

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 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, 2021

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

For the transition period from _____ to _____ .

Commission File Number: 000-26727

BioMarin Pharmaceutical Inc.

(Exact name of registrant as specified in its charter)

Delaware

(State or other jurisdiction of
incorporation or organization)

68-0397820

(I.R.S. Employer
Identification No.)

770 Lindaro Street

San Rafael

California

94901

(Address of principal executive offices)

(Zip Code)

(415) 506-6700

(Registrant's telephone number including area code)

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

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, par value \$0.001	BMRN	The Nasdaq Global Select Market

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 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, a 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.

Filer	Large Accelerated	<input checked="" type="checkbox"/>	Accelerated Filer	<input type="checkbox"/>
	Non-accelerated Filer	<input type="checkbox"/>	Smaller Reporting Company	<input type="checkbox"/>
Company	Emerging Growth	<input type="checkbox"/>		

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 12b-2 of the Exchange Act.) Yes No

Applicable only to corporate issuers:

Indicate the number of shares outstanding of each of the issuer's classes of common stock, as of the latest practicable date: 183,593,434 shares of common stock, par value \$0.001, outstanding as of October 26, 2021.

Unless the context suggests otherwise, references in this Quarterly Report on Form 10-Q to “BioMarin,” the “Company,” “we,” “us,” and “our” refer to BioMarin Pharmaceutical Inc. and, where appropriate, its wholly owned subsidiaries.

BioMarin®, Brineura®, Kuvan®, Naglazyme®, Palynziq® and Vimizim® are our registered trademarks. VOXZOGO™ is our trademark. Aldurazyme® is a registered trademark of BioMarin/Genzyme LLC. All other brand names and service marks, trademarks and other trade names appearing in this report are the property of their respective owners.

Forward-Looking Statements

This Quarterly Report on Form 10-Q contains “forward-looking statements” as defined under securities laws. Many of these statements can be identified by the use of terminology such as “believes,” “expects,” “intends,” “anticipates,” “plans,” “may,” “will,” “could,” “would,” “projects,” “continues,” “estimates,” “potential,” “opportunity” or the negative versions of these terms and other similar expressions. Our actual results or experience could differ significantly from the forward-looking statements. Factors that could cause or contribute to these differences include those discussed in “Risk Factors,” in Part II, Item 1A of this Quarterly Report on Form 10-Q as well as information provided elsewhere in this Quarterly Report on Form 10-Q and our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the Securities and Exchange Commission (the SEC) on February 26, 2021. You should carefully consider that information before you make an investment decision.

You should not place undue reliance on these types of forward-looking statements, which speak only as of the date that they were made. These forward-looking statements are based on the beliefs and assumptions of the Company’s management based on information currently available to management and should be considered in connection with any written or oral forward-looking statements that the Company may issue in the future as well as other cautionary statements the Company has made and may make. Except as required by law, the Company does not undertake any obligation to release publicly any revisions to these forward-looking statements after completion of the filing of this Quarterly Report on Form 10-Q to reflect later events or circumstances or the occurrence of unanticipated events.

The discussion of the Company’s financial condition and results of operations should be read in conjunction with the Company’s Condensed Consolidated Financial Statements and the related Notes thereto included in this Quarterly Report on Form 10-Q.

Risk Factors Summary

The following is a summary of the principal risks that could adversely affect our business, financial condition, operating results, cash flows or stock price. Discussion of the risks listed below, and other risks that we face, are discussed in the section titled “Risk Factors” in Part II, Item 1A of this Quarterly Report on Form 10-Q.

Business and Operational Risks

- The COVID-19 pandemic could continue to materially adversely affect our business, results of operations, and financial condition.
 - Because the target patient populations for our products are small, we must achieve significant market share and maintain high per-patient prices for our products to achieve and maintain profitability.
 - If we fail to obtain and maintain an adequate level of coverage and reimbursement for our products by third-party payers, the sales of our products would be adversely affected or there may be no commercially viable markets for our products.
 - If we fail to compete successfully with respect to product sales, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product and our revenues could be adversely affected.
 - Changes in methods of treatment of disease could reduce demand for our products and adversely affect revenues.
 - If we fail to develop new products and product candidates or compete successfully with respect to acquisitions, joint ventures, licenses or other collaboration opportunities, our ability to continue to expand our product pipeline and our growth and development would be impaired.
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- The sale of generic versions of Kuvan by generic manufacturers has adversely affected and will continue to adversely affect our revenues and results of operations.
- If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

Regulatory Risks

- If we fail to obtain regulatory approval to commercially market and sell our product candidates, or if approval of our product candidates is delayed, we will be unable to generate revenues from the sale of these product candidates, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will increase.
- Any product for which we have obtained regulatory approval, or for which we obtain approval in the future, is subject to, or will be subject to, extensive ongoing regulatory requirements by the Food and Drug Administration (FDA), the European Medicines Agency (EMA) and other comparable international regulatory authorities, and if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, we may be subject to penalties, we will be unable to generate revenues from the sale of such products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.
- To obtain regulatory approval to market our products, preclinical studies and costly and lengthy clinical trials are required and the results of the studies and trials are highly uncertain. Likewise, preliminary, initial or interim data from clinical trials should be considered carefully and with caution because the final data may be materially different from the preliminary, initial or interim data, particularly as more patient data become available.
- Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenues and results of operations.
- Government healthcare reform could increase our costs and adversely affect our revenues and results of operations.

Risks Related to Valoctocogene Roxaparvovec

- Our valoctocogene roxaparvovec program is based on a gene therapy approach, which, as a novel technology, presents additional development and treatment risks in relation to our other, more traditional drug development programs.
- As compared to our other, more traditional products, our gene therapy product candidate valoctocogene roxaparvovec, if approved, may present additional problems with respect to the pricing, coverage, and reimbursement and acceptance of the product candidate.

Financial and Financing Risks

- If we continue to incur operating losses or are unable to sustain positive cash flows for a period longer than anticipated, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Manufacturing Risks

- If we fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.
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- If we are unable to successfully develop and maintain manufacturing processes for our product candidates to produce sufficient quantities at acceptable costs, we may be unable to support a clinical trial or be forced to terminate a program, or if we are unable to produce sufficient quantities of our products at acceptable costs, we may be unable to meet commercial demand, lose potential revenue, have reduced margins or be forced to terminate a program.
- Supply interruptions may disrupt our inventory levels and the availability of our products and product candidates and cause delays in obtaining regulatory approval for our product candidates, or harm our business by reducing our revenues.

Risks Related to International Operations

- We conduct a significant amount of our sales and operations outside of the United States (U.S.), which subjects us to additional business risks that could adversely affect our revenues and results of operations.
- A significant portion of our international sales are made based on special access programs, and changes to these programs could adversely affect our product sales and revenues in these countries.

Intellectual Property Risks

- If we are unable to protect our intellectual property, we may not be able to compete effectively or preserve our market shares.
 - Competitors and other third parties may have developed intellectual property that could limit our ability to market and commercialize our products and product candidates, if approved.
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PART I. FINANCIAL INFORMATION

Item 1. Financial Statements

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
September 30, 2021 and December 31, 2020
(In thousands, except share amounts)

ASSETS	September 30, 2021	December 31, 2020 ⁽¹⁾
	(unaudited)	
Current assets:		
Cash and cash equivalents	\$ 617,143	\$ 649,158
Short-term investments	462,333	416,228
Accounts receivable, net	374,937	448,351
Inventory	749,406	698,548
Other current assets	107,751	129,934
Total current assets	2,311,570	2,342,219
Noncurrent assets:		
Long-term investments	466,618	285,473
Property, plant and equipment, net	1,024,787	1,032,471
Intangible assets, net	388,487	417,271
Goodwill	196,199	196,199
Deferred tax assets	1,445,109	1,432,150
Other assets	144,705	142,237
Total assets	\$ 5,977,475	\$ 5,848,020
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	\$ 466,711	\$ 492,548
Short-term contingent consideration	48,187	—
Total current liabilities	514,898	492,548
Noncurrent liabilities:		
Long-term convertible debt, net	1,078,093	1,075,145
Long-term contingent consideration	15,204	60,130
Other long-term liabilities	103,131	114,195
Total liabilities	1,711,326	1,742,018
Stockholders' equity:		
Common stock, \$0.001 par value: 500,000,000 shares authorized; 183,567,424 and 181,740,999 shares issued and outstanding, respectively.	184	182
Additional paid-in capital	5,133,742	4,993,407
Company common stock held by Nonqualified Deferred Compensation Plan (the NQDC)	(10,225)	(9,839)
Accumulated other comprehensive income (loss)	10,239	(16,139)
Accumulated deficit	(867,791)	(861,609)
Total stockholders' equity	4,266,149	4,106,002
Total liabilities and stockholders' equity	\$ 5,977,475	\$ 5,848,020

(1) December 31, 2020 balances were derived from the audited Consolidated Financial Statements included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on February 26, 2021.

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE INCOME (LOSS)
Three and Nine Months Ended September 30, 2021 and 2020
(In thousands, except per share amounts)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
REVENUES:				
Net product revenues	\$ 393,840	\$ 460,741	\$ 1,348,279	\$ 1,368,816
Royalty and other revenues	14,902	16,043	48,186	39,522
Total revenues	408,742	476,784	1,396,465	1,408,338
OPERATING EXPENSES:				
Cost of sales	103,537	188,793	350,765	398,134
Research and development	157,869	147,053	467,701	471,449
Selling, general and administrative	183,333	179,450	541,812	542,157
Intangible asset amortization and contingent consideration	17,222	17,429	52,648	48,018
Gain on sale of nonfinancial assets	—	—	—	(59,495)
Total operating expenses	461,961	532,725	1,412,926	1,400,263
INCOME (LOSS) FROM OPERATIONS	(53,219)	(55,941)	(16,461)	8,075
Equity in the income (loss) of BioMarin/Genzyme LLC	177	(921)	(1,349)	(1,077)
Interest income	1,827	4,004	8,737	13,539
Interest expense	(3,870)	(9,597)	(11,491)	(24,560)
Other income, net	8,925	1,239	11,788	1,886
INCOME (LOSS) BEFORE INCOME TAXES	(46,160)	(61,216)	(8,776)	(2,137)
Benefit from income taxes	(9,666)	(846,019)	(2,594)	(839,138)
NET INCOME (LOSS)	\$ (36,494)	\$ 784,803	\$ (6,182)	\$ 837,001
NET INCOME (LOSS) PER SHARE, BASIC	\$ (0.20)	\$ 4.33	\$ (0.03)	\$ 4.63
NET INCOME (LOSS) PER SHARE, DILUTED	\$ (0.20)	\$ 4.01	\$ (0.03)	\$ 4.39
Weighted average common shares outstanding, basic	183,214	181,142	182,616	180,592
Weighted average common shares outstanding, diluted	183,214	197,674	182,616	194,959
COMPREHENSIVE INCOME (LOSS)	\$ (25,316)	\$ 765,138	\$ 20,196	\$ 827,222

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF STOCKHOLDERS' EQUITY
Three and Nine Months Ended September 30, 2021 and 2020
(In thousands)
(unaudited)

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Shares of common stock, beginning balances ⁽¹⁾	183,322	181,148	181,741	179,838
Issuances under equity incentive plans	246	344	1,827	2,172
Repurchase of common stock	—	—	—	(518)
Shares of common stock, ending balances	<u>183,568</u>	<u>181,492</u>	<u>183,568</u>	<u>181,492</u>
Total stockholders' equity, beginning balances ⁽¹⁾	\$ 4,241,571	\$ 3,236,679	\$ 4,106,002	\$ 3,122,381
Common stock:				
Beginning balances ⁽¹⁾	183	181	182	180
Issuances under equity incentive plans, net of tax	1	—	2	1
Ending balance	<u>184</u>	<u>181</u>	<u>184</u>	<u>181</u>
Additional paid-in capital:				
Beginning balance ⁽¹⁾	5,083,831	4,885,637	4,993,407	4,832,707
Issuances under equity incentive plans, net of tax	(460)	7,319	(11,551)	17,601
Stock-based compensation	50,353	44,757	151,500	136,688
Repurchase of common stock	—	—	—	(50,000)
Common stock held by the NQDC	18	78	386	795
Ending balance	<u>5,133,742</u>	<u>4,937,791</u>	<u>5,133,742</u>	<u>4,937,791</u>
Treasury stock:				
Beginning balance ⁽¹⁾	—	—	—	—
Purchase of treasury stock	—	—	—	(50,000)
Retirement of treasury stock	—	—	—	50,000
Ending balance	<u>—</u>	<u>—</u>	<u>—</u>	<u>—</u>
Company common stock held by the NQDC:				
Beginning balance ⁽¹⁾	(10,207)	(10,678)	(9,839)	(9,961)
Common stock held by the NQDC	(18)	(78)	(386)	(795)
Ending balance	<u>(10,225)</u>	<u>(10,756)</u>	<u>(10,225)</u>	<u>(10,756)</u>
Accumulated other comprehensive income (loss):				
Beginning balance ⁽¹⁾	(939)	30,050	(16,139)	20,164
Other comprehensive income (loss)	11,178	(19,665)	26,378	(9,779)
Ending balance	<u>10,239</u>	<u>10,385</u>	<u>10,239</u>	<u>10,385</u>
Accumulated Deficit:				
Beginning balance ⁽¹⁾	(831,297)	(1,668,511)	(861,609)	(1,720,709)
Net income (loss)	(36,494)	784,803	(6,182)	837,001
Ending balance	<u>(867,791)</u>	<u>(883,708)</u>	<u>(867,791)</u>	<u>(883,708)</u>
Total stockholders' equity, ending balances	<u>\$ 4,266,149</u>	<u>\$ 4,053,893</u>	<u>\$ 4,266,149</u>	<u>\$ 4,053,893</u>

(1) The beginning balances for the nine-month periods were derived from the audited Consolidated Financial Statements included in Company's Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on February 26, 2021.

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
Nine Months Ended September 30, 2021 and 2020
(In thousands)
(unaudited)

	Nine Months Ended September 30,	
	2021	2020
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income (loss)	\$ (6,182)	\$ 837,001
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Depreciation and amortization	82,053	77,814
Non-cash interest expense	3,114	14,766
Amortization of premium on investments	3,279	175
Stock-based compensation	153,372	142,125
Gain on sale of nonfinancial assets	—	(59,495)
Inventory reserves, net of stock-based compensation	—	75,609
Deferred income taxes	(12,020)	(854,199)
Unrealized foreign exchange (gain) loss	(1,347)	9,082
Non-cash changes in the fair value of contingent consideration	6,254	1,352
Other	(1,317)	388
Changes in operating assets and liabilities:		
Accounts receivable, net	65,513	(32,915)
Inventory	(19,125)	(73,310)
Other current assets	27,029	32,848
Other assets	(407)	(5,543)
Accounts payable and accrued liabilities	(7,129)	(76,174)
Other long-term liabilities	269	9,225
Net cash provided by operating activities	<u>293,356</u>	<u>98,749</u>
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property, plant and equipment	(66,840)	(83,286)
Maturities and sales of investments	502,112	345,224
Purchases of available-for-sale securities	(737,144)	(369,942)
Proceeds from sale of nonfinancial assets	—	67,159
Purchase of intangible assets	(8,026)	(14,369)
Investment in convertible note	—	(8,709)
Other	(994)	(725)
Net cash used in investing activities	<u>(310,892)</u>	<u>(64,648)</u>
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from exercises of awards under equity incentive plans	32,877	60,268
Taxes paid related to net share settlement of equity awards	(44,428)	(42,667)
Repurchase of common stock	—	(50,000)
Proceeds from convertible senior subordinated note offering, net	—	585,752
Principal repayments of financing leases	(2,492)	(6,080)
Other	(401)	—
Net cash provided by (used in) financing activities	<u>(14,444)</u>	<u>547,273</u>
Effect of exchange rate changes on cash	(35)	(3,145)
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	<u>(32,015)</u>	<u>578,229</u>
Cash and cash equivalents:		
Beginning of period	\$ 649,158	\$ 437,446
End of period	<u>\$ 617,143</u>	<u>\$ 1,015,675</u>
SUPPLEMENTAL CASH FLOW DISCLOSURES:		
Cash paid for income taxes	\$ 15,531	\$ 4,355
Cash paid for interest	\$ 6,673	\$ 5,615
SUPPLEMENTAL CASH FLOW DISCLOSURES FOR NON-CASH INVESTING AND FINANCING ACTIVITIES:		
Decrease in accounts payable and accrued liabilities related to fixed assets	\$ (7,690)	\$ (13,281)
Increase (decrease) in accounts payable and accrued liabilities related to intangible assets	\$ 9,389	\$ (3,043)

The accompanying notes are an integral part of these Condensed Consolidated Financial Statements.

