a result, our financial position, results of operations and cash flows can be affected by market fluctuations in the foreign currencies to U.S. dollar exchange rate, which are difficult to predict. A hypothetical 10 percent change in foreign exchange rates during any of the periods presented would not have had a material impact on our condensed consolidated financial statements.

ITEM 4. CONTROLS AND PROCEDURES

We maintain disclosure controls and procedures that are designed to ensure that information we are required to disclose in our Exchange Act reports is recorded, processed, summarized and reported within the time periods specified in the SEC's rules and forms, and that such information is accumulated and communicated to our management, including our Chief Executive Officer and Chief Financial Officer, as appropriate, to allow timely decisions regarding required disclosure. We design and evaluate our disclosure controls and procedures recognizing that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance and not absolute assurance of achieving the desired control objectives.

As of our most recently completed fiscal year and as of the end of the period covered by this Quarterly Report on Form 10-Q, we carried out an evaluation of the effectiveness of the design and operation of our disclosure controls and procedures, as defined in Rules 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934, as amended, under the supervision and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. Based on our evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of September 30, 2025. There have been no significant changes in our internal controls or in other factors that could significantly affect internal controls subsequent to September 30, 2025.

We also performed an evaluation of any changes in our internal controls over financial reporting that occurred during our last fiscal quarter and that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting. We conducted this evaluation under the supervision of and with the participation of our management, including our Chief Executive Officer and Chief Financial Officer. That evaluation did not identify any changes in our internal controls over financial reporting that occurred during our latest fiscal quarter and that have materially affected, or are reasonably likely to materially affect, our internal controls over financial reporting.

Index

PART II — OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

For details of legal proceedings, refer to Part I, Item 1, Note 14, *Legal Proceedings*, in the Notes to Condensed Consolidated Financial Statements.

ITEM 1A. RISK FACTORS

Investing in our securities involves a high degree of risk. You should carefully consider the following information about the risks described below, together with the other information contained in this report and in our other public filings in evaluating our business. If any of the following risks actually occur, our business could be materially harmed, and our financial condition and results of operations could be materially and adversely affected. As a result, the trading price of our securities could decline, and you might lose all or part of your investment. We have marked with an asterisk those risk factors that reflect substantive changes from the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2024.

Summary of Risk Factors

There are a number of risks related to our business and our securities. Some of the principal risks related to our business include the following:

- Our ability to generate substantial revenue from the sale of our medicines;
- The availability of adequate coverage and payment rates for our medicines;
- Our and our partners' ability to compete effectively;
- Our ability to successfully manufacture our medicines;
- Our ability to successfully develop and obtain marketing approvals for our medicines;
- Our ability to secure and maintain effective corporate partnerships;
- Our ability to sustain cash flows and achieve consistent profitability;
- Our ability to protect our intellectual property;
- Our ability to maintain the effectiveness of our personnel;
- The impacts of health epidemics, climate change, war and other events;
- Our dependence upon our own and third-party information technology systems; and
- The other factors set forth below.

Risks Related to the Commercialization of our Medicines

We have limited experience as a company in commercializing medicines and we will have to continue to invest significant resources to develop our capabilities. If we are unable to effectively establish or maintain an effective commercialization infrastructure, or enter into agreements with third parties to commercialize our medicines, we may not be able to successfully commercialize our medicines.

We have historically relied on third parties to commercialize our marketed medicines and have limited experience as a company in commercializing medicines. We currently have two independently launched medicines, TRYNGOLZA and DAWNZERA, and we expect to independently launch additional medicines in the future. Any failure to effectively commercialize our medicines, including our failure to allocate resources to our commercial launches efficiently or timely, could adversely impact the revenue we generate from our medicines. If the commercialization of our independently launched medicines and future sales of such are less successful than anticipated by us or our investors or securities analysts, our stock price could decline and our business may be harmed.

We will have to continue to invest significant financial and management resources to build and maintain the infrastructure required to successfully commercialize our medicines. We will need to establish and maintain effective sales teams for each of our independently launched medicines and there are significant risks involved in managing a sales organization, including our ability to hire, retain and incentivize qualified individuals, generate sufficient sales leads, provide adequate training to sales and marketing personnel, and effectively manage a geographically dispersed sales and marketing team. We must also continue to scale-up existing internal support functions to aid our commercialization efforts. Further, these existing support functions will need to work effectively in coordination with new commercial functional areas. Any failure to establish or maintain an effective commercialization infrastructure, including our sales, marketing, market access, distribution, and related capabilities, scale-up our existing support functions, or effectively integrate new functional areas, could adversely affect our ability to successfully commercialize our medicines.

Index

If we choose to rely on third parties to assist us in commercializing our medicines, we may not be able to enter into collaborations or hire consultants or external service providers on acceptable financial terms, or at all. In addition, if we continue to engage third parties to assist us in the commercialization of our medicines, our product revenues and profitability may be lower than if we commercialized such medicines ourselves.

The proximity of our planned upcoming independent launches could increase the likelihood that the risks set forth above will occur.

If the market does not accept our medicines, including our commercial medicines and our medicines in development, we are not likely to generate substantial revenues or become consistently profitable.

Even if our medicines are authorized for marketing, our success will depend upon the medical community, patients and third-party payers accepting our medicines as medically useful, cost-effective, safe and convenient. Even when the FDA or foreign regulatory authorities authorize our or our partners' medicines for commercialization, doctors may not prescribe our medicines to treat patients. Furthermore, we and our partners may not successfully commercialize additional medicines.

Additionally, in many of the markets where we or our partners may sell our medicines in the future, if we or our partners cannot agree with the government or other third-party payers regarding the price we can charge for our medicines, we may not be able to sell our medicines in that market. Similarly, cost control initiatives by governments or third-party payers could decrease the price received for our medicines or increase patient coinsurance to a level that makes our medicines, including our commercial medicines and our medicines in development, economically unviable. If the pricing of any of our medicines decreases for any reason, it will reduce our revenue for such medicine. For example, Biogen has in the past disclosed that SPINRAZA revenue decreased in part due to lower pricing in the U.S. and certain rest-of-world markets.

The degree of market acceptance for our medicines, including our commercial medicines and our medicines in development, depends upon several factors, including the:

- receipt and scope of marketing authorizations;
- establishment and demonstration in the medical and patient community of the efficacy and safety of our medicines, public perception regarding our medicines and their potential advantages over competing products;
- cost and effectiveness of our medicines compared to other available therapies;
- patient convenience of the dosing regimen for our medicines; and
- reimbursement policies of government and third-party payers.

Based on the profile of our medicines, physicians, patients, patient advocates, payers or the medical community in general may not accept or use any of the medicines that we or our partners may develop. For example, the product label for WAYLIVRA in the EU requires regular blood monitoring, which has negatively affected our ability to attract and retain patients for this medicine.

If government or other third-party payers fail to provide adequate coverage and payment rates for our medicines, including our commercial medicines and our medicines in development, our revenue will be limited.*

In both domestic and foreign markets, sales of our current and future products will depend in part upon the availability of coverage and reimbursement from third-party payers. The majority of patients in the U.S. who would fit within our target patient populations for our medicines have their healthcare supported by a combination of Medicare coverage, other government health programs such as Medicaid, managed care providers, private health insurers and other organizations. Coverage decisions may depend upon clinical and economic standards that disfavor new medicines when more established or lower cost therapeutic alternatives are already available or subsequently become available. Assuming coverage is approved, the resulting reimbursement payment rates might not be enough to make our medicines affordable. Even if favorable coverage status and adequate reimbursement rates are attained, less favorable coverage policies and reimbursement rates may be implemented in the future. Accordingly, our commercial medicines and our medicines in development will face competition from other therapies and medicines for limited financial resources. Furthermore, we or our partners may need to conduct post-marketing studies to demonstrate the cost-effectiveness of any future products to satisfy third-party payers. These studies might require us to commit a significant amount of management time and financial and other resources. In addition, third-party payers may never consider our future products as cost-effective and adequate third-party coverage and reimbursement might not be available to enable us to maintain price levels sufficient to realize an appropriate return on investment in product development.

Index

Third-party payers, whether foreign or domestic, or governmental or commercial, are developing increasingly sophisticated methods of controlling healthcare costs. In addition, in the U.S., no uniform policy of coverage and reimbursement for medicines exists among third-party payers. Therefore, coverage and reimbursement for medicines can differ significantly from payer to payer. For example, the Affordable Care Act, or ACA, was passed in March 2010, and substantially changed the way healthcare is financed by both governmental and private insurers and continues to significantly impact the U.S. pharmaceutical industry. There have been judicial and Congressional challenges to certain aspects of the ACA, as well as efforts to repeal or replace certain aspects of the ACA. It is unclear how future litigation and healthcare reform measures will impact the ACA and our business.

Further, we believe that future coverage, reimbursement and pricing will likely be subject to increased restrictions both in the U.S. and in international markets. In the U.S., recent health reform measures have resulted in reductions in Medicare and other healthcare funding, and there have been several recent U.S. Congressional inquiries, legislation and executive orders designed to, among other things, reduce drug prices, increase competition (including by enhancing support for generic and biosimilar drugs), lower out-of-pocket drug costs for patients, curtail spread pricing practices by pharmacy benefit managers, and foster scientific innovation to promote better health care and improved health. For example, on May 12, 2025, President Trump issued an executive order implementing the concept of most-favored nation pricing. Under this order, HHS, in coordination with other federal agencies, is directed to take actions to ensure that the price of prescription drugs paid by federal health insurers, including Medicare and Medicaid, is in line with the prices paid in comparably developed nations. These and similar actions and policies may significantly reduce U.S. drug prices, potentially impacting manufacturers' global pricing strategies and profitability, while increasing their operational costs and compliance risks.

In addition, the Inflation Reduction Act of 2022, or the IRA, includes key actions aimed at reducing the costs of prescription drugs and allows HHS to negotiate the price of certain single-source drugs covered under Medicare and establish a price cap on such drugs. The IRA, among other things, (1) directs HHS to negotiate the price of certain single-source drugs and biologics that have been on the market for at least seven years covered under Medicare, or the Medicare Drug Price Negotiation Program, and (2) imposes rebates under Medicare Part B and Medicare Part D to penalize price increases that outpace inflation. These provisions began to take effect progressively starting in fiscal year 2023, although the Medicare Drug Price Negotiation Program is currently subject to legal challenges. Under this program, HHS has already announced the agreed-upon prices of the first drugs that were subject to price negotiations and will announce the agreed-upon prices of additional drugs in the coming years. In response to an October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the CMS Innovation Center that will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. It is unclear whether or how these selected models or similar policy initiatives will impact prescription drug pricing in the future.

Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. Our future product sales may be subject to additional discounts from list price in the form of rebates and discounts provided to covered entities under the Public Health Service Act 340B drug pricing program. Changes to the 340B program or to Medicare or Medicaid programs at the federal or state level, including outcomes of ongoing litigation in our industry, may impact our product prices and rebate liability.

At the state level, legislatures have increasingly passed legislation and implemented regulations designed to control pharmaceutical and biological product pricing, including price or patient reimbursement constraints, discounts, restrictions on certain product access and marketing cost disclosure and transparency measures, and, in some cases, designed to encourage importation from other countries and bulk purchasing. For example, on January 5, 2024, the FDA approved Florida's Section 804 Importation Program, or SIP, proposal to import certain drugs from Canada for specific state healthcare programs. It is unclear how this program will be implemented, including which drugs will be chosen, and whether it will be subject to legal challenges in the United States or Canada. Other states have also submitted SIP proposals that are pending review by the FDA. Any such approved importation plans, when implemented, may result in lower drug prices for products covered by those programs. Third-party coverage and reimbursement for medicines may not be available or adequate in either the U.S. or international markets, which would negatively affect the potential commercial success of our products, our revenue and our profits.

If we or our partners fail to compete effectively, our medicines, including our commercial medicines and our medicines in development, will not generate significant revenues.

Our competitors engage in drug discovery throughout the world, are numerous, and include, among others, major pharmaceutical companies and specialized biopharmaceutical firms. In addition, other companies are engaged in developing RNA-targeted technology. Our competitors may succeed in developing medicines that are:

- priced lower than our medicines;
- reimbursed more favorably by government and other third-party payers than our medicines;
- safer than our medicines;
- more effective than our medicines; or
- more convenient to use than our medicines.

These competitive developments could make our medicines, including our commercial medicines and our medicines in development, obsolete or non-competitive.

Certain of our partners are pursuing other technologies or developing other medicines either on their own or in collaboration with others, including our competitors, to treat some of the same diseases that our own programs target. Competition may negatively impact a partner's focus on and commitment to our medicines and, as a result, could delay or otherwise negatively affect the commercialization of our medicines, including our commercial medicines and our medicines in development.

Many of our competitors have substantially greater financial, technical and human resources than we do. In addition, many of these competitors have significantly greater experience than we do in conducting preclinical testing and human clinical studies of new pharmaceutical products, in obtaining FDA and other regulatory authorizations of such products and in commercializing such products. Accordingly, our competitors may succeed in obtaining regulatory authorization for products earlier than we do or more successfully commercialize their products.

There are several pharmaceutical and biotechnology companies engaged in the development or commercialization in certain geographic markets of products against targets that are also targets of products in our development pipeline or of medicines we are commercializing. For example:

- Onasemnogene abeparvovec and risdiplam compete with SPINRAZA;
- Acoramidis, patisiran, tafamidis, tafamidis meglumine and vutrisiran compete with WAINUA;
- Nexiguran ziclumeran, ALXN2220 and NNC6019-0001 could compete with WAINUA;
- Plozasiran, pegozafermin and NST-1024 could compete with TRYNGOLZA and WAYLIVRA;
- Lanadelumab-flyo, C1 esterase inhibitor, berotralstat, C1 esterase inhibitor subcutaneous, garadacimab, deucrictibant, NTLA-2002 and STAR-0215 could compete with DAWNZERA;
- Olpasiran, zerlasiran, lepodisiran and muvalaplin could compete with pelacarsen;
- NI-005/AP-101 could compete with QALSODY;
- VIR-2218, VIR-3434, BRII-179, AB-729, selgantolimod, bersacapavir, REP 2139-Mg and VTP-300 could complete with bepirovirsen;
- Budesonide, sparsentan, atrasentan, iptacopan, zigakibart, sibeprenlimab, atacicept, ravulizumab, vemircopan, felzartamab, telitacicept and povetacicept could compete with sefaxersen; and
- GTX-102, alogabat and NNZ-2591 could compete with ION582.

SPINRAZA injection for intrathecal use is an antisense medicine indicated for the treatment of SMA patients of all ages approved in over 50 countries. Specifically, SPINRAZA faces competition from onasemnogene abeparvovec, a gene therapy product that was approved in the U.S. in May 2019 and in the EU in May 2020 for the treatment of SMA, as well as risdiplam, an oral product for the treatment of SMA that was approved in the U.S. in August 2020 and in the EU in March 2021. Biogen has in the past disclosed that SPINRAZA revenue decreased due to a reduction in demand as a result of increased competition and that future sales of SPINRAZA may be adversely affected by competing products.

Additionally, companies that are developing medicines that target the same patient populations as our medicines in development may compete with us to enroll participants in the clinical trials for such medicines, which could make it more difficult for us to complete enrollment for these clinical trials.

Our medicines could be subject to regulatory limitations following approval.

Following approval of a medicine, we and our partners must comply with comprehensive government regulations regarding the manufacture, marketing and distribution of medicines. The FDA and foreign regulatory bodies have the authority to impose significant restrictions on an approved medicine through the product label. We or our partners may not obtain the labeling claims necessary or desirable to successfully commercialize our medicines, including our commercial medicines and our medicines in development.

Promotional communications regarding prescription medicines must be consistent with the information in the product's approved labeling. Additionally, prescription medicines may be promoted only for the approved indication(s) in accordance with the approved label. The FDA and other regulatory authorities actively enforce the laws and regulations prohibiting the promotion of off-label uses, and a company that is found to have improperly promoted off-label uses may be subject to significant liability.

In addition, when approved, the FDA or a foreign regulatory authority may condition approval on the performance of post-approval clinical studies or patient monitoring, which could be time consuming and expensive. For example, in connection with the conditional marketing approval for WAYLIVRA in the EU, we are required to conduct a post-authorization safety study to evaluate the safety of WAYLIVRA on thrombocytopenia and bleeding in FCS patients taking WAYLIVRA. If the results of such post-marketing studies are not satisfactory, the FDA, EC or other foreign regulatory authorities may withdraw the marketing authorization or may condition continued marketing on commitments from us or our partners that may be expensive and time consuming to fulfill.

If we or others identify side effects after any of our medicines are on the market, or if manufacturing problems occur subsequent to regulatory approval, or if we, our CMOs or our partners fail to comply with regulatory requirements, we or our partners may, among other things, lose regulatory approval and be forced to withdraw products from the market, need to conduct additional clinical studies, incur restrictions on the marketing, distribution or manufacturing of the product, and/or change the labeling of our medicines.

We depend on our collaborations with Biogen for the development and commercialization of SPINRAZA and QALSODY.