BIOMARIN PHARMACEUTICAL INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS
(In thousands of U.S. Dollars, except per share amounts or as otherwise disclosed)

(1) NATURE OF OPERATIONS

BioMarin Pharmaceutical Inc. (the Company) is a global biotechnology company that develops and commercializes innovative therapies for people with serious and life-threatening rare diseases and medical conditions. The Company selects product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market or offer a significant benefit over existing products. The Company's portfolio consists of several commercial products and multiple clinical and preclinical product candidates for the treatment of various diseases. Voxzogo (formerly known as vosoritide) was granted marketing approval in the European Union (EU) on August 27, 2021.

The Company expects to continue to finance future cash needs that exceed its operating activities primarily through its current cash, cash equivalents and investments and through proceeds from debt or equity offerings, commercial borrowing, or through collaborative agreements with corporate partners. If the Company elects to increase its spending on development programs significantly above current long-term plans or enters into potential licenses and other acquisitions of complementary technologies, products or companies, the Company may need additional capital.

(2) BASIS OF PRESENTATION

The accompanying Condensed Consolidated Financial Statements have been prepared pursuant to United States generally accepted accounting principles (U.S. GAAP) and the rules and regulations of the Securities and Exchange Commission (the SEC) for Quarterly Reports on Form 10-Q and do not include all of the information and note disclosures required by U.S. GAAP for complete financial statements, although the Company believes that the disclosures herein are adequate to ensure that the information presented is not misleading. The Condensed Consolidated Financial Statements should therefore be read in conjunction with the Consolidated Financial Statements and Notes thereto for the fiscal year ended December 31, 2020 included in the Company's Annual Report on Form 10-K. The Condensed Consolidated Financial Statements include the accounts of the Company and its wholly owned subsidiaries. All intercompany transactions have been eliminated. The results of operations for the three and nine months ended September 30, 2021 are not necessarily indicative of the results that may be expected for the fiscal year ending December 31, 2021 or any other period.

U.S. GAAP requires management to make estimates and assumptions that affect amounts reported in the Condensed Consolidated Financial Statements and accompanying disclosures. Although these estimates are based on management's best knowledge of current events and actions that the Company may undertake in the future, actual results may be different from those estimates. The Condensed Consolidated Financial Statements reflect all adjustments of a normal, recurring nature that are, in the opinion of management, necessary for a fair presentation of results for these interim periods. The full extent to which the novel coronavirus (referred to as COVID-19) pandemic could continue to directly or indirectly impact the Company's business, results of operations and financial condition, including revenues, expenses, reserves and allowances, manufacturing, clinical trials and research and development costs, will depend on future developments that remain uncertain at this time, particularly as virus variants continue to spread. As events continue to evolve and additional information becomes available, the Company's estimates may change materially in future periods.

Management performed an evaluation of the Company's activities through the date of filing of this Quarterly Report on Form 10-Q, and has concluded that there were no subsequent events or transactions that occurred subsequent to the balance sheet date prior to filing this Quarterly Report on Form 10-Q that would require recognition or disclosure in the Condensed Consolidated Financial Statements.

(3) SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

There have been no material changes to the Company's significant accounting policies during the nine months ended September 30, 2021, as compared to the significant accounting policies disclosed in Note 3 – *Summary of Significant Accounting Policies* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

(4) RECENT ACCOUNTING PRONOUNCEMENTS

There have been no new accounting pronouncements adopted by the Company or new accounting pronouncements issued by the Financial Accounting Standards Board during the nine months ended September 30, 2021, as compared to the recent accounting pronouncements described in Note 4 of the Company's Annual Report on Form 10-K for the year ended December 31, 2020, that the Company believes are of significance or potential significance to the Company.

BIOMARIN PHARMACEUTICAL INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS - (continued)
(In thousands of U.S. Dollars, except per share amounts or as otherwise disclosed)

(5) FINANCIAL INSTRUMENTS

All marketable securities were classified as available-for-sale at September 30, 2021 and December 31, 2020.

The following tables show the Company's cash, cash equivalents and available-for-sale securities by significant investment category for each period presented:

September 30, 2021							
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Fair Value	Cash and Cash Equivalents	Short-term Marketable Securities ⁽¹⁾	Long-term Marketable Securities ⁽²⁾
Level 1:							
Cash	\$ 294,209	\$ —	\$ —	\$ 294,209	\$ 294,209	\$ —	\$ —
Level 2:							
Money market instruments	291,735	—	—	291,735	291,735	—	—
Corporate debt securities	560,004	1,230	(198)	561,036	703	177,468	382,865
U.S. government agency securities	210,444	416	(7)	210,853	12,999	161,207	36,647
Commercial paper	129,818	1	(1)	129,818	17,497	112,321	—
Asset-backed securities	55,182	26	(23)	55,185	—	8,272	46,913
Foreign and other	3,114	150	(6)	3,258	—	3,065	193
Subtotal	1,250,297	1,823	(235)	1,251,885	322,934	462,333	466,618
Total	<u>\$ 1,544,506</u>	<u>\$ 1,823</u>	<u>\$ (235)</u>	<u>\$ 1,546,094</u>	<u>\$ 617,143</u>	<u>\$ 462,333</u>	<u>\$ 466,618</u>

December 31, 2020							
	Amortized Cost	Gross Unrealized Gains	Gross Unrealized Losses	Aggregate Fair Value	Cash and Cash Equivalents	Short-term Marketable Securities ⁽¹⁾	Long-term Marketable Securities ⁽²⁾
Cash	\$ 370,325	\$ —	\$ —	370,325	370,325	\$ —	\$ —
Money market instruments	264,833	—	—	264,833	264,833	—	—
Corporate debt securities	413,137	3,261	(8)	416,390	—	220,551	195,839
U.S. government agency securities	265,298	1,555	(1)	266,852	14,000	192,488	60,364
Asset-backed securities	31,659	85	(2)	31,742	—	3,189	28,553
Foreign and other	549	168	—	717	—	—	717
Subtotal	975,476	5,069	(11)	980,534	278,833	416,228	285,473
Total	<u>\$ 1,345,801</u>	<u>\$ 5,069</u>	<u>\$ (11)</u>	<u>\$ 1,350,859</u>	<u>\$ 649,158</u>	<u>\$ 416,228</u>	<u>\$ 285,473</u>

(1) The Company's short-term marketable securities mature in one year or less.

(2) The Company's long-term marketable securities mature between one and five years.

As of September 30, 2021, the Company had the ability and intent to hold all investments that were in an unrealized loss position until maturity. The Company considered its intent and ability to hold the securities until recovery of amortized cost basis, the extent to which fair value is less than amortized cost basis, conditions specifically related to the security's industry and geography, payment structure and history and changes to the ratings (if any) in determining that the decline in fair value compared to carrying value is not related to a credit loss.

The Company has certain investments in non-marketable equity securities, measured using unobservable valuation inputs and remeasured on a nonrecurring basis, which are collectively considered strategic investments. As of September 30, 2021 and

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December 31, 2020, the fair value of the Company's strategic investments was \$16.3 million and \$10.5 million, respectively. These investments were recorded in Other Assets in the Company's Condensed Consolidated Balance Sheets.

(6) SUPPLEMENTAL BALANCE SHEET INFORMATION

Inventory consisted of the following:

	September 30, 2021	December 31, 2020
Raw materials	\$ 75,328	\$ 76,673
Work-in-process	412,434	308,286
Finished goods	261,644	313,589
Total inventory	<u>\$ 749,406</u>	<u>\$ 698,548</u>

Inventory as of September 30, 2021 included \$4.8 million of Voxzogo pre-launch manufacturing-related costs incurred during the third quarter of 2021 that are intended for the U.S. Voxzogo, which was granted marketing approval in the EU on August 27, 2021, is still a product candidate in other regions, including the U.S., for the treatment of achondroplasia in children, the most common form of disproportionate short stature in humans. The Company must receive marketing approval from the U.S. Food and Drug Administration (FDA) before the Voxzogo inventory can be sold commercially in the U.S. Starting in 2021, the Company believed that material uncertainties related to the ultimate regulatory approval of Voxzogo had been significantly reduced. A number of factors were taken into consideration, including the current status in the drug development process, pivotal clinical trial results for the underlying product candidate, results from meetings with the relevant regulatory authorities, historical experience, as well as potential impediments to the approval process such as product safety or efficacy, as well as commercialization and marketplace trends.

See Note 3 – *Summary of Significant Accounting Policies* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020 for additional information related to the Company's policies on inventory produced prior to regulatory approval.

Property, Plant and Equipment, Net consisted of the following:

	September 30, 2021	December 31, 2020
Property, plant and equipment, gross	\$ 1,724,702	\$ 1,668,066
Accumulated depreciation	(699,915)	(635,595)
Total property, plant and equipment, net	<u>\$ 1,024,787</u>	<u>\$ 1,032,471</u>

Depreciation expense, net of amounts capitalized into inventory, for the three and nine months ended September 30, 2021 was \$11.4 million and \$35.7 million, respectively. Depreciation expense, net of amounts capitalized into inventory, for the three and nine months ended September 30, 2020 was \$11.1 million and \$31.1 million, respectively.

Intangible Assets, Net consisted of the following:

	September 30, 2021	December 31, 2020
Finite-lived intangible assets	\$ 661,781	\$ 644,087
Less: Accumulated amortization	(273,294)	(226,816)
Net carrying value	<u>\$ 388,487</u>	<u>\$ 417,271</u>

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Accounts Payable and Accrued Liabilities consisted of the following:

	September 30, 2021	December 31, 2020
Accounts payable and accrued operating expenses	\$ 203,321	\$ 191,429
Accrued compensation expense	158,130	165,023
Accrued rebates payable	68,329	65,526
Accrued royalties payable	14,512	17,155
Lease liabilities	9,659	11,754
Forward foreign currency exchange contracts	5,323	17,798
Value added taxes payable	1,412	9,562
Accrued income taxes	564	9,661
Other	5,461	4,640
Total accounts payable and accrued liabilities	<u>\$ 466,711</u>	<u>\$ 492,548</u>

(7) FAIR VALUE MEASUREMENTS

The Company measures certain financial assets and liabilities at fair value in accordance with the policy described in Note 3 – *Summary of Significant Accounting Policies* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

The following tables present the classification within the fair value hierarchy of financial assets and liabilities not disclosed elsewhere in these Condensed Consolidated Financial Statements that are remeasured on a recurring basis as of September 30, 2021 and December 31, 2020. Other than the Company's fixed-rate convertible debt disclosed in Note 9 – *Debt*, there were no financial assets or liabilities that were remeasured using a quoted price in active markets for identical assets (Level 1) as of September 30, 2021 or December 31, 2020.

	Fair Value Measurements as of September 30, 2021		
	Significant Other Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:			
Other current assets:			
NQDC Plan assets	\$ 2,089	\$ —	\$ 2,089
Other assets:			
NQDC Plan assets	22,521	—	22,521
Restricted investments ⁽¹⁾	2,835	—	2,835
Total other assets	<u>25,356</u>	<u>—</u>	<u>25,356</u>
Total assets	<u>\$ 27,445</u>	<u>\$ —</u>	<u>\$ 27,445</u>
Liabilities:			
Current liabilities:			
NQDC Plan liability	\$ 2,089	\$ —	\$ 2,089
Contingent consideration	—	48,187	48,187
Total current liabilities	<u>2,089</u>	<u>48,187</u>	<u>50,276</u>
Other long-term liabilities:			
NQDC Plan liability	22,521	—	22,521
Contingent consideration	—	15,204	15,204
Total other long-term liabilities	<u>22,521</u>	<u>15,204</u>	<u>37,725</u>
Total liabilities	<u>\$ 24,610</u>	<u>\$ 63,391</u>	<u>\$ 88,001</u>

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	Fair Value Measurements as of December 31, 2020		
	Significant Observable Inputs (Level 2)	Significant Unobservable Inputs (Level 3)	Total
Assets:			
Other current assets:			
NQDC Plan assets	\$ 2,415	\$ —	\$ 2,415
Other assets:			
NQDC Plan assets	19,962	—	19,962
Restricted investments ⁽¹⁾	4,487	—	4,487
Total other assets	24,449	—	24,449
Total assets	\$ 26,864	\$ —	\$ 26,864
Liabilities:			
Current liabilities:			
NQDC Plan liability	\$ 2,415	\$ —	\$ 2,415
Other long-term liabilities:			
NQDC Plan liability	19,962	—	19,962
Contingent consideration	—	60,130	60,130
Total other long-term liabilities	19,962	60,130	80,092
Total liabilities	\$ 22,377	\$ 60,130	\$ 82,507

(1) The restricted investments at September 30, 2021 and December 31, 2020 secure the Company's irrevocable standby letters of credit obtained in connection with certain commercial agreements.

There were no transfers between levels during the three and nine months ended September 30, 2021.

Liabilities measured at fair value using Level 3 inputs primarily consisted of contingent consideration. The following tables represent a roll-forward of contingent consideration.

Contingent consideration as of December 31, 2020	\$ 60,130
Changes in the fair value of contingent consideration	6,254
Foreign exchange remeasurement of Euro denominated contingent consideration	(2,993)
Contingent consideration as of September 30, 2021	\$ 63,391

(8) DERIVATIVE INSTRUMENTS AND HEDGING STRATEGIES

The Company uses foreign currency exchange forward contracts (forward contracts) to protect against the reduction in value of forecasted foreign currency cash flows resulting from product revenues, royalty revenues and operating expenses denominated in currencies other than the U.S. Dollar (USD), primarily the Euro. Certain of these forward contracts are designated as cash flows hedges and have maturities of up to two years. The Company also enters into forward contracts to manage foreign exchange risk related to asset or liability positions denominated in currencies other than USD. Such forward contracts are considered to be economic hedges, are not designated as hedging instruments and have maturities of up to three months. The Company does not use derivative instruments for speculative trading purposes. The Company is exposed to counterparty credit risk on its derivatives. The Company has established and maintains strict counterparty credit guidelines and enters into hedging

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agreements with financial institutions that are investment grade or better to minimize the Company's exposure to potential defaults. The Company is not required to pledge collateral under these agreements.

The following table summarizes the aggregate notional amounts for the Company's derivatives outstanding as of the periods presented.

Foreign Exchange Contracts	September 30, 2021	December 31, 2020
Derivatives designated as hedging instruments:		
Sell	\$ 654,516	\$ 782,327
Purchase	\$ 168,080	\$ 189,540
Derivatives not designated as hedging instruments:		
Sell	\$ 77,040	\$ 98,343
Purchase	\$ 37,285	\$ 12,277

The fair value carrying amounts of the Company's derivatives, as classified within the fair value hierarchy, were as follows:

Balance Sheet Location	September 30, 2021	December 31, 2020
Derivatives designated as hedging instruments:		
Asset Derivatives - Level 2 ⁽¹⁾		
Other current assets	\$ 11,883	\$ 6,268
Other assets	4,320	3,148
Subtotal	\$ 16,203	\$ 9,416
Liability Derivatives - Level 2 ⁽¹⁾		
Accounts payable and accrued liabilities	\$ 5,257	\$ 17,551
Other long-term liabilities	1,486	11,020
Subtotal	\$ 6,743	\$ 28,571
Derivatives not designated as hedging instruments:		
Asset Derivatives - Level 2 ⁽¹⁾		
Other current assets	\$ 252	\$ 84
Liability Derivatives - Level 2 ⁽¹⁾		
Accounts payable and accrued liabilities	\$ 66	\$ 247
Total Derivatives Assets	\$ 16,455	\$ 9,500
Total Derivatives Liabilities	\$ 6,809	\$ 28,818

(1) For additional discussion of fair value measurements, see Note 3 – *Summary of Significant Accounting Policies* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

The following tables summarize the impact of gains and losses from the Company's derivatives on its Condensed Consolidated Statements of Comprehensive Income (Loss) for the periods presented.

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	Three Months Ended September 30,			
	2021		2020	
Derivatives Designated as Cash Flow Hedging Instruments	Cash Flow Hedging Gains (Losses) Reclassified into Earnings		Cash Flow Hedging Gains (Losses) Reclassified into Earnings	
Net product revenues as reported	\$ 393,840	\$ 401	\$ 460,741	\$ 2,693
Operating expenses as reported	\$ 461,961	\$ (268)	\$ 532,725	\$ (815)
Derivatives Not Designated as Hedging Instruments	Gains (Losses) Recognized in Earnings		Gains (Losses) Recognized in Earnings	
Operating expenses	\$ 1,302		\$ 4,166	
	Nine Months Ended September 30,			
	2021		2020	
Derivatives Designated as Cash Flow Hedging Instruments	Cash Flow Hedging Gains (Losses) Reclassified into Earnings		Cash Flow Hedging Gains (Losses) Reclassified into Earnings	
Net product revenues as reported	\$ 1,348,279	\$ (5,034)	\$ 1,368,816	\$ 17,301
Operating expenses as reported	\$ 1,412,926	\$ 81	\$ 1,400,263	\$ (4,274)
Derivatives Not Designated as Hedging Instruments	Gains (Losses) Recognized in Earnings		Gains (Losses) Recognized in Earnings	
Operating expenses	\$ 2,310		\$ 9,600	

As of September 30, 2021, the Company expects to reclassify unrealized gains of \$6.2 million from Accumulated Other Comprehensive Income (AOCI) to earnings as the forecasted revenues and operating expense transactions occur over the next 12 months. For additional discussion of balances in AOCI see Note 10 – *Accumulated Other Comprehensive Income*.

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(9) DEBT
Convertible Notes

As of September 30, 2021, the Company had outstanding fixed-rate notes with varying maturities for an undiscounted aggregate principal amount of \$1.1 billion (collectively the Notes). The Notes are senior subordinated convertible obligations, and interest is payable in arrears, semi-annually. The following table summarizes information regarding the Company's convertible debt:

	September 30, 2021	December 31, 2020
1.25% senior subordinated convertible notes due in May 2027 (the 2027 Notes)	\$ 600,000	\$ 600,000
Unamortized discount net of deferred offering costs	(11,478)	(12,995)
2027 Notes, net	<u>588,522</u>	<u>587,005</u>
0.599% senior subordinated convertible notes due in August 2024 (the 2024 Notes)	495,000	495,000
Unamortized discount net of deferred offering costs	(5,429)	(6,860)
2024 Notes, net	<u>489,571</u>	<u>488,140</u>
Total convertible debt, net	<u>\$ 1,078,093</u>	<u>\$ 1,075,145</u>
Fair value of fixed rate convertible debt ⁽¹⁾:		
2027 Notes	\$ 600,858	\$ 627,090
2024 Notes	510,954	530,714
Total fair value of fixed rate convertible debt	<u>\$ 1,111,812</u>	<u>\$ 1,157,804</u>

(1) The fair value of the Company's fixed-rate convertible debt is based on open market trades and is classified as Level 1 in the fair value hierarchy. For additional discussion of fair value measurements, see Note 3 – *Summary of Significant Accounting Policies* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020.

Interest expense on the Company's convertible debt consisted of the following:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Coupon interest expense	\$ 2,617	\$ 4,255	\$ 7,849	\$ 9,443
Accretion of discount on convertible notes	835	4,696	2,503	13,201
Amortization of debt issuance costs	148	535	445	1,565
Total interest expense on convertible debt	<u>\$ 3,600</u>	<u>\$ 9,486</u>	<u>\$ 10,797</u>	<u>\$ 24,209</u>

See Note 13 - *Debt* included in the Company's Annual Report on Form 10-K for the year ended December 31, 2020 for additional information related to the Company's convertible debt.

Revolving Credit Facility

In October 2018, the Company entered into an unsecured revolving credit facility of up to \$200.0 million which includes a letter of credit subfacility and a swingline loan subfacility. The credit facility is intended to finance ongoing working capital needs and for other general corporate purposes. In May 2021, the Company entered into an amendment agreement in respect of the credit facility, extending the maturity date from October 19, 2021 to May 28, 2024, among other changes. The amended credit facility contains financial covenants including a maximum leverage ratio and a minimum interest coverage ratio. As of September 30, 2021, there were no amounts outstanding under the credit facility and the Company and certain of its subsidiaries that serve as guarantors were in compliance with all covenants.

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(10) ACCUMULATED OTHER COMPREHENSIVE INCOME (LOSS)

The following tables summarize changes in the accumulated balances for each component of Accumulated Other Comprehensive Income (Loss) (AOCI), including current-period other comprehensive income (loss) and reclassifications out of AOCI, for the periods presented.

	Three Months Ended September 30, 2021			
	Unrealized Gains (Losses) on Cash Flow Hedges	Unrealized Gains (Losses) on Available for-Sale Debt Securities	Other	Total
AOCI balance at June 30, 2021	\$ (2,760)	\$ 1,821	\$ —	\$ (939)
Other comprehensive income (loss) before reclassifications	11,914	(786)	—	11,128
Less: gain (loss) reclassified from AOCI	133	—	—	133
Tax effect	—	183	—	183
Net current-period other comprehensive income (loss)	11,781	(603)	—	11,178
AOCI balance at September 30, 2021	\$ 9,021	\$ 1,218	\$ —	\$ 10,239

	Three Months Ended September 30, 2020			
	Unrealized Gains (Losses) on Cash Flow Hedges	Unrealized Gains (Losses) on Available for-Sale Debt Securities	Other	Total
AOCI balance at June 30, 2020	\$ 22,963	\$ 7,087	\$ —	\$ 30,050
Other comprehensive income (loss) before reclassifications	(16,094)	(2,201)	—	(18,295)
Less: gain (loss) reclassified from AOCI	1,878	—	—	1,878
Tax effect	—	508	—	508
Net current-period other comprehensive income (loss)	(17,972)	(1,693)	—	(19,665)
AOCI balance at September 30, 2020	\$ 4,991	\$ 5,394	\$ —	\$ 10,385

	Nine Months Ended September 30, 2021			
	Unrealized Gains (Losses) on Cash Flow Hedges	Unrealized Gains (Losses) on Available for-Sale Debt Securities	Other	Total
AOCI balance at December 31, 2020	\$ (20,028)	\$ 3,889	\$ —	\$ (16,139)
Other comprehensive income (loss) before reclassifications	24,096	(3,470)	—	20,626
Less: gain (loss) reclassified from AOCI	(4,953)	—	—	(4,953)
Tax effect	—	799	—	799
Net current-period other comprehensive income (loss)	29,049	(2,671)	—	26,378
AOCI balance at September 30, 2021	\$ 9,021	\$ 1,218	\$ —	\$ 10,239

	Nine Months Ended September 30, 2020			
	Unrealized Gains (Losses) on Cash Flow Hedges	Unrealized Gains (Losses) on Available for-Sale Debt Securities	Other	Total
AOCI balance at December 31, 2019	\$ 16,614	\$ 3,565	\$ (15)	\$ 20,164
Other comprehensive income (loss) before reclassifications	1,404	2,379	15	3,798
Less: gain (loss) reclassified from AOCI	13,027	—	—	13,027
Tax effect	—	(550)	—	(550)
Net current-period other comprehensive income (loss)	(11,623)	1,829	15	(9,779)
AOCI balance at September 30, 2020	\$ 4,991	\$ 5,394	\$ —	\$ 10,385

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For additional discussion of reclassifications from AOCI see Note 8 – *Derivative Instruments and Hedging Strategies*.

(11) REVENUE, CREDIT CONCENTRATIONS AND GEOGRAPHIC INFORMATION

The Company operates in one business segment, which primarily focuses on the development and commercialization of innovative therapies for people with serious and life-threatening rare diseases and medical conditions. The Company considers there to be revenue concentration risks for regions where Net Product Revenues exceed 10% of consolidated Net Product Revenues. The concentration of the Company's Net Product Revenues within the regions below may have a material adverse effect on the Company's revenues and results of operations if sales in the respective regions experience difficulties.

The following table disaggregates Total Revenues from external customers and collaborative partners by geographic region. Net product revenues by geographic region are based on patient location for the Company's commercial products, except for Aldurazyme, which is sold exclusively to Sanofi Genzyme (Genzyme) who markets and sells Aldurazyme worldwide. Aldurazyme revenues earned by the Company are included in the U.S. region as the transactions are with Genzyme, whose headquarters is located in the U.S.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Total revenues by geographic region:				
United States	\$ 196,239	\$ 252,948	\$ 608,670	\$ 729,672
Europe	115,497	121,158	450,016	375,453
Latin America	38,958	44,064	140,911	141,852
Rest of world	58,048	58,614	196,868	161,361
Total revenues	<u>\$ 408,742</u>	<u>\$ 476,784</u>	<u>\$ 1,396,465</u>	<u>\$ 1,408,338</u>

The following table disaggregates total Net Product Revenues by product.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Net product revenues by product:				
Vimizim	\$ 136,744	\$ 147,891	\$ 466,697	\$ 401,789
Naglazyme	71,172	76,323	297,321	271,585
Kuvan	67,687	123,993	217,257	368,604
Palynziq	60,729	46,092	173,702	121,354
Brineura	32,984	25,455	90,641	75,223
Voxzogo	144	—	144	—
Firdapse	—	—	—	1,316
Total net product revenues marketed by the Company	<u>\$ 369,460</u>	<u>\$ 419,754</u>	<u>\$ 1,245,762</u>	<u>\$ 1,239,871</u>
Aldurazyme net product revenues marketed by Genzyme	24,380	40,987	\$ 102,517	\$ 128,945
Total net product revenues	<u>\$ 393,840</u>	<u>\$ 460,741</u>	<u>\$ 1,348,279</u>	<u>\$ 1,368,816</u>

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The table below disaggregates total Net Product Revenues based on patient location for products sold directly by the Company, and global sales of Aldurazyme, which is marketed by Genzyme.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
United States	\$ 166,554	\$ 203,892	\$ 491,028	\$ 582,734
Europe	108,568	115,548	424,144	360,718
Latin America	38,958	44,064	140,911	141,852
Rest of world	55,380	56,250	189,679	154,567
Total net product revenues marketed by the Company	\$ 369,460	\$ 419,754	\$ 1,245,762	\$ 1,239,871
Aldurazyme net product revenues marketed by Genzyme	24,380	40,987	102,517	128,945
Total net product revenues	\$ 393,840	\$ 460,741	\$ 1,348,279	\$ 1,368,816

The following table illustrates the percentage of the Company's total Net Product Revenues attributed to the Company's largest customers for the periods presented.

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Customer A	20 %	16 %	17 %	15 %
Customer B	16 %	14 %	14 %	14 %
Customer C	11 %	11 %	10 %	12 %
Total	47 %	41 %	41 %	41 %

On a consolidated basis, two customers accounted for 31% and 14% of the Company's September 30, 2021 accounts receivable balance, respectively, compared to December 31, 2020, when two customers accounted for 24% and 22% of the accounts receivable balance, respectively. As of September 30, 2021, and December 31, 2020, the accounts receivable balance for Genzyme included \$83.9 million and \$72.1 million, respectively, of unbilled accounts receivable, which becomes payable to the Company when the product is sold through by Genzyme. The Company does not require collateral from its customers, but does perform periodic credit evaluations of its customers' financial condition and requires prepayments in certain circumstances.

The COVID-19 pandemic continues to affect economies and business around the world. The Company's global revenue sources, mostly in the form of demand interruptions such as missed patient infusions and delayed treatment starts for new patients, and its business operations were impacted by the COVID-19 pandemic during the nine months ended September 30, 2021 and 2020, and the Company anticipates a continued impact due to COVID-19 on its financial results in the remainder of 2021. The extent and duration of such effects remain uncertain and difficult to predict, particularly as virus variants continue to spread. The Company is actively monitoring and managing its response and assessing actual and potential impacts to its operating results and financial condition, as well as developments in its business, which could further impact developments, trends and expectations. See the risk factor related to the impact of the coronavirus pandemic, "The COVID-19 pandemic could continue to materially adversely affect our business, results of operations and financial condition." described in "Risk Factors" in Part II, Item 1A of this Quarterly Report, for additional details on the impact of the COVID-19 pandemic.

The Company is mindful that conditions in the current macroeconomic environment could affect the Company's ability to achieve its goals. The Company sells its products in countries that face economic volatility and weakness. Although the Company has historically collected receivables from customers in certain countries, sustained weakness or further deterioration of the local economies and currencies and effects of the impact of the ongoing COVID-19 pandemic may cause customers in those countries to delay payment or be unable to pay for the Company's products. The Company believes that the allowances for doubtful accounts related to these countries, if any, are adequate based on its analysis of the specific business circumstances and expectations of collection for each of the underlying accounts in these countries. The Company will continue to monitor these conditions and will attempt to adjust its business processes, as appropriate, to mitigate macroeconomic risks to its business.

(12) STOCK-BASED COMPENSATION

The Company has stockholder-approved equity incentive plans that provide for the granting of service-based restricted stock units (RSUs), market-based RSUs, performance-based RSUs, stock options and other types of awards to its employees,

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officers and non-employee directors. Compensation expense included in the Company's Condensed Consolidated Statements of Comprehensive Income (Loss) for all stock-based compensation arrangements was as follows:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Cost of sales	\$ 4,339	\$ 10,342	\$ 16,907	\$ 20,381
Research and development	17,866	15,705	56,199	45,333
Selling, general and administrative	26,821	24,122	80,266	76,411
Total stock-based compensation expense	<u>\$ 49,026</u>	<u>\$ 50,169</u>	<u>\$ 153,372</u>	<u>\$ 142,125</u>

(13) NET INCOME (LOSS) PER COMMON SHARE

Potentially issuable shares of common stock include shares issuable upon the exercise of outstanding employee stock option awards, common stock issuable under the Company's Employee Share Purchase Plan (ESPP), unvested RSUs, the Company's common stock held by the NQDC and contingent issuances of common stock related to the Company's convertible debt.