We have entered into separate collaborative arrangements with Biogen to develop and commercialize SPINRAZA and QALSODY. We entered into these collaborations primarily to:

- fund our development activities for SPINRAZA and QALSODY;
- seek and obtain regulatory approvals for SPINRAZA and QALSODY; and
- successfully commercialize SPINRAZA and QALSODY.

We are relying on Biogen to obtain additional regulatory approvals for SPINRAZA and QALSODY, generate additional clinical data for SPINRAZA and QALSODY, manufacture SPINRAZA and QALSODY, and successfully commercialize SPINRAZA and QALSODY. In general, we cannot control the amount and timing of resources that Biogen devotes to our collaborations. If Biogen fails to further develop SPINRAZA or QALSODY, obtain additional regulatory approvals for SPINRAZA or QALSODY, manufacture SPINRAZA or QALSODY, or successfully commercialize SPINRAZA or QALSODY, or if Biogen's efforts in any of these respects are ineffective, revenues for SPINRAZA or QALSODY would be negatively affected.

In addition, our collaborations with Biogen may not continue for various reasons. Biogen can terminate our collaborations at any time. If Biogen stops developing or commercializing SPINRAZA or QALSODY, we would have to seek or spend additional funding, and SPINRAZA's or QALSODY's commercialization may be harmed.

We depend on our collaboration with AstraZeneca for the joint development and commercialization of WAINUA.

We have entered into a collaborative arrangement with AstraZeneca to develop and commercialize WAINUA. Under the terms of the collaboration agreement, we and AstraZeneca are co-developing and co-commercializing WAINUA in the U.S. and AstraZeneca has the sole right to commercialize WAINUA in all other countries. As a company we do not have experience with co-commercialization arrangements. We also do not have control over (1) the amount and timing of resources that AstraZeneca devotes to our collaboration, particularly outside of the U.S; (2) the pricing and reimbursement strategies for WAINUA; and (3) whether AstraZeneca elects to terminate the collaborative arrangement. If the co-commercialization arrangement for WAINUA is not successful for any reason, WAINUA may not meet our commercial objectives and our revenues for WAINUA may be limited.

In addition, a Joint Steering Committee, or JSC, having equal membership from us and AstraZeneca, and various subcommittees oversee and coordinate the development, manufacturing, commercialization and other exploitation activities for WAINUA in the U.S. by mutual agreement. If any subcommittee cannot reach unanimous agreement on any matter within its respective scope of authority, such matter may be referred to the JSC for resolution. If the JSC cannot come to a mutual agreement on any particular matter, this could delay our ability to develop or commercialize WAINUA.

If we are not successful in expanding our manufacturing capabilities or cannot manufacture our medicines or contract with a third party to manufacture our medicines at costs that allow us to charge competitive prices to buyers, we cannot market our products profitably.*

To successfully commercialize any of our medicines, we need to optimize and manage large-scale commercial manufacturing capabilities either on a standalone basis or through a third-party manufacturer. As our drug development and commercial pipeline increases and matures, we will have a greater need for clinical trial and commercial manufacturing capacity. We will also need to ensure that we have the manufacturing capabilities in place to support advances in our drug development activities, such as new chemistries. While we believe our current capabilities and those we obtain through third-party manufacturers support our manufacturing needs now, it will be important to expand our manufacturing infrastructure in the future, which will likely require substantial expenditures. If we are not successful in executing this expansion, it could limit our ability to meet our manufacturing requirements and commercial objectives in the future.

In addition, we have limited experience manufacturing pharmaceutical products of the chemical class represented by our medicines, called oligonucleotides, on a commercial scale for the systemic administration of a medicine. There are a small number of suppliers for certain capital equipment and raw materials that we use to manufacture our medicines, and some of these suppliers will need to increase their scale of production to meet our projected needs for commercial manufacturing. If a supplier chooses to devote more resources to other products, especially products with higher manufacturing capacity needs, that could impact such supplier's capability to deliver our requirements timely. Further, we must continue to improve our manufacturing processes to allow us to reduce our drug costs. We or our partners may not be able to manufacture our medicines at a cost or in quantities necessary to make commercially successful products.

Manufacturers, including us, must adhere to the FDA's cGMP regulations and similar regulations in foreign countries, which the applicable regulatory authorities enforce through facilities inspection programs. We, our partners and our contract manufacturers may not comply or maintain compliance with cGMP, or similar foreign regulations. Non-compliance could significantly delay or prevent receipt of marketing authorizations for our medicines, including authorizations for our commercial medicines and our medicines in development, or could result in enforcement action after authorization that might limit the commercial success of our medicines.

We rely on third-party manufacturers to supply the drug substance and drug product for TRYNGOLZA and WAINUA and drug product for WAYLIVRA. The operations of our suppliers, many of which are located outside of the United States, are subject to additional risks that are beyond our control. For example, tariffs on the raw materials, components, or equipment we use to manufacture our products, or on our drug substance or finished products, will increase our manufacturing costs. There have also been Congressional legislative proposals to discourage contracting with Chinese companies for the development or manufacturing of pharmaceutical products. In addition, merger and acquisition activity within the commercial manufacturing space could reduce the availability of resources from our third-party manufacturers. Delays or disruption to our own or third-party commercial manufacturing capabilities for any reason could limit the commercial success of our medicines.

Risks Related to the Development and Regulatory Approval of our Medicines

If we or our partners fail to obtain regulatory approval for our medicines and additional approvals for our commercial medicines, we or our partners cannot sell them in the applicable markets.*

We cannot guarantee that any of our medicines will be considered safe and effective or will be approved for commercialization. In addition, it is possible that our commercial medicines may not be approved in additional markets or for additional indications. We and our partners must conduct time-consuming, extensive and costly clinical studies to demonstrate the safety and efficacy of each of our medicines before they can be approved or receive additional approvals for sale. We and our partners must conduct these studies in compliance with FDA regulations and with comparable regulations in other countries.

We and our partners may not obtain necessary regulatory approvals on a timely basis, if at all, for our medicines. It is possible that regulatory authorities will not approve our medicines for marketing or our commercial medicines in additional markets or for additional indications. If the FDA or another regulatory authority believes that we or our partners have not sufficiently demonstrated the safety or efficacy of any of our medicines, including our commercial medicines or our medicines in development, the authority will not approve the specific medicine or will require additional studies, which could be time consuming and expensive and delay or harm commercialization of the medicine. For example, in August 2018 we received a complete response letter from the FDA regarding the new drug application for WAYLIVRA in which the FDA determined that the safety concerns identified with WAYLIVRA in our clinical development program outweighed the expected benefits of triglyceride lowering in patients with FCS. We also received a Notice of Non-Compliance Withdrawal Letter, or Non-W, from Health Canada for WAYLIVRA in November 2018.

The FDA or other comparable foreign regulatory authorities can delay, limit or deny approval of a medicine for many reasons, including:

- such authorities may disagree with the design or implementation of our clinical studies;
- we or our partners may be unable to demonstrate to the satisfaction of the FDA or other regulatory authorities that a medicine is safe and effective for any indication;
- such authorities may not accept clinical data from studies conducted at clinical facilities that have deficient clinical practices or that are in countries where the standard of care is potentially different from the U.S.;
- we or our partners may be unable to demonstrate that our medicine's clinical and other benefits outweigh its safety risks to support approval;
- such authorities may disagree with the interpretation of data from preclinical or clinical studies;
- such authorities may find deficiencies in the manufacturing processes or facilities of third-party manufacturers who manufacture clinical and commercial supplies for our medicines; and
- the approval policies or regulations of such authorities or their prior guidance to us or our partners during clinical development may significantly change in a manner rendering our clinical data insufficient for approval.

For example, while we continue to activate sites in the U.S., Canada, U.K., Australia and Japan, we are revising the study protocol for the REVEAL study of ION582 to address changes requested by EU regulators and plan to resubmit the protocol and initiate EU sites for this study next year. Importantly, we believe we are on track to complete enrollment for this study in 2026.

Failure to receive marketing authorization for our medicines in development, or failure to receive additional marketing authorizations for our commercial medicines, or delays in these authorizations, could prevent or delay commercial introduction of the medicine, and, as a result, could negatively impact our ability to generate revenue from product sales.

If the results of clinical testing indicate that any of our medicines are not suitable for commercial use, we may need to abandon one or more of our drug development programs.

Drug discovery and drug development have inherent risks and the historical failure rate for drugs is high. Antisense medicines are a relatively new approach to therapeutics. If we cannot demonstrate that our medicines are safe and effective for human use in the intended indication(s), we may need to abandon one or more of our drug development programs.

Even if our medicines are successful in preclinical and human clinical studies, the medicines may not be successful in late-stage clinical studies. Similarly, topline, preliminary or interim data we release for any of our clinical studies may not be indicative of full or final results from such study.