The following table sets forth the computation of basic and diluted earnings per common share (common shares in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Numerator:				
Net Income (loss), basic	\$ (36,494)	\$ 784,803	\$ (6,182)	\$ 837,001
Add: Interest on convertible notes	—	7,070	—	18,333
Net Income (loss), diluted	<u>\$ (36,494)</u>	<u>\$ 791,873</u>	<u>\$ (6,182)</u>	<u>\$ 855,334</u>
Denominator:				
Weighted-average common shares outstanding, basic	183,214	181,142	182,616	180,592
Effect of dilutive securities:				
Options to purchase common stock	—	1,731	—	1,728
Common stock issuable under the 2020 notes	—	3,983	—	3,983
Common stock issuable under the 2024 notes	—	3,970	—	3,970
Common stock issuable under the 2027 notes	—	4,365	—	2,373
Unvested RSUs	—	1,926	—	1,765
Common stock potentially issuable for ESPP purchases	—	346	—	337
The Company's common stock held by the NQDC	—	211	—	211
Weighted-average common shares outstanding, diluted	<u>183,214</u>	<u>197,674</u>	<u>182,616</u>	<u>194,959</u>
Net income (loss) per common share, basic	<u>\$ (0.20)</u>	<u>\$ 4.33</u>	<u>\$ (0.03)</u>	<u>\$ 4.63</u>
Net income (loss) per common share, diluted	<u>\$ (0.20)</u>	<u>\$ 4.01</u>	<u>\$ (0.03)</u>	<u>\$ 4.39</u>

BIOMARIN PHARMACEUTICAL INC.
NOTES TO CONDENSED CONSOLIDATED FINANCIAL STATEMENTS - (continued)
(In thousands of U.S. Dollars, except per share amounts or as otherwise disclosed)

In addition to the equity instruments included in the table above, the table below presents potential shares of common stock that were excluded from the computation of basic and diluted income (loss) per common share as they were anti-dilutive (in thousands):

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Options to purchase common stock	6,649	5,172	6,649	5,175
Common stock issuable under the 2024 Notes	3,970	—	3,970	—
Common stock issuable under the 2027 Notes	4,365	—	4,365	—
Unvested RSUs	5,292	2,900	5,292	3,060
Common stock potentially issuable for ESPP purchases	582	193	582	204
The Company's common stock held by the NQDC	197	—	197	—
Total number of potentially issuable shares	21,055	8,265	21,055	8,439

The Company's 1.50% senior subordinated convertible notes due in October 2020 (the 2020 Notes) matured on October 15, 2020 and were settled in cash. The potential effect of the capped call transactions and potential shares issuable under the 2020 Notes were excluded from the calculation of diluted net income (loss) per share in the three and nine months ended September 30, 2020, as the Company's closing price on September 30, 2020 did not exceed the conversion price of \$94.15 per share. There is no similar capped call transaction associated with the 2024 Notes or the 2027 Notes.

(14) COMMITMENTS AND CONTINGENCIES

Contingencies

From time to time the Company is involved in legal actions arising in the normal course of its business. The process of resolving matters through litigation or other means is inherently uncertain and it is possible that an unfavorable resolution of these matters could adversely affect the Company, its results of operations, financial condition or cash flows. The Company's general practice is to expense legal fees as services are rendered in connection with legal matters, and to accrue for liabilities when losses are probable and reasonably estimable.

Contingent Payments

As of September 30, 2021, the Company was subject to contingent payments totaling approximately \$708.8 million upon achievement of certain development and regulatory activities and commercial sales milestones if they occur before certain dates in the future. Of this amount, \$70.0 million were considered probable and comprised of commercial milestones related to the acquisition of certain rights and other assets with respect to Kuvan and Palynziq from a third party, \$405.5 million were considered reasonably possible and primarily related to development milestones and \$233.3 million were considered remote as the Company is no longer developing the related programs.

As of September 30, 2021, the fair value of contingent liabilities recorded on the Company's Condensed Consolidated Balance Sheet was \$63.4 million of which \$48.2 million was short term. See Note 7 – *Fair Value Measurements* to these Condensed Consolidated Financial Statements for further information regarding the fair value of the Company's contingent consideration.

Other Commitments

The Company uses experts and laboratories at universities and other institutions to perform certain research and development (R&D) activities. These amounts are included as R&D expense as services are provided. In the normal course of business, the Company enters into various firm purchase commitments primarily related to active pharmaceutical ingredients, certain inventory-related items and certain third-party R&D services. As of September 30, 2021, such commitments and other minimum contractual obligations for clinical and post-marketing services were estimated at approximately \$107.7 million. The Company has also licensed technology, for which it is required to pay royalties upon future sales, subject to certain annual minimums.

Item 2. Management's Discussion and Analysis of Financial Condition and Results of Operations

The following discussion of our financial condition and results of operations should be read in conjunction with our Condensed Consolidated Financial Statements and the related Notes thereto included in this Quarterly Report on Form 10-Q. This discussion contains forward-looking statements that involve risks and uncertainties. When reviewing the discussion below, you should keep in mind the substantial risks and uncertainties that could impact our business. In particular, we encourage you to review the risk factor related to the impact of the coronavirus pandemic, "The COVID-19 pandemic could continue to materially adversely affect our business, results of operations and financial condition." described in "Risk Factors" in Part II, Item 1A in this Quarterly Report on Form 10-Q, amongst the other risk factors. These risks and uncertainties could cause actual results to differ significantly from those projected in forward-looking statements contained in this report or implied by past results and trends. Forward-looking statements are statements that attempt to forecast or anticipate future developments in our business, financial condition or results of operations. See the section titled "Forward-Looking Statements" that appears at the beginning of this Quarterly Report on Form 10-Q. These statements, like all statements in this report, speak only as of the date of this Quarterly Report on Form 10-Q (unless another date is indicated), and, except as required by law, we undertake no obligation to update or revise these statements in light of future developments. Our Condensed Consolidated Financial Statements have been prepared in accordance with United States (U.S.) generally accepted accounting principles (U.S GAAP) and are presented in U.S. Dollars (USD).

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions, except as otherwise disclosed)

Overview

We are a global biotechnology company that develops and commercializes innovative therapies for people with serious and life-threatening rare diseases and medical conditions. We select product candidates for diseases and conditions that represent a significant unmet medical need, have well-understood biology and provide an opportunity to be first-to-market or offer a significant benefit over existing products.

Our portfolio consists of several commercial therapies and multiple clinical and preclinical product candidates. A summary of our commercial products, as of September 30, 2021, is provided below:

Commercial Products	Indication	United States Orphan Drug Exclusivity Expiration ⁽¹⁾	United States Biologic Exclusivity Expiration ⁽²⁾	European Union Orphan Drug Exclusivity Expiration ⁽¹⁾
Aldurazyme (laronidase)	MPS I (3)	Expired	Expired	Expired
Brineura (cerliponase alfa)	CLN2 (4)	2024	2029	2027
Kuvan (sapropterin dihydrochloride)	PKU (5)	Expired	Not Applicable	Expired
Naglazyme (galsulfase)	MPS VI (6)	Expired	Expired	Expired
Palyzniq (pegvaliase-pqpz)	PKU (7)	2025	2030	2029
Vimizim (elosulfase alpha)	MPS IVA (8)	Expired	2026	2024
Voxzogo (vosoritide) (9)	Achondroplasia	Not Applicable	Not Applicable	2031

- (1) See "Government Regulation—Orphan Drug Designation" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on February 26, 2021 for further discussion
- (2) See "Government Regulation— Healthcare Reform" in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2020 for further discussion
- (3) For the treatment of Mucopolysaccharidosis I (MPS I)
- (4) For the treatment of late infantile neuronal ceroid lipofuscinosis type 2 (CLN2)
- (5) For the treatment of phenylketonuria (PKU)
- (6) For the treatment of Mucopolysaccharidosis VI (MPS VI)
- (7) For adult patients with PKU
- (8) For the treatment of Mucopolysaccharidosis IV Type A (MPS IVA)
- (9) Voxzogo (formerly known as vosoritide) was approved by the European Commission (EC) in August 2021 and our New Drug Application (NDA) submission for Voxzogo is under review by the U.S. Food and Drug Administration (FDA) with a Prescription Drug User Fee Act (PDUFA) target action date of November 20, 2021.

A summary of our on-going major development programs, as of September 30, 2021, is provided below:

Major Product Candidates in Development	Target Indication	U.S. Orphan Designation	EU Orphan Designation	Stage
Valoctocogene roxaparvec	Severe Hemophilia A	Yes	Yes	Clinical Phase 3
Voxzogo (1)	Achondroplasia	Yes	Yes	Clinical Phase 3
BMN 307	PKU	Yes	Yes	Clinical Phase 1/2

- (1) In August 2021, the EC granted marketing approval for Voxzogo in Europe and our NDA submission for Voxzogo is under review by the FDA.

Uncertainty Relating to the COVID-19 Pandemic

The COVID-19 pandemic continues to affect economies and business around the world. Our global revenue sources, mostly in the form of demand interruptions such as missed patient infusions and delayed treatment starts for new patients, and our overall business operations were impacted by the COVID-19 pandemic during the nine months ended September 30, 2021 and 2020, and we anticipate a continued impact due to the COVID-19 pandemic on our financial results for the remainder of 2021. The extent and duration of such effects remain uncertain and difficult to predict, particularly as virus variants continue to spread. We are

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions, except as otherwise disclosed)

actively monitoring and managing our response and assessing actual and potential impacts to our operating results and financial condition, as well as developments in our business, which could further impact the developments, trends and expectations described below. See the risk factor related to the impact of the coronavirus pandemic, "The COVID-19 pandemic could continue to materially adversely affect our business, results of operations and financial condition." described in "Risk Factors" in Part II, Item 1A of this Quarterly Report, for additional details on the impact of the COVID-19 pandemic.

Business Developments

We continued to advance our product candidate pipeline during 2021. We believe that the combination of our internal research programs, acquisitions and partnerships will allow us to continue to develop and commercialize innovative therapies for people with serious and life-threatening rare diseases and medical conditions. Below is a summary of key business developments:

Continued Emphasis on Research and Development

- **Voxzogo** – During the quarter, the EC approved Voxzogo for the treatment of children, ages two years and older. The commercial launch of Voxzogo in Europe is underway, with revenues for the remainder of 2021 expected from France, Germany and select early-access countries. Marketing authorization reviews are in process in Japan, Brazil and Australia, with potential approvals in those countries in 2022. The FDA is reviewing the Voxzogo NDA with the PDUFA target action date of November 20, 2021.
- **Valoctocogene roxaparvovec** – The European Medicines Agency (EMA) validated our Marketing Authorization Application for valoctocogene roxaparvovec resulting in an anticipated Committee for Medicinal Products for Human Use opinion in the first half of 2022, assuming favorable results from the two-year follow-up safety and efficacy data from the GENE8-1 study. In the U.S., we are targeting a Biologics License Application resubmission for valoctocogene roxaparvovec in the second quarter of 2022 also assuming favorable results from the two-year follow-up safety and efficacy data from the GENE8-1 study, followed by an expected six-month review procedure by the FDA.

In July 2021, we announced new data from our Phase 3 study, GENE8-1, at the International Society on Thrombosis and Haemostasis (ISTH) 2021 Virtual Congress. The pivotal study demonstrated superiority to Factor VIII prophylaxis in key clinical efficacy endpoints. Over 90 percent of all participants in the GENE8-1 study (N=134) had an Annualized Bleed Rate (ABR) of zero or a lower bleed rate than baseline after week 4 following treatment with valoctocogene roxaparvovec. Mean annualized Factor VIII utilization rate, among a pre-specified group of prior participants in a non-interventional baseline observational study (rollover population; N=112) decreased from baseline on Factor VIII prophylaxis by 99% from 3961.2 (median 3754.4) to 56.9 (median 0) IU/kg/year after week 4 after treatment with valoctocogene roxaparvovec (p-value <0.001).

In addition, we announced at ISTH new data from our open-label Phase 1/2 study with valoctocogene roxaparvovec. Five-year and four-year post-treatment follow-up of the 6e13 vg/kg and 4e13 vg/kg cohorts, respectively, demonstrated that all participants in both cohorts remain off prophylactic Factor VIII treatment. The mean ABR in year five for the 6e13 vg/kg cohort was 0.7 with an ABR reduction of 95% and Factor VIII use reduction of 96% through five years, compared to pre-infusion. The mean ABR in year four for the 4e13 vg/kg cohort was 1.7 with a mean cumulative ABR reduction of 92% and Factor VIII use reduction of 95% through four years, compared to pre-infusion. Mean Factor VIII activity levels of 11.6 IU/dL in year five for the 6e13 vg/kg cohort and 5.6 IU/dL in year four for the 4e13 vg/kg cohort as measured by the Chromogenic Substrate Assay.

- **BMN 307** – our gene therapy product candidate for PKU. In September 2021, the FDA placed a clinical hold on PHEarless, our Phase 1/2 study evaluating BMN 307, an investigational AAV5-phenylalanine hydroxylase gene therapy, in adults with PKU. The hold was based on pre-clinical study findings from a model designed to understand the durability of BMN 307 activity in mice bearing two germline mutations, one rendering the mice immunodeficient. The clinical significance of these findings is being evaluated to assure safe and appropriate use of BMN 307. To date, findings appear specific to mice and have no known translatability to humans or other gene therapy vectors. We are working with health authorities to address the clinical hold and resume study investigations, as appropriate.
- **BMN 255** – for the treatment of a subset of chronic renal disease. The Investigational New Drug application (IND) for BMN 255 is active and we are dosing subjects. Kidney damage can progress to end stage renal disease, and the availability of a potent, orally bioavailable, small molecule like BMN 255, may be able to significantly reduce disease and treatment burden in certain people with chronic renal disease.
- **BMN 331** – for the treatment of Hereditary Angioedema (HAE). We are leveraging our broad expertise in gene therapy to improve efficiencies in the development process of BMN 331. The IND for BMN 331 has been allowed by FDA and the first patient is expected to be enrolled around the end of 2021. Patients with HAE may experience benefit from the constitutive expression and stable C1-INH protein levels potentially provided by gene

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions, except as otherwise disclosed)

therapy, thus reducing the frequency and severity of attacks and reducing the burden associated with current standard of care.

- BMN 351 – an antisense oligonucleotide therapy for individuals with 51-skip-amenable Duchenne Muscular Dystrophy. IND-enabling studies continue. BMN 351 was developed using familiar chemistry and superior biology, by targeting a novel, upstream, splice enhancer site demonstrating improved binding affinity and metabolic stability in preclinical models. Preclinical data suggest that restored expression of near-full-length dystrophin protein at previously achieved levels of up to 40% will convert phenotypes from rapid loss to durable preservation of strength and ambulation. We anticipate filing an IND for BMN 351 in the first half of 2022.

Financial Highlights

Key components of our results of operations include the following:

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2021	2020	2021	2020
Total revenues	\$ 408.7	\$ 476.8	\$ 1,396.5	\$ 1,408.3
Cost of sales	\$ 103.5	\$ 188.8	\$ 350.8	\$ 398.1
Research and development (R&D) expense	\$ 157.9	\$ 147.1	\$ 467.7	\$ 471.4
Selling, general and administrative (SG&A) expense	\$ 183.3	\$ 179.5	\$ 541.8	\$ 542.2
Intangible asset amortization and contingent consideration	\$ 17.2	\$ 17.4	\$ 52.6	\$ 48.0
Gain on sale of nonfinancial assets	\$ —	\$ —	\$ —	\$ (59.5)
Non-operating income (expense), net	\$ 7.1	\$ (5.3)	\$ 7.7	\$ (10.2)
Benefit from income taxes	\$ (9.7)	\$ (846.0)	\$ (2.6)	\$ (839.1)
Net income (loss)	\$ (36.5)	\$ 784.8	\$ (6.2)	\$ 837.0

The Net Loss for the three months ended September 30, 2021 as compared to the Net Income for the three months ended September 30, 2020 was primarily attributed to:

- decreased benefit from income taxes of \$836.3 million, primarily due to the completion of an intra-entity transfer of certain intellectual property (IP) rights to an Irish subsidiary where our Ex-US regional headquarters are located and we have significant manufacturing and commercial operations, to better align ownership of IP rights with how the business operates, resulting in a tax benefit of \$835.1 million based on the fair value of the transferred IP rights in the three months ended September 30, 2020. There was no similar transaction in the three months ended September 30, 2021; partially offset by
- an increase in gross profit primarily driven by the absence of the \$81.2 million inventory charge related to pre-launch valoctocogene roxaparvec inventory reserves following regulatory responses received requesting additional data extending the anticipated regulatory approval timelines in the three months ended September 30, 2020.

The Net Loss for the nine months ended September 30, 2021 as compared to the Net Income for the nine months ended September 30, 2020 was primarily attributed to:

- decreased benefit from income taxes of \$836.5 million, primarily due to the completion of an intra-entity transfer of certain IP rights to an Irish subsidiary where our Ex-US regional headquarters are located and we have significant manufacturing and commercial operations, to better align ownership of IP rights with how the business operates, resulting in a tax benefit of \$835.1 million based on the fair value of the transferred IP rights in the three months ended September 30, 2020. There was no similar transaction in the three months ended September 30, 2021; and
- decreased gain on sale of nonfinancial assets of \$59.5 million due to the divestiture and sale of the Firdapse business in the three months ended March 31, 2020; partially offset by
- an increase in gross profit primarily driven by the absence of the \$81.2 million inventory charge related to pre-launch valoctocogene roxaparvec inventory reserves following regulatory responses received requesting additional data extending the anticipated regulatory approval timelines in the three months ended September 30, of 2020.

See "Results of Operations" below for additional information related to the Net Income fluctuations presented above. Our cash, cash equivalents and investments totaled \$1.55 billion as of September 30, 2021 compared to \$1.35 billion as of December 31, 2020. We have historically financed our operations primarily through our cash flows from operating activities and the issuance

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions, except as otherwise disclosed)

of common stock and convertible debt. We will be highly dependent on our net product revenues to supplement our current liquidity and fund our operations for the foreseeable future. We may in the future elect to supplement this with further debt or equity offerings or commercial borrowing. Further, depending on market conditions, our financial position and performance and other factors, we may in the future choose to use a portion of our cash, cash equivalents or investments to repurchase our convertible debt or other securities. See "Financial Position, Liquidity and Capital Resources" below for a further discussion of our liquidity and capital resources.

Critical Accounting Policies, Estimates and Judgments

In preparing our Condensed Consolidated Financial Statements in accordance with U.S. GAAP and pursuant to the rules and regulations promulgated by the Securities and Exchange Commission (the SEC), we make assumptions, judgments and estimates that can have a significant impact on our net income/loss and affect the reported amounts of certain assets, liabilities, revenues and expenses, and related disclosures. On an ongoing basis, we evaluate our estimates and discuss our critical accounting policies and estimates with the Audit Committee of our Board of Directors. We base our estimates on historical experience and various other assumptions that we believe to be reasonable under the circumstances. Actual results could differ materially from these estimates under different assumptions or conditions.

The full extent to which the ongoing COVID-19 pandemic could continue to directly or indirectly impact our business, results of operations and financial condition, including revenues, expenses, reserves and allowances, manufacturing, clinical trials and research and development costs will depend on future developments that continue to remain uncertain at this time, particularly as virus variants continue to spread. As events continue to evolve and additional information becomes available, our estimates may change materially in future periods.

There have been no significant changes to our critical accounting policies, estimates and judgments during the nine months ended September 30, 2021, compared to the critical accounting policies, estimates and judgments disclosed in "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, 2020.

Recent Accounting Pronouncements

See Note 4 to our accompanying Condensed Consolidated Financial Statements for a description of recent accounting pronouncements and our expectation of their impact on our results of operations and financial condition.

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

Results of Operations

Net Product Revenues

Net Product Revenues consisted of the following:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Net product revenues by product:						
Vimizim	\$ 136.9	\$ 147.9	\$ (11.0)	\$ 466.8	\$ 401.8	\$ 65.0
Naglazyme	71.2	76.3	(5.1)	297.3	271.6	25.7
Kuvan	67.7	124.1	(56.4)	217.3	368.7	(151.4)
Palynziq	60.7	46.1	14.6	173.7	121.4	52.3
Brineura	32.9	25.4	7.5	90.6	75.2	15.4
Voxzogo	0.1	—	0.1	0.1	—	0.1
Firdapse	—	—	—	—	1.2	(1.2)
Total net product revenues marketed by the Company	\$ 369.5	\$ 419.8	\$ (50.3)	\$ 1,245.8	\$ 1,239.9	\$ 5.9
Aldurazyme net product revenues marketed by Sanofi Genzyme	24.4	40.9	(16.5)	102.5	128.9	(26.4)
Total net product revenues	\$ 393.9	\$ 460.7	\$ (66.8)	\$ 1,348.3	\$ 1,368.8	\$ (20.5)

Net Product Revenues include revenues generated from our approved products. In the U.S., our commercial products, except for Palynziq and Aldurazyme, are generally sold to specialty pharmacies or end-users, such as hospitals, which act as retailers. Palynziq is distributed in the U.S. through certain certified specialty pharmacies under the Palynziq Risk Evaluation and Mitigation Strategy (REMS) program, and Aldurazyme is marketed worldwide by Sanofi Genzyme (Genzyme). Outside the U.S., our commercial products are sold to authorized distributors or directly to government purchasers or hospitals, which act as the end-users. In certain countries, governments place large periodic orders for our products. The timing of these large government orders can be inconsistent and can create significant quarter to quarter variation in our revenues.

The decrease in Net Product Revenues for the three months ended September 30, 2021 as compared to the three ended September 30, 2020 was primarily attributed to the following:

- a decrease in Kuvan product revenues primarily due to generic competition due to the loss of exclusivity in the U.S.;
- a decrease in Aldurazyme product revenues due to timing of product fulfillment to Genzyme; and
- a decrease in Vimizim and Naglazyme product revenues primarily driven by timing of orders from Europe and the Middle East; partially offset by
- an increase in Palynziq product revenues primarily due to a combination of revenues from more patients in the U.S. achieving maintenance dosing and new patients initiating therapy and to a lesser extent incremental growth in the European, Middle East and African (EMEA) region; and
- an increase in Brineura product revenues due to new patients initiating therapy driven by growth in EMEA and North America.

The decrease in Net Product Revenues for the nine months ended September 30, 2021 as compared to the nine ended September 30, 2020 was primarily attributed to the following:

- a decrease in Kuvan product revenues due to generic competition due to the loss of exclusivity in the U.S.;
- a decrease in Aldurazyme revenues due to timing of product fulfillment to Genzyme; partially offset by
- an increase in Vimizim and Naglazyme product revenues primarily driven by larger government orders primarily from Europe and the Middle East; and
- an increase in Palynziq revenues primarily due to a combination of revenue from more U.S. patients achieving maintenance dosing and new patients initiating therapy and to a lesser extent incremental growth in the EMEA region.

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

We anticipate the COVID-19 pandemic could have a continued impact on future Net Product Revenues during the remainder of 2021 as many of our products are administered via infusions in a clinic or hospital setting and/or by a healthcare professional. Although we worked with our patient community and health care providers to find alternative arrangements where necessary, such as providing infusions at home, the revenues from the doses of our products that were missed by patients and the lost revenues from delayed treatment starts for new patients will never be recouped. See the risk factor "The COVID-19 pandemic could continue to materially adversely affect our business, results of operations and financial condition" in "Risk Factors" included in Part II, Item 1A of this Quarterly Report for additional information.

In October 2020, we lost U.S market exclusivity for Kuvan. We anticipated and prepared for this loss of exclusivity and the reduction in our market share, as well as the adverse effect on our revenues and results of operations. We may continue to experience adverse effects on our market share and revenues in the future. See the risk factor "The sale of generic versions of Kuvan by generic manufacturers has adversely affected and will continue to adversely affect our revenues and results of operations" in "Risk Factors" included in Part II, Item 1A of this Quarterly Report for additional information. Additionally, we received European approval for Voxzogo in the third quarter of 2021 and are focused on markets where early market access and reimbursement are possible, such as France and Germany.

We face exposure to movements in foreign currency exchange rates, primarily the Euro. We use foreign currency exchange contracts to hedge a percentage of our foreign currency exposure. The following table shows our Net Product Revenues denominated in USD and foreign currencies:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Sales denominated in USD	\$ 220.5	\$ 302.6	\$ (82.1)	\$ 732.5	\$ 846.4	\$ (113.9)
Sales denominated in foreign currencies	173.4	158.1	15.3	615.8	522.4	93.4
Total net product revenues	<u>\$ 393.9</u>	<u>\$ 460.7</u>	<u>\$ (66.8)</u>	<u>\$ 1,348.3</u>	<u>\$ 1,368.8</u>	<u>\$ (20.5)</u>

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Favorable (unfavorable) impact of foreign currency exchange rates on product sales denominated in currencies other than USD	\$ (0.7)	\$ (4.0)	\$ 3.3	\$ 1.8	\$ (14.8)	\$ 16.6

The unfavorable impact in the three months ended September 30, 2021 was primarily driven by the weakening of the Argentinian Peso relative to the USD, partially offset by the strengthening of the Canadian Dollar and Great British Pound. The favorable impact for the nine months ended September 30, 2021 was largely driven by the strengthening of the Euro, Great British Pound, Australian Dollar and Canadian Dollar, partially offset by the weakening of the Argentinian Peso and Brazilian Real relative to the USD. This compares to an unfavorable impact for the three and nine months ended September 30, 2020, which were driven primarily by weakening of currencies in certain Latin American markets, such as the Brazilian Real and Colombian Peso relative to the USD.

Royalty and Other Revenues

Royalty and Other Revenues include royalties earned on net sales of products sold and milestones achieved by licensees or sublicensees and rental income associated with the tenants in our facilities.

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Total royalty and other revenues	\$ 14.9	\$ 16.0	\$ (1.1)	\$ 48.2	\$ 39.5	\$ 8.7

The decrease in Royalty and Other Revenues for the three months ended September 30, 2021 compared to the same period in 2020 was primarily due to lower licensing revenues earned from third parties. The increase in Royalty and Other

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

Revenues for the nine months ended September 30, 2021 compared to the same period in 2020 was primarily due to a license payment received from a third party due to their achievement of a regulatory milestone in the three months ended March 31, 2021.

We expect to continue to earn royalties from third parties in the future.

Cost of Sales and Gross Margin

Cost of Sales includes raw materials, personnel and facility and other costs associated with manufacturing our commercial products. These costs include production materials, production costs at our manufacturing facilities, third-party manufacturing costs, and internal and external final formulation and packaging costs. Cost of Sales also includes royalties payable to third parties based on sales of our products and charges for inventory valuation reserves. Gross margin is calculated on Total Revenues, which includes Royalty and Other Revenues that usually do not have associated costs.

The following table summarizes our Cost of Sales and gross margin:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Total revenues	\$ 408.7	\$ 476.8	\$ (68.1)	\$ 1,396.5	\$ 1,408.3	\$ (11.8)
Cost of sales	\$ 103.5	\$ 188.8	\$ (85.3)	\$ 350.8	\$ 398.1	\$ (47.3)
Gross margin	74.7 %	60.4 %	14.3 %	74.9 %	71.7 %	3.2 %

Cost of Sales decreased for the three and nine months ended September 30, 2021 compared to the same periods in 2020 primarily due to the \$81.2 million pre-launch valoctocogene roxaparvovec inventory charge following regulatory responses received in third quarter of 2020 requesting additional data extending the anticipated regulatory approval timelines. Gross margin for the three and nine months ended September 30, 2021 compared to the same periods in 2020 increased primarily due to the pre-launch valoctocogene roxaparvovec inventory charge in the three months ended September 30, 2020.

Research and Development

R&D expense includes costs associated with the research and development of product candidates and post-marketing research commitments related to our approved products. R&D expense primarily includes preclinical and clinical studies, personnel and raw materials costs associated with manufacturing clinical product, quality control and assurance, other R&D activities, facilities and regulatory costs.

We manage our R&D expense by identifying the R&D activities we anticipate will be performed during a given period and then prioritizing efforts based on scientific data, probability of successful development, market potential, available human and capital resources and other similar considerations. We continually review our product pipeline and the development status of product candidates and, as necessary, reallocate resources among the research and development portfolio that we believe will best support the future growth of our business. Continued material investment in R&D activities that we have strategically prioritized remains a core component of our business model and future growth plans.

We evaluate the recoverability of costs associated with pre-launch manufacturing activities and capitalize the costs incurred if recoverability is highly likely. We have capitalized \$4.8 million of manufacturing-related costs for Voxzogo pre-launch inventory as of September 30, 2021. Voxzogo, which was granted marketing approval in the EU on August 27, 2021, is still a product candidate in other regions, including the U.S. See Note 6 to our accompanying Consolidated Financial Statements for additional information regarding our inventory.

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

R&D expense consisted of the following:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Research and early development	\$ 59.2	\$ 35.2	\$ 24.0	\$ 148.7	\$ 123.6	\$ 25.1
Valoctocogene roxaparovec	29.1	28.4	0.7	84.0	92.6	(8.6)
Voxzogo	26.1	30.7	(4.6)	99.0	97.8	1.2
Approved products	25.8	31.2	(5.4)	80.5	97.5	(17.0)
BMN 307	14.6	18.6	(4.0)	44.7	53.7	(9.0)
Other	3.1	3.0	0.1	10.8	6.2	4.6
Total R&D expense	\$ 157.9	\$ 147.1	\$ 10.8	\$ 467.7	\$ 471.4	\$ (3.7)

The increase in R&D expense for the three months ended September 30, 2021 as compared to the same period in 2020 primarily comprised the following:

- higher spend in research and early development programs due to increased pre-clinical activities and a \$10.0 million development milestone earned by a third party in the three months ended September 30, 2021; partially offset by
- a reduction in clinical activities related to approved products as the long-term post marketing studies were completed;
- a decrease in Voxzogo manufacturing costs for which capitalization began in the three months ended March 31, 2021 for estimated European demand; and
- a decrease in BMN 307 manufacturing costs due to clinical manufacturing activities that occurred during 2020.

The decrease in R&D expense for the nine months ended September 30, 2021 as compared to the same period in 2020 primarily comprised the following:

- a reduction in clinical activities related to approved products as the long-term post marketing studies were completed;
- a decrease in BMN 307 manufacturing costs due to clinical manufacturing activities that occurred during 2020;
- a decrease in clinical trial activities related to valoctocogene roxaparovec as patients transitioned to the monitoring phase of the study; partially offset by
- higher spend in research and early development programs due to increased pre-clinical activities and a \$10.0 million development milestone earned by a third party in the three months ended September 30, 2021.

We expect R&D expense to increase in future periods, primarily due to increased activities for our research and early development programs while we continue to develop our later stage programs.

Selling, General and Administrative

Sales and marketing (S&M) expense primarily consisted of employee-related expenses for our sales group, brand marketing, patient support groups and pre-commercialization expenses related to our product candidates. General and

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

administrative (G&A) expense primarily consisted of corporate support and other administrative expenses, including administrative employee-related expenses.

SG&A expenses consisted of the following:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
S&M expense	\$ 97.0	\$ 101.1	\$ (4.1)	\$ 292.0	\$ 293.0	\$ (1.0)
G&A expense	86.3	78.4	7.9	249.8	249.2	0.6
Total SG&A expense	<u>\$ 183.3</u>	<u>\$ 179.5</u>	<u>\$ 3.8</u>	<u>\$ 541.8</u>	<u>\$ 542.2</u>	<u>\$ (0.4)</u>

S&M expenses by product were as follows:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
PKU Products (Kuvan and Palynziq)	\$ 29.9	\$ 30.0	\$ (0.1)	\$ 91.9	\$ 91.8	\$ 0.1
MPS Products (Aldurazyme, Naglazyme and Vimizim)	23.9	25.4	(1.5)	76.0	78.0	(2.0)
Voxzogo	18.5	8.2	10.3	52.9	19.9	33.0
Valoctocogene roxaparovec	13.1	26.9	(13.8)	37.6	70.6	(33.0)
Brineura	8.9	8.5	0.4	26.1	27.3	(1.2)
Other	2.7	2.1	0.6	7.5	5.4	2.1
Total S&M expense	<u>\$ 97.0</u>	<u>\$ 101.1</u>	<u>\$ (4.1)</u>	<u>\$ 292.0</u>	<u>\$ 293.0</u>	<u>\$ (1.0)</u>

The decrease in S&M expense for the three and nine months ended September 30, 2021 as compared to the same periods in 2020 was primarily due to a reduction in valoctocogene roxaparovec activities based on a change in anticipated timelines for potential approval following regulatory responses received in the third quarter of 2020 requesting additional data, partially offset by an increase in pre-commercialization activities related to Voxzogo.