Successful results in preclinical or initial human clinical studies, including the Phase 2 results for some of our medicines in development, may not predict the results of subsequent clinical studies. If any of our medicines in Phase 3 clinical studies do not show sufficient safety and efficacy in patients with the targeted indication, or if such studies are discontinued for any other reason, it could negatively impact our development and commercialization goals for these medicines and our stock price could decline. In addition, we may release topline, preliminary or interim data for any of our clinical studies. The interim, topline or preliminary results we report may differ from future results of the same studies, or different conclusions or considerations may qualify such results, once additional data have been received and fully evaluated. As a result, such data should be viewed with caution until the final data are available.

Index

In the past, we have invested in clinical studies of medicines that have not met the primary clinical endpoints in their Phase 3 studies or have been discontinued for other reasons. For example, in October 2021, Biogen reported that QALSODY did not meet the primary clinical endpoint in the Phase 3 VALOR study; however, trends favoring QALSODY were seen across multiple secondary and exploratory measures of disease activity and clinical function. In addition, in March 2021, Roche decided to discontinue dosing in the Phase 3 GENERATION HD1 study of tominersen in patients with manifest Huntington's disease based on the results of a pre-planned review of data from the Phase 3 study conducted by an unblinded Independent Data Monitoring Committee. Similar results could occur in clinical studies for our other medicines.

There are a number of factors that could cause a clinical study to fail or be delayed, including:

- the clinical study may produce negative or inconclusive results;
- regulators may require that we hold, suspend or terminate clinical research for noncompliance with regulatory requirements;
- we, our partners, the FDA or foreign regulatory authorities could suspend or terminate a clinical study due to adverse side effects of a medicine on subjects or lack of efficacy in the trial;
- we or our partners may decide, or regulators may require us, to conduct additional preclinical testing or clinical studies;
- enrollment in our clinical studies may be slower than we anticipate;
- we or our partners, including our independent clinical investigators, contract research organizations and other third-party service providers on which we rely, may not identify, recruit or train suitable clinical investigators at a sufficient number of study sites or timely enroll a sufficient number of study subjects in the clinical study;
- the institutional review board for a prospective site might withhold or delay its approval for the study;
- people who enroll in the clinical study may later drop out due to adverse events, a perception they are not benefiting from participating in the study, fatigue with the clinical study process or personal issues;
- a clinical study site may deviate from the protocol for the study;
- the cost of our clinical studies may be greater than we anticipate;
- our partners may decide not to exercise any existing options to license and conduct additional clinical studies for our medicines; and
- the supply or quality of our medicines or other materials necessary to conduct our clinical studies may be insufficient, inadequate or delayed.

Further, the FDA or other regulatory authorities could request, among other things, additional information or commitments before we can start or continue a clinical study, protocol amendments, increased safety monitoring, additional product labeling information, and post-approval commitments. This happened in connection with the conditional marketing approval for WAYLIVRA in the EU, as the European Commission is requiring us to conduct a post-authorization safety study to evaluate the safety of WAYLIVRA on thrombocytopenia and bleeding in FCS patients taking WAYLIVRA. In addition, under accelerated approval the FDA is requiring completion of the ongoing Phase 3 trial for QALSODY to confirm the clinical benefit of QALSODY.

Moreover, our commercial medicines are chemically similar to each other. As a result, a safety observation we encounter with one of our medicines could have, or be perceived by a regulatory authority to have, an impact on a different medicine we are developing. This could cause the FDA or other regulators to ask questions or take actions that could harm or delay our ability to develop and commercialize our medicines or increase our costs. Any failure or delay in our clinical studies could reduce the commercial potential or viability of our medicines.

We depend on third parties to conduct clinical studies for our medicines and any failure of those parties to fulfill their obligations could adversely affect our development and commercialization plans.

We depend on independent clinical investigators, contract research organizations and other third-party service providers to conduct our clinical studies for our medicines and expect to continue to do so in the future. For example, we use clinical research organizations, such as Icon Clinical Research Limited, Medpace, Inc., Parexel International Corporation, Syneos Health, Inc. and Thermo Fisher Scientific Inc. for the clinical studies for our medicines, including WAINUA for the treatment of ATTR-CM, DAWNZERA, olezarsen, ulefnersen, zilganersen and ION582. We rely heavily on these parties for successful execution of our clinical studies, but do not control many aspects of their activities. For example, the investigators are not our employees, but we are responsible for ensuring that such investigators conduct each of our clinical studies in accordance with the general investigational plan and approved protocols for the study. Third parties may not complete activities on schedule or may not conduct our clinical studies in accordance with regulatory requirements or our stated protocols. For example, some of our key vendors have in the past experienced labor shortages, which impacted their ability to perform services for us for certain of our clinical trials. Subsequent failures of these third parties to carry out their obligations, or a termination of our relationship with such third parties, could delay or prevent the development, marketing authorization and commercialization of our medicines.

Index

In addition, while we do not have any clinical trial sites in Russia, Ukraine or Gaza, we do have a limited number of clinical trial sites in Israel that may be materially impacted by the ongoing military conflicts in Israel and elsewhere in the Middle East and could result in difficulties enrolling or completing our clinical trials in such areas on schedule.

Since corporate partnering is part of our strategy to fund the advancement and commercialization of some of our development programs, if any of our collaborative partners fail to fund our collaborative programs, or if we cannot obtain additional partners, we may have to delay or stop progress on those drug development programs.*

To date, corporate partnering has played a significant role in our strategy to fund our development programs and to add key development resources. While we are now commercializing some of our medicines independently, we still plan to continue to rely on additional collaborative arrangements to develop and commercialize some of our unpartnered medicines. However, we may not be able to negotiate favorable collaborative arrangements for these drug programs. If we cannot continue to secure additional collaborative partners, our revenues could decrease and the development of our medicines could suffer.

Our corporate partners are developing and funding many of the medicines in our development pipeline. For example, we are relying on:

- AstraZeneca for the joint development and funding of WAINUA;
- Novartis for development and funding of pelacarsen;
- GSK for development and funding of bepirovirsen; and
- Roche for development and funding of sefaxersen.

If any of these pharmaceutical companies stops developing and funding these medicines, our business could suffer and we may not have, or be willing to dedicate, the resources available to develop these medicines on our own. Our collaborators can terminate their relationships with us under certain circumstances, many of which are outside of our control. For example, in 2022, Pfizer and Bayer decided to discontinue the clinical development programs for vupanorsen and fesomersen, respectively. Similarly, Novartis decided to return the clinical development program we licensed to Novartis in August 2023 as a follow-on to pelacarsen to pursue a different molecule that is further along in development. Novartis remains fully committed to pelacarsen with Phase 3 data on track for the first half of 2026.

Even with funding from corporate partners, if our partners do not effectively perform their obligations under our agreements with them, it would delay or stop the progress of our drug development and commercial programs.

In addition to receiving funding, we enter into collaborative arrangements with third parties to:

- conduct clinical studies;
- seek and obtain marketing authorizations; and
- manufacture and commercialize our medicines.

Once we have secured a collaborative arrangement to further develop and commercialize one of our drug development programs, such as our collaborations with AstraZeneca, Biogen, GSK, Novartis, Otsuka and Roche, these collaborations may not continue or result in commercialized medicines, or may not progress as quickly as we anticipated.

For example, a collaborator such as AstraZeneca, Biogen, GSK, Novartis, Otsuka or Roche, could determine that it is in its financial interest to:

- pursue alternative technologies or develop alternative products that may be competitive with the medicine that is part of the collaboration with us;
- pursue higher-priority programs or change the focus of its own development programs; or
- choose to devote fewer resources to our medicines than it does to its own medicines.

If any of these occur, it could affect our partner's commitment to the collaboration with us and could delay or otherwise negatively affect the commercialization of our medicines, including QALSODY, SPINRAZA, WAINUA, bepirovirsen, sefaxersen and pelacarsen.

Index

We may not be able to benefit from designations for our medicines from regulatory authorities that are intended to confer benefits such as financial incentives or an accelerated regulatory pathway.