The increase in G&A expense for the three months ended September 30, 2021 as compared to the same period in 2020 was primarily due to the idle plant time related to maintaining our valoctocogene roxaparovec manufacturing capabilities.

G&A expense for the nine months ended September 30, 2021 compared to the same period in 2020 was relatively flat.

We expect SG&A expense to increase in future periods as a result of preparing to launch new products and support of our global business as it grows.

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

Intangible Asset Amortization and Contingent Consideration and Gain on Sale of Nonfinancial Assets

Changes during the periods presented for Intangible Asset Amortization and Contingent Consideration and Gain on Sale of Nonfinancial Assets were as follows:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Changes in the fair value of contingent consideration (gain) / loss	\$ 1.8	\$ 1.9	\$ (0.1)	\$ 6.3	\$ 1.4	\$ 4.9
Amortization of intangible assets	15.4	15.5	(0.1)	46.3	46.6	(0.3)
Total intangible asset amortization and contingent consideration	<u>\$ 17.2</u>	<u>\$ 17.4</u>	<u>\$ (0.2)</u>	<u>\$ 52.6</u>	<u>\$ 48.0</u>	<u>\$ 4.6</u>
Gain on sale of nonfinancial assets	\$ —	\$ —	\$ —	\$ —	\$ 59.5	\$ (59.5)

Fair value of contingent consideration – the increase in the fair value of contingent consideration for the nine months ended September 30, 2021 as compared to the same period in 2020 was attributable to changes in the estimated probability of achieving sales milestones related to our PKU products.

Amortization of intangible assets – the expense for the three and nine months ended September 30, 2021 as compared to the same periods in 2020 was relatively flat.

Gain on Sale of Nonfinancial Assets – the decrease in the nine months ended September 30, 2021 is due to the recognition of a gain of \$59.5 million in the nine months ended September 30, 2020 related to the divestiture and sale of the Firdapse business.

Interest Income

We invest our cash equivalents and investments in U.S. government securities and other high credit quality debt securities in order to limit default and market risk. Interest Income was as follows:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Interest income	\$ 1.8	\$ 4.0	\$ (2.2)	\$ 8.7	\$ 13.5	\$ (4.8)

Interest Income for the three and nine months ended September 30, 2021 decreased as compared to same period in 2020 primarily due to lower interest rates and total portfolio returns.

We expect interest income to be lower over the next 12 months due to lower interest rates and yields on our cash equivalents and investments.

Interest Expense

We incur interest expense primarily on our convertible debt. Interest Expense for the periods presented was as follows:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Interest expense	\$ 3.9	\$ 9.6	\$ (5.7)	\$ 11.5	\$ 24.6	\$ (13.1)

Interest Expense for the three and nine months ended September 30, 2021 compared to 2020 was lower due primarily to the settlement of the 2020 Notes in the fourth quarter of 2020.

We do not expect interest expense to fluctuate significantly over the next 12 months.

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

Other Income, Net

Other Income, Net for the periods presented was as follows:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Other income, net	\$ 8.9	\$ 1.2	\$ 7.7	\$ 11.8	\$ 1.9	\$ 9.9

Other Income, Net for the three and nine months September 30, 2021 increased compared to the same periods in 2020 primarily due to the receipt of insurance proceeds in excess of direct costs incurred in the third quarter of 2021.

Benefit from Income Taxes

The following table summarizes our income tax benefit:

	Three Months Ended September 30,			Nine Months Ended September 30,		
	2021	2020	Change	2021	2020	Change
Benefit from income taxes	\$ (9.7)	\$ (846.0)	\$ 836.3	\$ (2.6)	\$ (839.1)	\$ 836.5

Tax benefit was computed using a forecasted annual effective tax rate for the three and nine months ended September 30, 2021 and 2020. The Benefit from Income Taxes for the three and nine months ended September 30, 2021 and 2020 consisted of state, federal and foreign current tax expense which was offset by tax benefits related to stock option exercises and deferred tax benefits from federal orphan drug credits and R&D credits.

In the three month ended September 30, 2020, we completed an intra-entity transfer of certain IP rights to an Irish subsidiary where our Ex-US regional headquarters are located. The transaction did not result in a taxable gain however, our Irish subsidiary recognized a deferred tax asset for the book and tax basis difference of the transferred IP. As a result, we recognized a deferred tax asset of \$835.1 million, and related tax benefit on our Condensed Consolidated Financial Statements based on the fair value of the transferred intellectual property rights.

Financial Position, Liquidity and Capital Resources

As of September 30, 2021, we had \$1.55 billion in cash, cash equivalents and investments. We expect to fund our operations with our net product revenues from our commercial products, cash, cash equivalents and investments, supplemented as may become necessary by proceeds from equity or debt financings and loans, or collaborative agreements with corporate partners. We believe that our existing cash, cash equivalents and investments and cash we expect to generate from operations will be sufficient to satisfy our liquidity requirements for the next 12 months. We may require additional financing to fund the repayment of our convertible debt, future milestone payments and our future operations, including the commercialization of our products and product candidates currently under development, preclinical studies and clinical trials, and potential licenses and acquisitions. We will need to raise additional funds from equity or debt securities, loans or collaborative agreements if we are unable to satisfy our liquidity requirements. The timing and mix of our funding options could change depending on many factors, including how much we elect to spend on our development programs, potential licenses and acquisitions of complementary technologies, products and companies or if we elect to settle all or a portion of our convertible debt in cash. Our ability to raise additional capital may also be adversely impacted by potential worsening global economic conditions and the recent disruptions to, and volatility in, financial markets in the U.S. and worldwide resulting from the ongoing COVID-19 pandemic.

In managing our liquidity needs in the U.S., we do not rely on unrepatriated earnings as a source of funds. As of September 30, 2021, \$192.3 million of our \$1.55 billion balance of cash, cash equivalents and investments was held in non-U.S. subsidiaries, a significant portion of which is required to fund the liquidity needs of these non-U.S. subsidiaries. For additional discussion regarding income taxes, see Note 18 to our Consolidated Financial Statements included in our Annual Report on Form 10-K for the year ended December 31, 2020.

We are mindful that conditions in the current macroeconomic environment could affect our ability to achieve our goals. We sell our products in countries that face economic volatility and weakness. Although we have historically collected receivables from customers in such countries, sustained weakness or further deterioration of the local economies and currencies and adverse effects of the impact of the ongoing COVID-19 pandemic may cause customers in those countries to be unable to pay for our products. We will continue to monitor these conditions and will attempt to adjust our business processes, as appropriate, to mitigate macroeconomic risks to our business.

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

Our liquidity and capital resources as of September 30, 2021 and December 31, 2020 were as follows:

	September 30, 2021	December 31, 2020	Change
Cash and cash equivalents	\$ 617.1	\$ 649.2	\$ (32.1)
Short-term investments	462.3	416.2	46.1
Long-term investments	466.7	285.5	181.2
Cash, cash equivalents and investments	<u>\$ 1,546.1</u>	<u>\$ 1,350.9</u>	<u>\$ 195.2</u>
Total convertible debt, net	\$ 1,078.1	\$ 1,075.1	\$ 3.0

Our cash flows for the nine months ended September 30, 2021 and 2020 are summarized as follows:

	September 30, 2021	September 30, 2020	Change
Cash and cash equivalents at the beginning of the period	\$ 649.2	\$ 437.4	\$ 211.8
Net cash provided by operating activities	293.4	98.7	194.7
Net cash used in investing activities	(310.9)	(64.6)	(246.3)
Net cash provided by (used in) financing activities	(14.4)	547.3	(561.7)
Foreign exchange impact	(0.2)	(3.1)	2.9
Cash and cash equivalents at the end of the period	\$ 617.1	\$ 1,015.7	\$ (398.6)
Short-term and long-term investments	929.0	755.1	173.9
Cash, cash equivalents and investments	<u>\$ 1,546.1</u>	<u>\$ 1,770.8</u>	<u>\$ (224.7)</u>

Cash Provided by Operating Activities

Net cash provided by operating activities increased by \$194.7 million to \$293.4 million in the nine months ended September 30, 2021, compared to cash provided by operating activities of \$98.7 million in the nine months ended September 30, 2020. The increase was primarily attributed to the timing of cash receipts from our customers and licensees, lower employee compensation related payments and tax refund proceeds.

Cash Used in Investing Activities

Net cash used in investing activities increased by \$246.3 million to \$310.9 million in the nine months ended September 30, 2021, compared to cash used in investing activities of \$64.6 million in the nine months ended September 30, 2020. The increase in cash used in investing activities was primarily attributable to higher net purchases of available-for-sale debt securities and the absence of the proceeds received from divestiture and sale of Firdapse to a third party in the first quarter of 2020 partially offset by lower purchases of property, plant and equipment.

Cash Provided by (Used in) Financing Activities

Net cash used in financing activities increased by \$561.7 million to \$14.4 million in the nine months ended September 30, 2021, compared to cash provided by financing activities of \$547.3 million in the nine months ended September 30, 2020 primarily due to the proceeds from the issuance of the 2027 Notes in the second quarter of 2020.

Other Information

Our \$1.1 billion (undiscounted) of total convertible debt as of September 30, 2021 will impact our liquidity due to the semi-annual cash interest payments. As of September 30, 2021, our indebtedness consisted of our 0.599% senior subordinated convertible notes due in 2024 (the 2024 Notes) and our 1.25% senior subordinated convertible notes due in 2027 (the 2027 Notes and together with the 2024 Notes, the Notes), which, if not converted, will be required to be repaid in cash at maturity in August 2024 and May 2027, respectively. We will need cash not only to pay the ongoing interest due on the Notes during their term, but also to repay the principal amount of the Notes if not converted.

In October 2018, we entered into an unsecured revolving credit facility of up to \$200.0 million which includes a letter of credit subfacility and a swingline loan subfacility. The credit facility is intended to finance ongoing working capital needs and for other general corporate purposes. In May 2021, we amended the credit facility agreement, extending the maturity date from October 19, 2021 to May 28, 2024, among other changes. The amended credit facility contains financial covenants including a

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions of U.S. dollars, except as otherwise disclosed)

maximum leverage ratio and a minimum interest coverage ratio. As of September 30, 2021, there were no amounts outstanding under the credit facility and we and certain of our subsidiaries that serve as guarantors were in compliance with all covenants.

For additional information related to our convertible debt see Note 9 to our accompanying Condensed Consolidated Financial Statements and Note 13 - *Debt* included in our Annual Report on Form 10-K for the year ended December 31, 2020.

Funding Commitments

We cannot estimate with certainty the cost to complete any of our product development programs. Additionally, we cannot precisely estimate the time to complete any of our product development programs or when we expect to receive net cash inflows from any of our product development programs. Please see "Risk Factors" included in Part II, Item 1A of this Quarterly Report on Form 10-Q, for a discussion of the reasons we are unable to estimate such information.

Our investment in our product development programs and continued development of our existing commercial products has a major impact on our operating performance. Our R&D expenses for the period since inception as of September 30, 2021 were as follows:

	Since Program Inception
Valoctocogene roxaparovec	\$ 794.0
Voxzogo	\$ 669.7
BMN 307	\$ 224.6
Approved products	\$ 2,345.2

We may need or elect to increase our spending above our current long-term plans to be able to achieve our long-term goals. This may increase our capital requirements, including: costs associated with the commercialization of our products; additional clinical trials; investments in the manufacturing of our commercial products; preclinical studies and clinical trials for our product candidates; potential licenses and other acquisitions of complementary technologies, products and companies; and general corporate purposes.

Our future capital requirements will depend on many factors, including, but not limited to:

- our ability to successfully market and sell our products;
- the time and cost necessary to develop commercial manufacturing processes, including quality systems, and to build or acquire manufacturing capabilities;
- the progress and success of our preclinical studies and clinical trials (including the manufacture of materials for use in such studies and trials);
- the timing, number, size and scope of our preclinical studies and clinical trials;
- the time and cost necessary to obtain regulatory approvals and the costs of post-marketing studies which may be required by regulatory authorities; and
- the progress of research programs carried out by us.

Off-Balance Sheet Arrangements

We do not have any off-balance sheet arrangements that are currently material or reasonably likely to be material to our consolidated financial position or results of operations.

Contractual and Commercial Obligations

We have contractual and commercial obligations under our convertible debt, leases and other obligations related to R&D activities, purchase commitments, licenses and sales royalties with annual minimums. As of September 30, 2021, such commitments and other minimum contractual obligations for clinical and post-marketing services were estimated at approximately \$107.7 million.

As of September 30, 2021, we were also subject to contingent payments totaling approximately \$708.8 million upon achievement of certain development and regulatory activities and commercial sales milestones if they occur before certain dates in the future. Of this amount, \$70.0 million were considered probable and comprised of commercial milestones related to the

Management's Discussion and Analysis of Financial Condition and Results of Operations (continued)
(In millions, except as otherwise disclosed)

acquisition of certain rights and other assets with respect to Kuvan and Palynziq from a third party, \$405.5 million were considered reasonably possible and primarily related to development milestones and \$233.3 million were considered remote as we are no longer developing the related programs.

As of September 30, 2021, the fair value of the contingent liabilities recorded on our Condensed Consolidated Balance Sheet was \$63.4 million, of which \$48.2 million was short term.

Other than as set forth above, there have been no material changes to our contractual and commercial obligations during the nine months ended September 30, 2021, as compared to the obligations disclosed in Management's Discussion and Analysis in our Annual Report on Form 10-K for the year ended December 31, 2020.

Item 3. Quantitative and Qualitative Disclosures About Market Risk

Our market risks during the nine months ended September 30, 2021 have not materially changed from those discussed in Part II, Item 7A of our Annual Report on Form 10-K for the year ended December 31, 2020.

Item 4. Controls and Procedures

(a) Controls and Procedures

An evaluation was carried out, under the supervision of and with the participation of our management, including our Chief Executive Officer and our Chief Financial Officer, of the effectiveness 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 (the Exchange Act)), as of the end of the period covered by this report.

Based on the evaluation, our Chief Executive Officer and our Chief Financial Officer have concluded that our disclosure controls and procedures were effective, at the reasonable assurance level, as of September 30, 2021.

In designing and evaluating our disclosure controls and procedures, our management recognizes that any controls and procedures, no matter how well designed and operated, can provide only reasonable assurance of achieving the desired control objectives, and our management must apply its judgment in evaluating the cost-benefit relationship of possible controls and procedures. Accordingly, our disclosure controls and procedures are designed to provide reasonable, not absolute, assurance that the objectives of our disclosure controls system are met.

(b) Change in Internal Control over Financial Reporting

There were no changes in our internal control over financial reporting, as such term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act, during our most recently completed quarter that have materially affected or are reasonably likely to materially affect our internal control over financial reporting. We continue to utilize the Committee of Sponsoring Organizations of the Treadway Commission (COSO) 2013 Framework on internal control.

PART II. OTHER INFORMATION

Item 1. Legal Proceedings

On September 25, 2020, a purported shareholder class action lawsuit was filed against us, our Chief Executive Officer, our President of Worldwide Research and Development and our Chief Financial Officer in the United States District Court in the Northern District of California, alleging violations under Sections 10(b) and 20(a) of the Securities Exchange Act of 1934 as amended (the Exchange Act). The complaint alleges that the Company made materially false or misleading statements regarding the clinical trials and Biologics License Application (BLA) for valoctocogene roxaparovec by purportedly failing to disclose that differences between the Company's Phase 1/2 and Phase 3 clinical studies limited the ability of the Phase 1/2 study to support valoctocogene roxaparovec's durability of effect and, as a result, that it was foreseeable that the FDA would not approve the BLA without additional data. The complaint seeks an unspecified amount of damages, pre-judgment and post-judgment interest, attorneys' fees, expert fees, and other costs. In December 2020, the court hearing the case appointed Arbejdsmarkedets Tillægspension as lead plaintiff. The lead plaintiff filed an amended complaint in February 2021, dropping our Chief Financial Officer as a defendant, and asserting that the Company misled investors about the progress of the FDA's review of our BLA for valoctocogene roxaparovec. Our motion to dismiss the complaint was filed on April 22, 2021. We believe that the claims have no merit and we intend to vigorously defend this action.

On October 22, 2021, a purported securities class action lawsuit was filed against us, our Chief Executive Officer, our current and prior Chief Financial Officers, and our President of Worldwide Research & Development in the United States District Court for the Northern District of California, alleging violations under Sections 10(b) and 20(a) of the Exchange Act. The complaint alleges that the Company made materially false or misleading statements regarding BMN 307 by purportedly failing to disclose information about BMN 307's safety profile, and by purportedly overstating BMN 307's clinical and commercial prospects. The complaint seeks an unspecified amount of damages, pre-judgment and post-judgment interest, attorneys' fees, expert fees, and other costs. We believe that the claims have no merit and we intend to vigorously defend this action.

Item 1A. Risk Factors

An investment in our securities involves a high degree of risk. We operate in a dynamic and rapidly changing industry that involves numerous risks and uncertainties. The risks and uncertainties described below are not the only ones we face. Other risks and uncertainties, including those that we do not currently consider material, may impair our business. If any of the risks discussed below actually occur, our business, financial condition, operating results or cash flows could be materially adversely affected. This could cause the value of our securities to decline, and you may lose all or part of your investment.

We have marked with an asterisk (*) those risk factors below that include a substantive change from or update to the risk factors included in our Annual Report on Form 10-K for the year ended December 31, 2020, which was filed with the SEC on February 26, 2021.

Business and Operational Risks

***The COVID-19 pandemic could continue to materially adversely affect our business, results of operations, and financial condition.**

The COVID-19 pandemic has resulted in travel restrictions, quarantines, "work-from-home" and "shelter-in-place" orders and extended shutdown of certain businesses around the world, including in many countries in which we operate. Our global revenue sources, mostly in the form of demand interruptions such as missed patient infusions and delayed treatment starts for new patients, and our overall business operations were impacted by the COVID-19 pandemic, and we expect that the pandemic will continue to adversely impact our financial results and our business generally for at least the remainder of 2021 and potentially longer if the pandemic continues to impact countries in which we operate. Ongoing and future effects of the COVID-19 pandemic (or any future pandemic) on all aspects of our business and operations, including revenues, expenses, reserves and allowances, manufacturing, clinical trials and research and development costs, and the duration of such effects, are highly uncertain and difficult to predict.

The COVID-19 pandemic has adversely affected and will likely continue to adversely impact our product development programs, including preclinical study and clinical trial operations. We have been, and will likely continue to be, unable to initiate or continue conducting clinical trials as originally planned due to the prioritization of hospital resources toward the outbreak, difficulty in recruiting and retaining healthcare providers and staff due to their diversion toward treating COVID-19 patients or their heightened exposure to COVID-19, potential unwillingness of patients to enroll or continue in trials for fear of exposure to COVID-19 at sites, or the inability of patients to comply with clinical trial protocols as quarantines or travel restrictions impede patient movement or otherwise interrupt healthcare services. For example, we experienced delays in certain clinical trials and have had to reevaluate expected timelines for those trials. In addition, we rely on independent clinical investigators, contract research organizations (CROs) and other third-party service providers to assist us in managing, monitoring and otherwise carrying out our preclinical studies and clinical trials, and the outbreak may affect their ability to devote sufficient time and resources to our programs or to travel to sites to perform work for us. Additionally, the COVID-19 pandemic has delayed, and may continue to

postpone, necessary regulatory inspections and other interactions with regulators regarding our products in development, which could delay review or approval of our regulatory submissions.

COVID-19 could adversely affect our ability to source materials and supplies and successfully manufacture and distribute our product candidates and products. The outbreak could result in reduced operations of third-party suppliers of raw materials and supplies upon whom we rely or otherwise limit our ability to obtain sufficient materials and supplies necessary for production of our therapies. Our manufacturing facilities and those of our contract manufacturers are located in areas impacted by the COVID-19 pandemic, which may result in delays or disruptions in our ability to produce product candidates and products. If we or any third party in our supply or distribution chain are adversely impacted by the COVID-19 pandemic, including as a result of required closures, staffing shortages, production slowdowns and disruptions in delivery systems, our operations may be disrupted, limiting our ability to manufacture and distribute our product candidates for clinical trials and research and development operations and our products for commercial sales.

Our commercial operations have also been, and will likely continue to be, adversely impacted by the COVID-19 pandemic. Many of our products are administered via infusions in a clinic or hospital setting and/or by a healthcare professional. Treating COVID-19 patients has become the priority for many healthcare facilities and workers, so it has become, and may continue to be, difficult for some of our patients to receive our therapies that are administered by infusion. Although we are working with our patient community and healthcare providers to find alternative arrangements where necessary, such as providing infusions at home, the revenue from doses of our products that are missed by patients and the lost revenues from delayed treatment starts for new patients will never be recouped. Moreover, some patients may choose to skip infusions because they do not want to risk exposure to COVID-19 by having a healthcare provider administer the therapy at a healthcare facility or at home. The pandemic has also hindered our ability to find new patients and start treating newly found patients, and it has limited our sales force's ability to promote our products to distributors, hospitals, clinics, doctors and pharmacies, which could adversely affect our revenues and results of operations. In addition, the COVID-19 pandemic could adversely affect our workforce and the employees of companies with which we do business, thereby disrupting our business operations. We have implemented work-from-home policies for employees whose jobs do not require them to be onsite. Increased reliance by us and the companies with which we do business on personnel working from home may negatively impact productivity, increase cyber security risk, create data accessibility issues, increase the risk for communication disruptions, or otherwise disrupt or delay normal business operations. For our employees whose jobs require them to be onsite, we have taken precautions to avoid the spread of COVID-19 among our employees, but we cannot guarantee our workforce will not face an outbreak that could adversely impact our operations.

While the long-term economic impact and the duration of the COVID-19 pandemic may be difficult to predict, the pandemic has resulted in, and may continue to result in, significant disruption of global financial markets, which could reduce our ability to access capital and could negatively affect our liquidity and the liquidity and stability of markets for our common stock and convertible notes. In addition, a recession, further market correction or depression resulting from the COVID-19 pandemic could materially adversely affect our business and the value of our common stock and convertible notes.

To the extent the COVID-19 pandemic continues to adversely affect our business and financial results, it may also have the effect of heightening many of the other risks described in this Risk Factors section, such as those relating to our conducting a significant amount of our sales and operations outside of the U.S., exposure to changes in foreign exchange rates, our substantial indebtedness, our need to generate sufficient cash flows to service our indebtedness and finance our operations, our ability to comply with the covenants contained in the agreements that govern our indebtedness and the volatility of our stock price.

***Because the target patient populations for our products are small, we must achieve significant market share and maintain high per-patient prices for our products to achieve and maintain profitability.**

All of our products target diseases with small patient populations. As a result, our per-patient prices must be relatively high in order to recover our development and manufacturing costs and achieve and maintain profitability. For Brineura, Naglazyme and Vimizim in particular, we must market worldwide to achieve significant market penetration of the product. In addition, because the number of potential patients in each disease population is small, it is not only important to find patients who begin therapy to achieve significant market penetration of the product, but we also need to be able to maintain these patients on therapy for an extended period of time. Due to the expected costs of treatment for our products, we may be unable to maintain or obtain sufficient market share at a price high enough to justify our product development efforts and manufacturing expenses.

***If we fail to obtain and maintain an adequate level of coverage and reimbursement for our products by third-party payers, the sales of our products would be adversely affected or there may be no commercially viable markets for our products.**

The course of treatment for patients using our products is expensive. We expect patients to need treatment for extended periods, and for some products throughout the lifetimes of the patients. We expect that most families of patients will not be capable of paying for this treatment themselves. There will be no commercially viable market for our products without coverage and reimbursement from third-party payers. Additionally, even if there is a commercially viable market, if the level of reimbursement is below our expectations, our revenues and gross margin will be adversely affected.

Third-party payers, such as government or private healthcare insurers, carefully review and increasingly challenge the prices charged for drugs. Reimbursement rates from private companies vary depending on the third-party payer, the insurance plan and other factors. Obtaining coverage and adequate reimbursement for our products may be particularly difficult because of the higher prices often associated with drugs administered under the supervision of a physician. Reimbursement systems in international markets vary significantly by country and by region, and reimbursement approvals must be obtained on a country-by-country basis.

Government authorities and other third-party payers are developing increasingly sophisticated methods of controlling healthcare costs, such as by limiting coverage and the amount of reimbursement for particular medications. Increasingly, third-party payers are requiring that drug companies provide them with predetermined discounts from list prices as a condition of coverage, are using restrictive formularies and preferred drug lists to leverage greater discounts in competitive classes, and are challenging the prices charged for medical products. Further, no uniform policy requirement for coverage and reimbursement for drug products exists among third-party payers in the U.S. Therefore, coverage and reimbursement for drug products can differ significantly from payer to payer. As a result, the coverage determination process is often a time-consuming and costly process that will require us to provide scientific and clinical support for the use of our products to each payer separately, with no assurance that coverage and adequate reimbursement will be applied consistently or obtained in the first instance.

We cannot be sure that coverage and reimbursement will be available for any product that we commercialize or will continue to be available for any product that we have commercialized and, if reimbursement is available, what the level of reimbursement will be. Even if favorable coverage and reimbursement status is attained for one or more products for which we receive regulatory approval, less favorable coverage policies and reimbursement rates may be implemented in the future. Coverage and reimbursement may impact the demand for, or the price of, any product candidate for which we obtain marketing approval. If coverage and reimbursement are not available or reimbursement is available only to limited levels, we may not successfully commercialize any product candidate for which we obtain marketing approval or continue to market any product that has already been commercialized.

Reimbursement in the European Union (EU) and many other territories must be negotiated on a country-by-country basis and in many countries the product cannot be commercially launched until reimbursement is approved. The timing to complete the negotiation process in each country is highly uncertain, and in some countries, we expect that it will exceed 12 months. Even after a price is negotiated, countries frequently request or require reductions to the price and other concessions over time.

For our future products, we will not know what the reimbursement rates will be until we are ready to market the product and we actually negotiate the rates. If we are unable to obtain sufficiently high reimbursement rates for our products, they may not be commercially viable or our future revenues and gross margin may be adversely affected.

If we fail to compete successfully with respect to product sales, we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product and our revenues could be adversely affected.

Our competitors may develop, manufacture and market products that are more effective or less expensive than ours. They may also obtain regulatory approvals for their products faster than we can obtain them (including those products with orphan drug designation, which may prevent us from marketing our product entirely) or commercialize their products before we do. With respect to valoctocogene roxaparovec, if the product candidate is approved, we will face a highly developed and competitive market for hemophilia A treatments. As we commercialize valoctocogene roxaparovec, if approved, we may face intense competition from large pharmaceutical companies with extensive resources and established relationships in the hemophilia A community. If we do not compete successfully, our revenues would be adversely affected, and we may be unable to generate sufficient sales to recover our expenses related to the development of a product program or to justify continued marketing of a product.

Changes in methods of treatment of disease could reduce demand for our products and adversely affect revenues.

Even if our product candidates are approved, if doctors elect a course of treatment which does not include our products, this decision would reduce demand for our products and adversely affect revenues. For example, if gene therapy becomes widely used as a treatment of genetic diseases, the use of enzyme replacement therapy, such as Aldurazyme, Naglazyme, and Vimizim in MPS diseases, could be greatly reduced. Moreover, if we obtain regulatory approval for valoctocogene roxaparovec, the commercial success of valoctocogene roxaparovec will still depend, in part, on the acceptance of physicians, patients and healthcare payers of gene therapy products in general, and our product candidate in particular, as medically necessary, cost effective and safe. Changes in treatment method can be caused by the introduction of other companies' products or the development of new technologies or surgical procedures which may not directly compete with ours, but which have the effect of changing how doctors decide to treat a disease.

If we fail to develop new products and product candidates or compete successfully with respect to acquisitions, joint ventures, licenses or other collaboration opportunities, our ability to continue to expand our product pipeline and our growth and development would be impaired.

Our future growth and development depend in part on our ability to successfully develop new products from our research and development activities. The development of biopharmaceutical products is very expensive and time intensive and involves a great degree of risk. The outcomes of research and development programs, especially for innovative biopharmaceuticals, are inherently uncertain and may not result in the commercialization of any products.

Our competitors compete with us to attract organizations for acquisitions, joint ventures, licensing arrangements or other collaborations. To date, several of our former and current product programs have been acquired through acquisitions and several of our former and current product programs have been developed through licensing or collaborative arrangements, such as Aldurazyme, Kuvan and Naglazyme. These collaborations include licensing proprietary technology from, and other relationships with, academic research institutions. Our future success will depend, in part, on our ability to identify additional opportunities and to successfully enter into partnering or acquisition agreements for those opportunities. If our competitors successfully enter into partnering arrangements or license agreements with academic research institutions, we will then be precluded from pursuing those specific opportunities. Because each of these opportunities is unique, we may not be able to find a substitute. Several pharmaceutical and biotechnology companies have already established themselves in the field of genetic diseases. These companies have already begun many drug development programs, some of which may target diseases that we are also targeting, and have already entered into partnering and licensing arrangements with academic research institutions, reducing the pool of available opportunities.

Universities and public and private research institutions also compete with us. While these organizations primarily have educational or basic research objectives, they may develop proprietary technology and acquire patents that we may need for the development of our product candidates. We will attempt to license this proprietary technology, if available. These licenses may not be available to us on acceptable terms, if at all. If we are unable to compete successfully with respect to acquisitions, joint venture and other collaboration opportunities, we may be limited in our ability to develop new products and to continue to expand our product pipeline.

***The sale of generic versions of Kuvan by generic manufacturers has adversely affected and will continue to adversely affect our revenues and results of operations.**

The Drug Price Competition and Patent Term Restoration Act of 1984, known as the Hatch-Waxman Act, permits the Food and Drug Administration (FDA) to approve abbreviated new drug applications (ANDAs) for generic versions of branded drugs. We refer to this process as the ANDA process. The ANDA process permits competitor companies to obtain marketing approval for a drug with the same active ingredient as a branded drug, but does not generally require the conduct and submission of clinical efficacy studies for the generic product. In place of such clinical studies, an ANDA applicant usually needs only to submit data demonstrating that its product is bioequivalent to the branded product.

Pursuant to the Hatch-Waxman Act, companies were permitted to file ANDA applications for proposed generic versions of Kuvan at any time after December 2011. We own several patents that cover Kuvan, and we have listed those patents in conjunction with that product in the FDA's Approved Drug Products with Therapeutic Equivalence Evaluations (the Orange Book). The Hatch-Waxman Act requires an ANDA applicant seeking FDA approval of its proposed generic product prior to the expiration of our Orange Book-listed patents to certify that the applicant believes that our patents are invalid or will not be infringed by the manufacture, use or sale of the drug for which the application has been submitted (a paragraph IV certification) and notify us of such certification (a paragraph IV notice). Upon receipt of a paragraph IV notice, the Hatch-Waxman Act allows us, with proper basis, to bring an action for patent infringement against the ANDA filer, asking that the proposed generic product not be approved until after our patents expire. If we commence a lawsuit within 45 days from receipt of the paragraph IV notice, the Hatch-Waxman Act provides a 30-month stay, during which time the FDA cannot finally approve the applicant's ANDA. If the litigation is resolved in favor of the ANDA applicant during the 30-month stay period, the stay is lifted and the FDA may approve the ANDA if it is otherwise ready for approval. The discovery, trial and appeals process in such a lawsuit is costly, time consuming, and may result in generic competition if the ANDA applicant prevails.