In the U.S., under the Orphan Drug Act, the FDA may designate a medicine as an Orphan Drug if it is intended to treat a rare disease or condition affecting fewer than 200,000 individuals in the U.S. Orphan Drug designation does not convey any advantage in, or shorten the duration of, the regulatory review and approval process, but it can provide financial incentives, such as tax advantages and user-fee waivers, as well as longer regulatory exclusivity periods. The FDA has granted Orphan Drug designation to TRYNGOLZA for the treatment of patients with FCS, to WAINUA for the treatment of patients with ATTR, to ulefnersen for the treatment of patients with FUS-ALS, to ION582 for the treatment of patients with Angelman syndrome, and to some of our earlier stage medicines. The FDA and EMA have granted Orphan Drug designation to DAWNZERA for the treatment of patients with HAE, to WAYLIVRA for the treatment of patients with FCS, to tominersen for the treatment of patients with HD, and to some of our earlier stage medicines. In addition, the EMA has granted Orphan Drug designation to WAYLIVRA for the treatment of patients with FPL. Even if approval is obtained on a medicine that has been designated as an Orphan Drug, we may lose Orphan Drug exclusivity if the FDA or EMA determines that the request for designation was materially defective or if we cannot assure sufficient quantity of the applicable medicine to meet the needs of patients with the rare disease or condition, or if a competitor is able to gain approval for the same or a substantially similar medicine in a safer or more effective form or that makes a major contribution to patient care. If we lose Orphan Drug exclusivity on any of our medicines, we may face increased competition and lose market share for such medicine.

We may also seek rare pediatric disease designation for some of our medicines. The FDA defines "rare pediatric disease" as a serious or life-threatening disease in which the serious or life-threatening manifestations primarily affect individuals aged from birth to 18 years or is a rare disease or condition within the meaning of the Orphan Drug Act. Designation of a medicine as a medicine for a rare pediatric disease does not guarantee that a marketing application for such

medicine will meet the eligibility criteria for a rare pediatric disease priority review voucher, or PRV, at the time the application is approved. Under the FDCA, we will need to request a rare pediatric disease PRV in our original marketing application for any potential medicine for which we have received rare pediatric disease designation. The FDA may determine that a marketing application for any such medicine, if approved, does not meet the eligibility criteria for a PRV. Under the current statutory sunset provisions, after December 20, 2024, the FDA may only award a PRV for an approved rare pediatric disease application if the sponsor has rare pediatric disease designation for the drug or biologic that is the subject of such application, and that designation was granted by December 20, 2024. After September 30, 2026, the FDA may not award any rare pediatric disease PRVs. However, it is possible the authority for FDA to award rare pediatric disease PRV will be further extended by Congress.

Risks Associated with our Businesses as a Whole

Risks related to our financial condition

If we fail to obtain timely funding, we may need to curtail or abandon some of our programs.

Many of our medicines are undergoing clinical studies or are in the early stages of research and development. Most of our programs will require significant additional research, development, manufacturing, preclinical and clinical testing, marketing authorizations, preclinical activities and commitment of significant additional resources prior to their successful commercialization. In addition, as we commercialize more medicines on our own, we will need to invest significant financial resources to continue developing the infrastructure required to successfully commercialize our medicines, including building and maintaining new support functions and scaling up existing internal support functions and expanding our manufacturing capabilities. All of these activities will require significant cash. As of September 30, 2025, we had cash, cash equivalents and short-term investments equal to $2.2 billion. If we or our partners do not meet our goals to successfully commercialize our medicines, including our commercial medicines, or to license certain medicines and proprietary technologies, we will need additional funding in the future. Our future capital requirements will depend on many factors such as:

- successful commercialization of our commercial medicines;
- the profile and launch timing of our medicines in development;
- changes in existing collaborative relationships and our ability to establish and maintain additional collaborative arrangements;
- continued scientific progress in our research, drug discovery and development programs;
- the size of our programs and progress with preclinical and clinical studies;
- the time and costs involved in obtaining marketing authorizations;
- competing technological and market developments, including the introduction by others of new therapies that address our markets; and
- our manufacturing requirements and capacity to fulfill such requirements.

Index

If we need additional funds, we may need to raise them through public or private financing. Additional financing may not be available on acceptable terms or at all. If we raise additional funds by issuing equity securities, the shares of existing stockholders will be diluted and the price, as well as the price of our other securities, may decline. For example, in September 2024, we completed an underwritten public offering of 11,500,000 shares of our common stock for total net proceeds, after deducting underwriting discounts and commissions and other offering expenses payable by us, of approximately $489.1 million. If adequate funds are not available or not available on acceptable terms, we may have to cut back on one or more of our research, drug discovery or development programs, or commercial operations. Alternatively, we may obtain funds through arrangements with collaborative partners or others, which could require us to give up rights to certain of our technologies or medicines.

We have incurred losses, and our business will suffer if we fail to consistently achieve profitability in the future.

Because drug discovery and development require substantial lead-time and money prior to commercialization, our expenses have generally exceeded our revenue since we were founded in January 1989. As of September 30, 2025, we had an accumulated deficit of approximately $2.4 billion and stockholders' equity of approximately $0.6 billion. Most of our income has historically come from collaborative arrangements, including commercial revenue from royalties and R&D revenue, with additional income from research grants and the sale or licensing of our patents, as well as interest income. We will now and continuing into the foreseeable future need to invest significant financial resources to commercialize medicines on our own and expect that our income in the future will be driven primarily by commercial sales. If we do not earn substantial revenue from commercial sales, we may incur additional operating losses in the future, which could restrict our ability to successfully develop additional medicines or sustain future profitability.

We may not be entitled to obtain additional milestone payments under our royalty monetization agreement with Royalty Pharma.

In January 2023, we entered into a Royalty Purchase Agreement with Royalty Pharma Investments. In addition to the $500 million we received at closing, this agreement makes available to us up to an additional $625 million in milestone payments. However, these additional milestone payments are subject to satisfaction of certain conditions related to the regulatory approval or commercial sales of pelacarsen, in certain cases by specific deadlines. Should we not satisfy such conditions by the applicable deadlines, or if we fail to meet our obligations or default under this agreement, the actual amount of additional payments to us could be substantially less than the maximum amounts available thereunder.

Risks related to our intellectual property

If we cannot protect our patent rights or our other proprietary rights, others may compete more effectively against us.

Our success depends to a significant degree upon whether we can continue to develop, secure and maintain intellectual property rights to proprietary products and services. However, we may not receive issued patents on any of our pending patent applications in the U.S. or in other countries and we may not be able to obtain, maintain or enforce our patents and other intellectual property rights, any of which could impact our ability to compete effectively. In addition, the scope of any of our issued patents may not be sufficiently broad to provide us with a competitive advantage. Furthermore, other parties may successfully challenge, invalidate or circumvent our issued patents or patents licensed to us so that our patent rights do not create an effective competitive barrier or revenue source.

We cannot be certain that the U.S. Patent and Trademark Office, or U.S. PTO, and courts in the U.S. or the patent offices and courts in foreign countries will consider the claims in our patents and applications covering our commercial medicines, or any of our medicines in development, as patentable. Method-of-use patents protect the use of a product for the specified method. This type of patent does not prevent a competitor from making and marketing a product that is identical to our product for an indication that is outside the scope of the patented method. Moreover, even if competitors do not actively promote their product for our targeted indications, physicians may prescribe these products off-label. Although off-label prescriptions may infringe or contribute to the infringement of method-of-use patents, the practice is common and such infringement is difficult to prevent, even through legal action.

If we or any licensor partner loses or cannot obtain patent protection for our commercial medicines or any of our medicines in development, it could have a material adverse impact on our business.

Intellectual property litigation could be expensive and prevent us from pursuing our programs.*

From time to time, we have to defend our intellectual property rights. If we are involved in an intellectual property dispute, we may need to litigate to defend our rights or assert them against others. Disputes can involve arbitration, litigation or proceedings declared by the U.S. PTO or the International Trade Commission or foreign patent authorities. Even if resolved in our favor, litigation or other legal proceedings relating to intellectual property claims may cause us to incur significant expenses and could distract our technical and management personnel from their normal responsibilities. In addition, there could be public announcements of the results of hearings, motions or other interim proceedings or developments and if securities analysts or investors perceive these results to be negative, it could have a substantial adverse effect on the price of our common stock. For example, in September 2025, we filed a claim against Arrowhead Pharmaceuticals, Inc., or Arrowhead, for patent infringement over Arrowhead's planned commercialization of plozasiran, and Arrowhead filed a separate lawsuit against us seeking to invalidate that same patent.

If a third party claims that our medicines or technology infringe its patents or other intellectual property rights, we may have to discontinue an important product or product line, alter our products and processes, pay license fees or cease certain activities. We may not be able to obtain a license to needed intellectual property on favorable terms, if at all. There are many patents issued or applied for in the biotechnology industry, and we may not be aware of patents or patent applications held by others that relate to our business. This is especially true since patent applications in the U.S. are filed confidentially for the first 18 months. Moreover, the validity and breadth of biotechnology patents involve complex legal and factual questions for which important legal issues remain.

Risks related to product liability

We are exposed to potential product liability claims, and insurance against these claims may not be available to us at a reasonable rate in the future or at all.

Our business exposes us to potential product liability risks that are inherent in the testing, manufacturing, marketing and sale of therapeutic products, including potential product liability claims related to our commercial medicines and our medicines in development. We have clinical study insurance coverage and commercial product liability insurance coverage. However, this insurance coverage may not be adequate to cover claims against us, or be available to us at an acceptable cost, if at all. Regardless of their merit or eventual outcome, product liability claims may result in decreased demand for our medicines, injury to our reputation, withdrawal of clinical study volunteers and loss of revenues. Thus, whether or not we are insured, a product liability claim or product recall may result in losses that could be material.

Risks related to our personnel

The loss of key personnel, or the inability to attract and retain highly skilled personnel, could make it more difficult to run our business and reduce our likelihood of success.

We are dependent on the principal members of our management, scientific and commercial staff. We do not have employment agreements with any of our employees that would prevent them from leaving us. The loss of our key management, scientific or commercial employees might slow the achievement of important research and development or commercial goals. It is also critical to our success that we recruit and retain qualified scientific personnel to perform research and development work and that we recruit and retain qualified marketing, sales, market access, distribution, and related personnel to commercialize our medicines. We may not be able to attract and retain skilled and experienced personnel on acceptable terms because of intense competition for experienced personnel among many pharmaceutical and health care companies, universities and non-profit research institutions. In addition, failure to succeed in clinical studies or in commercializing our medicines may make it more challenging to recruit and retain qualified personnel.

Risks related to health epidemics, climate change and other events

Our business may be adversely affected by health epidemics, climate change, extreme weather events, fires, earthquakes, war, civil or political unrest, terrorism or disruptions of the U.S. government.*

Our business could be adversely affected by health epidemics in regions where we or our partners are commercializing our medicines, have concentrations of clinical trial sites or other business operations, and could cause disruption in the operations of third-party manufacturers and contract research organizations upon whom we rely. For example, enrollment in some of our clinical trials was delayed due to the COVID-19 pandemic.

In recent years, extreme weather events and changing weather patterns have become more common. As a result, we are potentially exposed to varying natural disaster or extreme weather risks such as fires, hurricanes, tornadoes, droughts, floods, or other events that may result from the impact of climate change on the environment, any of which could impact our business and manufacturing operations. The potential impacts of climate change may also include increased operating costs associated with additional regulatory requirements and investments in reducing energy, water use and greenhouse gas emissions. In addition, we currently manufacture most of our research and clinical supplies in a manufacturing facility located in Carlsbad, California, and various regions within California have recently experienced numerous catastrophic wildfires. We manufacture the finished drug product for TRYNGOLZA, WAYLIVRA and eplontersen for ongoing clinical trials at third-party contract manufacturers. Biogen manufactures the finished drug product for SPINRAZA and QALSODY and AstraZeneca is responsible for WAINUA's commercial drug supply. The facilities and the equipment we, our partners and our contract manufacturers use to research, develop and manufacture our medicines would be costly to replace and could require substantial lead time to repair or replace.

Our facilities or those of our partners or contract manufacturers may be harmed by natural disasters or other events outside our control, such as earthquakes, war, civil or political unrest, deliberate acts of sabotage, terrorism or industrial accidents such as fire and explosion, whether due to human or equipment error, and if such facilities are affected by a disaster or other event, our development and commercialization efforts would be delayed. Although we possess property damage and business interruption insurance coverage, this insurance may not be sufficient to cover all of our potential losses and may not continue to be available to us on acceptable terms, or at all.

In addition, our development and commercialization activities could be harmed or delayed by staffing shortages or a shutdown or other significant disruption of the U.S. government, including the FDA or the U.S. PTO.

Risks related to personal information, cybersecurity, social media and artificial intelligence

We are dependent on data as well as information technology systems and infrastructure, which exposes us to data protection risks.

We are dependent upon our own and third-party data as well as information technology systems and infrastructure, including mobile technologies, to operate our business. The personal information we process subjects us to stringent and evolving U.S. and foreign laws, rules and regulations, contractual obligations, industry standards and other obligations related to data privacy and security. Our personal information obligations require us to implement and maintain certain practices, including those in relation to cross-border transfers of personal information. The multitude and complexity of our information technology systems and infrastructure make them vulnerable to a variety of evolving threats that may result in systems or data interruption, corruption, destruction, disruption of data integrity, malicious intrusion, or random attacks or other compromise (such as due to malfunctions, software vulnerabilities, natural disasters, telecommunications failures,

malicious actors and personnel error). Data privacy or security incidents or breaches pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons. Cyber-attacks are increasing in their frequency, sophistication and intensity, particularly as companies (including us) continue to move to more remote work structures. In addition, the number and frequency of cybersecurity events globally may be heightened during times of geopolitical tension or instability between countries, including, for example, the ongoing war between Russia and Ukraine and military conflicts in the Middle East and the surrounding areas, or collectively, conflicts in Eastern Europe and the Middle East, as well as related political or economic responses and counter-responses by various global actors.

Cybersecurity related events could include the deployment or use of harmful malware or malicious code, denial-of-service attacks, credential stuffing attacks, credential harvesting attacks, social engineering attacks (including deep fakes), ransomware and other means to affect the confidentiality, integrity or availability of our data as well as information systems and infrastructure. Our current, past and prospective business partners face similar risks and any security breaches of their systems could adversely affect our security posture. A security breach or privacy violation (including perceived breaches or violations) could result in any of the following, any of which could disrupt our business and result in increased costs or loss of revenue:

- harm our reputation;
- delay progress on the development of our medicines;
- compel us to comply with applicable security or data breach notification obligations (including laws);
- result in the diversion of monetary funds and other company resources;
- subject us to financial or other penalties, regulatory investigations or actions, including mandatory and costly corrective actions; and
- require us to verify the correctness of database contents and otherwise subject us to litigation or other liabilities.

Risk mitigation strategies such as liability limitations in our contracts and insurance coverage may prove inadequate if there is a security breach or privacy violation. While we have invested, and continue to invest, in the protection of our data and information technology systems and infrastructure, our efforts may not be successful. Non-compliance with relevant data protection obligations or a failure to secure our data, information technology systems or infrastructure could adversely affect our business and operations and result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us.

The increasing use of social media platforms and artificial intelligence based software presents new risks and challenges.

Social media is increasingly being used to communicate about our medicines and the diseases our therapies are designed to treat. Social media practices in the biopharmaceutical industry continue to evolve and regulations relating to such use are not always clear and create uncertainty and risk of noncompliance with regulations applicable to our business. There is also a risk of inappropriate disclosure of sensitive information or negative or inaccurate posts or comments about us on social media. We may also encounter criticism on social media regarding our company, management, or medicines. Our reputation could be damaged by negative publicity or if adverse information concerning us is posted on social media platforms or similar mediums, which we may not be able to reverse. If any of these events were to occur or we otherwise fail to comply with applicable regulations, we could incur liability, face restrictive regulatory actions or incur other harm to our business.

Additionally, artificial intelligence, or AI, based software is increasingly being used in the biopharmaceutical industry. Use of AI based software may lead to the release of confidential proprietary information, which may impact our ability to realize the benefit of our intellectual property.

Risks related to our securities and the global credit markets

If we do not progress in our programs as anticipated, the price of our securities could decrease.

For planning purposes, we estimate and may disclose the timing of a variety of clinical, regulatory and other milestones, such as when we anticipate a certain medicine will enter clinical trials, when we anticipate disclosing clinical data, when we anticipate completing a clinical study, when we anticipate filing an application for, or obtaining, marketing authorization, or when we or our partners plan to commercially launch a medicine. We base our estimates on present facts and a variety of assumptions, many of which are outside of our control. If we do not achieve milestones in accordance with our or our investors' or securities analysts' expectations, including milestones related to our commercial medicines and medicines in development, the price of our securities could decrease. In addition, our share price may be dependent upon the valuations and recommendations of the analysts who cover our business. If our results do not meet these analysts' forecasts, the expectations of our investors or the financial guidance we provide to investors in any period, the market price of our common stock could decline. Our ability to meet analysts' forecasts, investors' expectations and our financial guidance is substantially dependent on our ability to maintain or increase sales of our commercial medicines, both partnered and unpartnered.

If the price of our securities continues to be highly volatile, this could make it harder to liquidate your investment and could increase your risk of suffering a loss.*

The market price of our common stock, like that of the securities of many other biopharmaceutical companies, has been and is likely to continue to be highly volatile. These fluctuations in our common stock price may significantly affect the trading price of our securities. During the 12 months preceding September 30, 2025, the closing market price of our common stock ranged from $65.42 to $25.51 per share. Many factors can affect the market price of our securities, including, for example, fluctuations in our operating results, financing transactions, announcements of collaborations, clinical study results, technological innovations or new products being developed by us or our competitors, the commercial success of our approved medicines, governmental regulation, marketing authorizations, changes in payers' reimbursement policies, developments in patent or other proprietary rights and public concern regarding the safety of our medicines.

Broad market factors may materially harm the market price of our common stock irrespective of our operating performance. For example, events such as recent tariffs announcements and the ongoing conflicts in Eastern Europe and the Middle East have caused disruptions of global financial markets and resulted in increased volatility in the trading price of our common stock. In addition, industry factors may materially harm the market price of our common stock. Nasdaq, and the market for biotechnology companies in particular, have historically experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of the particular companies affected. The trading prices and valuations of these stocks, and of ours, may not be predictable. A loss of investor confidence in the market for biotechnology or pharmaceutical stocks or the stocks of other companies that investors perceive to be similar to us, the opportunities in the biotechnology and pharmaceutical market or the stock market in general, could depress our stock price regardless of our business, prospects, financial conditions or results of operations.

Negative conditions in the global credit markets and financial services and other industries may adversely affect our business, financial condition or stock price.*

The global credit and financial markets have experienced extreme volatility and disruptions recently, including as a result of tariffs announcements and the ongoing conflicts in Eastern Europe and the Middle East. These disruptions can result in severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. There can be no assurance that further deterioration in credit and financial markets and confidence in economic conditions will not occur. If the current equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult, more costly and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our operations, growth plans, financial performance or stock price. In addition, our insurance carriers and insurance policies covering all aspects of our business may become financially unstable or may not be sufficient to cover any or all of our losses and may not continue to be available to

us on acceptable terms, or at all.

A variety of risks associated with operating our business and marketing our medicines internationally could adversely affect our business. In addition to our U.S. operations, we are commercializing WAYLIVRA in the EU, Latin America and certain Caribbean countries. We face risks associated with our international operations, including possible unfavorable regulatory, pricing and reimbursement, political, tax and labor conditions, which could harm our business. Because we have international operations, we are subject to numerous risks associated with international business activities, including:

- compliance with differing or unexpected regulatory requirements for our medicines and foreign employees;
- complexities associated with managing multiple payer reimbursement regimes, government payers or patient self-pay systems;
- difficulties in staffing and managing foreign operations;
- in certain circumstances, increased dependence on the commercialization efforts and regulatory compliance of third-party distributors or strategic partners;
- foreign government taxes, regulations and permit requirements;
- U.S. and foreign government tariffs, trade and export restrictions, price and exchange controls and other regulatory requirements;
- anti-corruption laws, including the Foreign Corrupt Practices Act, or the FCPA, and its equivalent in foreign jurisdictions;
- economic weakness, including inflation, natural disasters, war, acts of terrorism, political instability or public health issues or health epidemics, in particular foreign countries or globally;
- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenue, and other obligations related to doing business in another country;
- the potential for a local seller, faced with higher local prices, importing medicines from an international market with lower prices rather than buying such medicines locally, which is referred to as parallel importation;
- compliance with tax, employment, privacy, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the U.S.; and
- changes in diplomatic and trade relationships.

Our business activities outside of the U.S. are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate, including the United Kingdom's Bribery Act 2010. In many other countries, the healthcare providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. There is no certainty that all employees and third-party business partners (including our contract research organizations, contract manufacturing organizations, distributors, wholesalers, agents, contractors and other partners) will comply with anti-bribery laws. Importantly, we do not control the actions of manufacturers and other third-party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have an adverse impact on our business and financial condition.

Index

Provisions in our certificate of incorporation, bylaws, convertible notes documents, call spread hedge transaction documents and Delaware law may prevent stockholders from receiving a premium for their shares.*

Our certificate of incorporation provides for classified terms for the members of our board of directors. Our certificate also includes a provision that requires at least 66 2/3 percent of our voting stockholders to approve a merger or certain other business transactions with, or proposed by, any holder of 15 percent or more of our voting stock, except in cases where certain directors approve the transaction or certain minimum price criteria and other procedural requirements are met.

Our certificate of incorporation also requires that any action required or permitted to be taken by our stockholders must be taken at a duly called annual or special meeting of stockholders and may not be taken by written consent. In addition, only our board of directors, chairperson of the board or chief executive officer can call special meetings of our stockholders. We have in the past, and may in the future, implement a stockholders' rights plan, also called a poison pill, which could make it uneconomical for a third party to acquire our company on a hostile basis. In addition, our board of directors has the authority to fix the rights and preferences of, and issue shares of preferred stock, which may have the effect of delaying or preventing a change in control of our company without action by our stockholders.

The provisions of our convertible senior notes could make it more difficult or more expensive for a third party to acquire us. Upon the occurrence of certain transactions constituting a fundamental change, holders of the notes will have the right, at their option, to require us to repurchase all of their notes or a portion of their notes, which may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over the then-current market prices.

In 2023, we completed a $575 million offering of 1.75% Notes and used $488.2 million of the net proceeds from the issuance of the 1.75% Notes to repurchase $504.4 million of our 0.125% Notes. In 2024, we used $44.5 million of the net proceeds to settle the remaining principal balance of our 0.125% Notes upon maturity. In 2021, we completed a $632.5 million offering of 0% Notes and used $319.0 million of the net proceeds from the issuance of the 0% Notes to repurchase the remaining $309.9 million of our 1% Notes. In 2019, we entered into privately negotiated exchange and/or subscription agreements with certain new investors and certain holders of our existing 1% Notes to exchange $375.6 million of our 1% Notes for $439.3 million of our 0.125% Notes, and to issue $109.5 million of our 0.125% Notes. Additionally, in connection with the pricing of our 0% Notes and 0.125% Notes, we entered into call spread transactions in which we purchased note hedges and sold warrants. For our 0.125% Notes, the note hedges expired upon maturity of the 0.125% Notes and the warrants fully expired in June 2025. Terminating or unwinding the call spread transactions for our 0% Notes could require us to make substantial payments to the counterparties under those agreements or may increase our stock price. The costs or any increase in stock price that may arise from terminating or unwinding such agreements could make an acquisition of our company significantly more expensive to the purchaser.

These provisions, as well as Delaware law, including Section 203 of the Delaware General Corporation Law, and other of our agreements, may discourage certain types of transactions in which our stockholders might otherwise receive a premium for their shares over then-current market prices, and may limit the ability of our stockholders to approve transactions that they think may be in their best interests.

Future sales of our common stock in the public market could adversely affect the trading price of our securities.

Future sales of substantial amounts of our common stock in the public market, or the perception that such sales could occur, could adversely affect trading prices of our securities. For example, we may issue approximately 21.6 million shares of our common stock upon conversion of our 1.75% Notes and 0% Notes. In connection with the issuance of the 0% Notes, we entered into certain call spread transactions covering 10.9 million shares that we expect will offset the dilution to holders of common stock upon any conversion of those notes. However, the anti-dilutive effect of the convertible note hedges is offset by certain warrant transactions we entered into in connection with the issuance of the 0% Notes. The addition of any of these shares into the public market may have an adverse effect on the price of our securities.

In addition, pursuant to the call spread transactions we entered into in connection with the pricing of our 0% Notes, the counterparties are likely to modify their hedge positions from time to time at or prior to the conversion or maturity of the notes by purchasing and selling shares of our common stock, other of our securities, or other instruments, including over-the-counter derivative instruments, that they may wish to use in connection with such hedging, which may have a negative effect on the conversion value of those notes and an adverse impact on the trading price of our common stock. The call spread transactions are expected generally to reduce potential dilution to holders of our common stock upon any conversion of our 0% Notes or offset any cash payments we are required to make in

excess of the principal amount of the converted 0% Notes, as the case may be. However, the warrant transactions could separately have a dilutive effect to the extent that the market value per share of our common stock exceeds the applicable strike price of the warrants.

Index

Risks related to compliance with laws

Our operations are subject to extensive legal and regulatory requirements affecting the health care industry.

Our operations are subject to extensive legal and regulatory requirements affecting the health care industry, including federal and state anti-kickback laws, false claims laws, transparency laws, such as the federal Sunshine Act, and health information privacy and security laws, which are subject to change at any time. It is possible that governmental authorities will conclude that our business practices may not comply with current or future statutes, regulations or case law involving applicable fraud and abuse or other healthcare laws and regulations. Penalties for violations of applicable healthcare laws and regulations may include significant civil, criminal and administrative penalties, damages, disgorgement, fines, imprisonment, exclusion of products from government funded healthcare programs, such as Medicare and Medicaid, and additional reporting requirements and oversight if we enter into a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws. In addition, violations may also result in reputational harm, diminished profits and future earnings.

Because we use biological materials, hazardous materials, chemicals and radioactive compounds, if we do not comply with laws regulating the protection of the environment and health and human safety, our business could be adversely affected.

Our research, development and manufacturing activities involve the use of potentially harmful biological materials as well as materials, chemicals and various radioactive compounds that could be hazardous to human health and safety or the environment. We store most of these materials and various wastes resulting from their use at our facilities in Carlsbad, California pending ultimate use and disposal. We cannot completely eliminate the risk of contamination, which could cause:

- interruption of our research, development and manufacturing efforts;
- injury to our employees and others;
- environmental damage resulting in costly clean up; and
- liabilities under federal, state and local laws and regulations governing health and human safety, as well as the use, storage, handling and disposal of these materials and resultant waste products.

In such an event, we may be held liable for any resulting damages, and any liability could exceed our resources. Although we carry insurance for pollution liability in amounts and types that we consider commercially reasonable, the coverage or coverage limits of our insurance policies may not be adequate. If our losses exceed our insurance coverage, our financial condition would be adversely affected.

Our business is subject to changing regulations for corporate governance and public disclosure that has increased both our costs and the risk of noncompliance.

Each year we are required to evaluate our internal control systems to allow management to report on, and our Independent Registered Public Accounting Firm to attest to, our internal controls as required by Section 404 of the Sarbanes-Oxley Act. As a result, we continue to incur additional expenses and divert our management's time to comply with these regulations. In addition, if we cannot continue to comply with the requirements of Section 404 in a timely manner, we might be subject to sanctions or investigation by regulatory authorities, such as the SEC, the Public Company Accounting Oversight Board, or PCAOB, or The Nasdaq Global Select Market. Any such action could adversely affect our financial results and the market price of our common stock.

The SEC and other regulators have continued to adopt new rules and regulations and make additional changes to existing regulations that require our compliance. In July 2010, the Dodd-Frank Wall Street Reform and Protection Act, or the Dodd-Frank Act, was enacted, and in August 2022, the SEC adopted additional rules and regulations under the Dodd-Frank Act related to "say on pay" and proxy access. Stockholder activism, the current political environment and the current high level of government intervention and regulatory reform may lead to substantial new regulations and disclosure obligations, which has and may in the future lead to additional compliance costs and impact the manner in which we operate our business.

Risks related to taxes

Our ability to use our net operating loss carryovers and certain other tax attributes may be limited.

Under the Internal Revenue Code of 1986, as amended, or the Code, a corporation is generally allowed a deduction for net operating losses, or NOLs, carried over from a prior taxable year. Under the Code, we can carry forward our NOLs to offset our future taxable income, if any, until such NOLs are used or expire. The same is true of other unused tax attributes, such as tax credits.

Index

Under the current U.S. federal income tax law, U.S. federal NOLs generated in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of such U.S. federal NOLs is limited to 80 percent of taxable income.

In addition, under Sections 382 and 383 of the Code, and corresponding provisions of state law, if a corporation undergoes an "ownership change," which is generally defined as a greater than 50 percentage-point cumulative change, by value, in its equity ownership over a three-year period, the corporation's ability to use its pre-change NOL carryforwards and other pre-change tax attributes to offset its post-change income or taxes may be limited. We may experience ownership changes in the future as a result of subsequent shifts in our stock ownership, some of which may be outside of our control. If an ownership change occurs and our ability to use our NOL carryforwards or other tax attributes is materially limited, it would harm our future operating results by effectively increasing our future tax obligations. As a result of our merger with Akcea Therapeutics, Inc. in 2020, or the Akcea Merger, we are subject to the separate return limitation year, or SRLY, rules. Under the SRLY rules, our utilization of Akcea's pre-merger NOL and tax credit carryforwards is limited to the amount of income that Akcea contributes to our consolidated taxable income. The Akcea pre-merger tax attributes cannot be used to offset any of the income that Ionis contributes to our consolidated taxable income. In addition, at the state level, there may be periods during which the use of NOLs is suspended or otherwise limited, which could accelerate or permanently increase state taxes owed. For example, in June 2024, California enacted Senate Bill 167, or SB 167, which, with certain exceptions, suspends the ability to use California net operating losses to offset California income and limits the ability to use California business tax credits to offset California taxes, for taxable years beginning after 2023 and before 2027.

Our future taxable income could be impacted by changes in tax laws, regulations and treaties.

A change in tax laws, treaties or regulations, or their interpretation, of any country in which we operate could materially affect us.

We could be subject to additional tax liabilities.

We are subject to U.S. federal, state, local and foreign income taxes, sales taxes in the U.S., withholding taxes and transaction taxes in foreign jurisdictions. Significant judgment is required in evaluating our tax positions and our worldwide provision for taxes. During the ordinary course of business, there are many activities and transactions for which the ultimate tax determination is uncertain. In addition, our tax obligations and effective tax rates could be adversely affected by changes in the relevant tax, accounting and other laws, regulations, principles and interpretations, including those relating to income tax nexus, by recognizing tax

losses or lower than anticipated earnings in jurisdictions where we have lower statutory rates and higher than anticipated earnings in jurisdictions where we have higher statutory rates, by changes in foreign currency exchange rates, or by changes in the valuation of our deferred tax assets and liabilities. In particular, our tax obligations and effective tax rate in the jurisdictions in which we conduct business could increase in the future as a result of the base erosion and profit shifting, or BEPS, project led by the Organization for Economic Co-operation and Development, or OECD, and other initiatives led by the OECD or the European Commission. The OECD is leading work on an iteration of the BEPS project based on two "pillars" (subject to certain revenue thresholds), involving the reallocation of taxing rights in respect of certain multinational enterprises above a fixed profit margin to the jurisdictions in which they carry on business) (referred to as "Pillar One") and imposing a minimum effective corporate tax rate on certain multinational enterprises (referred to as "Pillar Two"). Based on the minimum revenue thresholds we do not expect to fall within the scope of these requirements in the near term.

We may be audited in various jurisdictions, and such jurisdictions may assess additional income, sales and value-added or other taxes against us. Although we believe our tax estimates are reasonable, the final determination of any tax audits or litigation could be materially different from our historical tax provisions and accruals, which could have a material adverse effect on our operating results or cash flows in the period for which a determination is made.

Index

ITEM 2. UNREGISTERED SALES OF EQUITY SECURITIES AND USE OF PROCEEDS

Not applicable.

ITEM 3. DEFAULT UPON SENIOR SECURITIES

Not applicable.

ITEM 4. MINE SAFETY DISCLOSURES

Not applicable.

ITEM 5. OTHER INFORMATION

Trading Plans

During the quarter ended September 30, 2025, our directors and officers (as defined in Rule 16a-1(f) under the Exchange Act), or Section 16 officers and directors, adopted or terminated contracts, instructions or written plans for the purchase or sale of our securities as noted in the table below.

* Contract, instruction or written plan intended to satisfy the affirmative defense conditions of Rule 10b5-1(c) under the Exchange Act.
** "Non-Rule 10b5-1 trading arrangement" as defined in item 408(c) of Regulation S-K under the Exchange Act.

				Trading Arrangement		Total Shares	
Name	Title	Action	Date	Rule 10b5-1*	Non-Rule 10b5-1**	to be Sold	Expiration Date
Spencer Berthelsen	Board Member	Adoption	September 12, 2025	X		16,000	The earlier to occur of (i) July 1, 2026, and (ii) Upon the execution of all instructions provided in the plan

Index

ITEM 6. EXHIBITS

a. Exhibits

Exhibit Number	Description of Document
31.1	Certification by Chief Executive Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.
31.2	Certification by Chief Financial Officer pursuant to Rules 13a-14(a) and 15d-14(a) under the Securities Exchange Act of 1934, as amended.
32.1*	Certification Pursuant to 18 U.S.C. Section 1350 as Adopted Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002.
101	The following financial statements from the Ionis Pharmaceuticals, Inc. Quarterly Report on Form 10-Q for the quarter ended September 30, 2025, formatted in Inline Extensible Business Reporting Language (iXBRL): (i) condensed consolidated balance sheets, (ii) condensed consolidated statements of operations, (iii) condensed consolidated statements of comprehensive income (loss), (iv) condensed consolidated statements of stockholders' equity, (v) condensed consolidated statements of cash flows and (vi) notes to condensed consolidated financial statements (detail tagged).
104	Cover Page Interactive Data File (formatted in iXBRL and included in exhibit 101).

* This certification is deemed not filed for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, or otherwise subject to the liability of that section, nor shall it be deemed incorporated by reference into any filing under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended.

Index

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the Registrant and in the capacities and on the dates indicated.

Signatures	Title	Date
/s/ BRETT P. MONIA Brett P. Monia, Ph.D.	Director and Chief Executive Officer (Principal executive officer)	October 29, 2025

/s/ ELIZABETH L. HOUGEN	Executive Vice President, Finance and Chief Financial Officer	
Elizabeth L. Hougen	(Principal financial and accounting officer)	October 29, 2025