Between 2014 and 2016 we received paragraph IV notice letters from two pharmaceutical companies notifying us that each had filed ANDAs seeking approval of proposed generic versions of Kuvan. We filed lawsuits alleging patent infringement against each company, and between 2015 and 2017 we entered into settlement agreements with the companies that resolved the patent litigation in the U.S. The settlement agreements granted the companies non-exclusive licenses to our Kuvan-related patents to allow them to market generic versions of sapropterin dihydrochloride in the U.S. for the indications approved for Kuvan beginning on October 1, 2020, or earlier under certain circumstances. Generic versions of Kuvan first became available in the U.S. in October 2020, and as expected, our U.S. sales of Kuvan in the fiscal quarters since October 2020 have significantly declined as compared to prior periods. We expect that the continued availability of generic versions of sapropterin dihydrochloride in the U.S. will continue to adversely affect our U.S. sales of Kuvan.

Any future ANDA or related legal proceeding could have an adverse impact on our stock price, and litigation to enforce our patents has, and is likely to continue to, cost a substantial amount and require significant management attention. If the patents covering Kuvan and its use are not upheld in litigation, or if any ANDA filer we bring suit against is found to not infringe our asserted patents, the resulting generic competition following the expiration of regulatory exclusivity would have a material adverse effect on our revenues and results of operations. Moreover, generic competition following the settlements described above could have a material adverse effect on our revenues and results of operations.

We also face generic competition for Kuvan in certain non-U.S. countries, and there is a process equivalent to the ANDA process under Article 10 of Directive 2001/83/EC in the EU. Our ability to successfully market and sell Kuvan in many countries in which we operate is based upon patent rights or certain regulatory forms of exclusivity, or both. The scope of our patent rights and regulatory exclusivity for Kuvan vary from country to country and are dependent on the availability of meaningful legal remedies in each country. If our patent rights and regulatory exclusivity for Kuvan are successfully challenged, expire, or otherwise terminate in a particular country, the resulting generic competition could have a material adverse effect on our revenues and results of operations.

If we do not achieve our projected development goals in the timeframes we announce and expect, the commercialization of our product candidates may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

For planning purposes, we estimate the timing of the accomplishment of various scientific, clinical, regulatory and other product development goals, which we sometimes refer to as milestones. These milestones may include the commencement or completion of scientific studies and clinical trials and the submission of regulatory filings. From time to time, we publicly announce the expected timing of some of these milestones. All of these milestones are based on a variety of assumptions. The actual timing of these milestones can vary dramatically compared to our estimates, in many cases for reasons beyond our control. If we do not meet these milestones as publicly announced, the commercialization of our products may be delayed and the credibility of our management may be adversely affected and, as a result, our stock price may decline.

Regulatory Risks

If we fail to obtain regulatory approval to commercially market and sell our product candidates, or if approval of our product candidates is delayed, we will be unable to generate revenues from the sale of these product candidates, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will increase.

We must obtain regulatory approval to market and sell our product candidates. For example, in the U.S., we must obtain FDA approval for each product candidate that we intend to commercialize, and in the EU we must obtain approval from the European Commission, based on the opinion of the Committee for Medicinal Products for Human Use of the European Medicines Agency (EMA). The FDA and EMA approval processes are typically lengthy and expensive, and approval is never certain. Accordingly, there are no assurances that we will obtain regulatory approval for any of our product candidates. Furthermore, there can be no assurance that approval of one of our product candidates by one regulatory agency will mean that other agencies will also approve the same product candidate. Similarly, regulatory authorities may approve a product candidate for fewer or more limited indications than requested. In addition, regulatory authorities may not approve the labeling claims that are necessary or desirable for the successful commercialization of our product candidates.

We have had fewer interactions with regulatory authorities outside the U.S. and the EU as compared to our interactions with the FDA and EMA. The approval procedures vary among countries and can involve additional clinical testing, and the time required to obtain approval may differ from that required to obtain FDA or EMA approval. Moreover, clinical trials conducted in one country may not be accepted by regulatory authorities in other countries. Approval by the FDA or EMA does not ensure approval by regulatory authorities in other countries, and approval by one or more non-U.S. regulatory authorities does not ensure approval by regulatory authorities in other non-U.S. countries or by the FDA or EMA. However, a failure or delay in obtaining regulatory approval in one country may have a negative effect on the regulatory process in others. The non-U.S. regulatory approval process may include all of the risks associated with obtaining FDA or EMA approval. We may not obtain non-U.S. regulatory approvals on a timely basis, if at all. We may not be able to file for regulatory approvals and even if we file, we may not receive necessary approvals to commercialize our product candidates in any market.

Because of the risks and uncertainties in pharmaceutical development, our product candidates could take a significantly longer time to gain regulatory approval than we expect or may never gain approval. We also rely on independent third-party CROs to file some of our non-U.S. marketing applications and important aspects of the services performed for us by the CROs are out of our direct control. If we fail to adequately manage our CROs, if the CRO elects to prioritize work on our projects below other projects or if there is any dispute or disruption in our relationship with our CROs, the filing of our applications may be delayed.

Although the FDA and the EMA have programs to facilitate expedited development and accelerated approval processes, the timelines agreed under legislative goals or mandated by regulations are subject to the possibility of substantial delays. In

addition, the FDA, the EMA and other international regulatory authorities have substantial discretion over the approval process for pharmaceutical products. These regulatory agencies may not agree that we have demonstrated the requisite level of product safety and efficacy to grant approval and may require additional data. If we fail to obtain regulatory approval for our product candidates, we will be unable to market and sell those product candidates, which would have a negative effect on our business and financial condition.

With respect to valoctocogene roxaparvovec, we may experience challenges specific to gene therapy that cause significant delays or unanticipated costs, or that cannot be solved. Although numerous companies are currently advancing gene therapy product candidates through clinical trials, the FDA has only approved a very small number of vector-based gene therapy products thus far. Moreover, there are very few approved gene therapy products outside the U.S. As a result, it is difficult to determine how long it will take or how much it will cost to obtain regulatory approvals for valoctocogene roxaparvovec in any jurisdiction. Regulatory requirements governing gene and cell therapy products are still evolving and may continue to change in the future. For example, in October 2020, it was reported that the Director of the Center for Biologics Evaluation and Research, the center of the FDA responsible for reviewing marketing applications for gene therapies, stated that the FDA will assess the importance of durability of effect differently for a gene therapy that treats a disease that has no other available therapies versus a condition for which there are multiple approved treatments. Regulatory review agencies and the new requirements and guidelines they promulgate may lengthen the regulatory review process, require us to perform additional or larger studies, increase our development costs, lead to changes in regulatory positions and interpretations, delay or prevent approval and commercialization of our treatment candidate or lead to significant post-approval studies, limitations or restrictions. For example, on August 18, 2020 the FDA issued a Complete Response Letter (CRL) to our BLA for valoctocogene roxaparvovec for the treatment of adults with severe hemophilia A. In the CRL, the FDA introduced a new request for two-year follow-up safety and efficacy data on all study participants from our ongoing Phase 3 study of valoctocogene roxaparvovec. The trial will not complete two years of follow-up until November 2021. Continued delay or failure to obtain, or unexpected costs in obtaining, the regulatory approval necessary to bring valoctocogene roxaparvovec to market could have a negative effect on our business and financial condition. Even if we do obtain regulatory approval, ethical, social and legal concerns about gene therapy arising in the future could result in additional regulations restricting or prohibiting sale of our product.

In addition, some of our product candidates are intended to be used in combination with a delivery device, such as an injector or other delivery system. Medical products containing a combination of new drugs, biological products or medical devices may be regulated as “combination products” in the U.S. A combination product generally is defined as a product consisting of components from two or more regulatory categories (e.g., drug/device, device/biologic, drug/biologic). Each component of a combination product is subject to the requirements established by the FDA for that type of component, whether a new drug, biologic or device. In order to facilitate pre-market review of combination products, the FDA designates one of its centers to have primary jurisdiction for the pre-market review and regulation of the overall product based upon a determination by the FDA of the primary mode of action of the combination product. The determination whether a product is a combination product or two separately regulated products is made by the FDA on a case-by-case basis. Our product candidates intended for use with such devices, or expanded indications that we may seek for our products used with such devices, may not be approved or may be substantially delayed in receiving approval if the devices do not gain and/or maintain their own regulatory approvals or clearances. Where approval of the drug or biologic product and device is sought under a single application, the increased complexity of the review process may delay approval. The FDA review process and criteria are not well-established areas, which could also lead to delays in the approval process. In addition, because these delivery devices are provided by unaffiliated third-party companies, we are dependent on the sustained cooperation and effort of those third-party companies both to obtain regulatory approval and to maintain their own regulatory compliance. Failure of third-party companies to assist in the approval process or to maintain their own regulatory compliance could delay or prevent approval of our product candidates, or limit our ability to sell a product once it is approved.

From time to time during the development and regulatory approval process for our products and product candidates, we engage in discussions with the FDA and comparable international regulatory authorities regarding our development programs, including discussions about the regulatory requirements for approval. As part of these discussions, we sometimes seek advice in the design of our clinical programs from various regulatory agencies globally, but we do not always follow such guidance. This increases the chance of adverse regulatory actions, but we try to always provide appropriate scientific evidence to support approval. For example, when the FDA accepted our new drug application for Voxzogo (formerly known as vosoritide) in late 2020, the agency reiterated its position raised during the Voxzogo Pediatric Advisory Committee and Endocrinologic and Metabolic Drugs Advisory Committee held in May 2018, recommending two, two-year placebo-controlled trials in different age groups. Although our Voxzogo clinical program does not meet every element of the FDA's recommendation, we designed our studies of Voxzogo in a manner that we believe can demonstrate efficacy and safety of the product candidate for the target patient population. However, the FDA may ultimately disagree with our position that our Voxzogo trials support regulatory approval. Moreover, sometimes different regulatory agencies provide different or conflicting advice. While we attempt to harmonize the advice we receive from multiple regulatory authorities, it is not always practical to do so. Also, we may choose not to harmonize conflicting advice when harmonization would significantly delay clinical trial data or is otherwise inappropriate. If we are unable to effectively and efficiently resolve and comply with the inquiries and requests of the FDA and other non-U.S. regulatory authorities, the approval of our product candidates may be delayed and their value may be reduced.

***Any product for which we have obtained regulatory approval, or for which we obtain approval in the future, is subject to, or will be subject to, extensive ongoing regulatory requirements by the FDA, the EMA and other comparable international regulatory authorities, and if we fail to comply with regulatory requirements or if we experience unanticipated problems with our products, we may be subject to penalties, we will be unable to generate revenues from the sale of such products, our potential for generating positive cash flow will be diminished, and the capital necessary to fund our operations will be increased.**

Aldurazyme, Brineura, Kuvan, Naglazyme and Vimizim have received regulatory approval to be commercially marketed and sold in the U.S., the EU and certain other countries, Palynziq has received regulatory approval to be commercially marketed in the U.S., the EU, and Australia, and Voxzogo has received regulatory approval to be commercially marketed in the EU. Any product for which we have obtained regulatory approval, or for which we obtain regulatory approval in the future, along with the manufacturing processes and practices, post-approval clinical research, product labeling, advertising and promotional activities for such product, are subject to continual requirements of, and review by, the FDA, the EMA and other comparable international regulatory authorities. These requirements include submissions of safety and other post-marketing information and reports, registration and listing requirements, current good manufacturing practices (cGMP) requirements relating to manufacturing, quality control, quality assurance and corresponding maintenance of records and documents, import and export requirements and record keeping.

An example of the ongoing regulatory requirements our products are subject to is the Palynziq Risk Evaluation and Mitigation Strategy (REMS) program. In the U.S., Palynziq is only available through the REMS program, which is required by the FDA to mitigate the risk of anaphylaxis while using the product. Notable requirements of our REMS program include the following:

- prescribers must be certified by enrolling in the REMS program and completing training;
- prescribers must prescribe auto-injectable epinephrine with Palynziq;
- pharmacies must be certified with the REMS program and must dispense Palynziq only to patients who are authorized to receive it;
- patients must enroll in the REMS program and be educated about the risk of anaphylaxis by a certified prescriber to ensure they understand the risks and benefits of treatment with Palynziq; and
- patients must have auto-injectable epinephrine available at all times while taking Palynziq.

Failure of prescribers, pharmacies or patients to enroll in our REMS program or to successfully complete and comply with its requirements may result in regulatory action from the FDA or decreased sales of Palynziq. The restrictions and requirements under our REMS program, as well as potential changes to these restrictions and requirements in the future, subject us to increased risks and uncertainties, any of which could harm our business. The requirement for a REMS program can materially affect the potential market for and profitability of a drug. We cannot predict whether the FDA will request, seek to require or ultimately require modifications to, or impose additional requirements on, the Palynziq REMS program, or whether the FDA will permit modifications to the Palynziq REMS program that we consider warranted. Any modifications required or rejected by the FDA could make it more difficult or expensive for us to distribute Palynziq in the U.S., impair the safety profile of Palynziq, disrupt continuity of care for Palynziq patients and/or negatively affect sales of Palynziq.

Moreover, promotional communications with respect to prescription drugs, including biologics, are subject to a variety of legal and regulatory restrictions and must be consistent with the information in the product's approved labeling. In particular, a product may not be promoted for uses that are not approved by the FDA as reflected in the product's approved labeling. Although the FDA and other regulatory authorities do not regulate a physician's choice of drug treatment made in the physician's independent medical judgment, they do restrict promotional communications from companies or their sales force with respect to off-label uses of products for which marketing clearance has not been issued. The FDA and other agencies 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 civil, criminal and administrative penalties. Thus, we will not be able to promote any products we develop for indications or uses for which they are not approved.

Moreover, if original FDA approval for one of our product candidates is granted via the accelerated approval pathway, we will be required to conduct a post-marketing confirmatory trial to verify and describe the clinical benefit in support of full approval. An unsuccessful post-marketing study or failure to complete such a study with due diligence could result in the withdrawal of the FDA's marketing approval for a product candidate. In addition, the FDA often requires post-marketing testing and surveillance to monitor the effects of products. The FDA, the EMA and other comparable international regulatory agencies may condition approval of our product candidates on the completion of such post-marketing clinical studies. These post-marketing studies may suggest that a product causes undesirable side effects or may present a risk to the patient.

Discovery after approval of previously unknown problems with any of our products, manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in actions such as:

- restrictions on our ability to conduct clinical trials, including full or partial clinical holds on ongoing or planned trials;
- restrictions on product manufacturing processes;
- restrictions on the marketing of a product;
- restrictions on product distribution;
- requirements to conduct post-marketing clinical trials;
- untitled or warning letters or other adverse publicity;
- withdrawal of the products from the market;
- refusal to approve pending applications or supplements to approved applications that we submit;
- recall of products;
- refusal to permit the import or export of our products;
- product seizure;
- fines, restitution or disgorgement of profits or revenue;
- injunctions; or
- imposition of civil or criminal penalties.

If such regulatory actions are taken, our value and our operating results will be adversely affected. Additionally, if the FDA, the EMA or any other comparable international regulatory agency withdraws its approval of a product, we will be unable to generate revenues from the sale of that product in the relevant jurisdiction, our potential for generating positive cash flow will be diminished and the capital necessary to fund our operations will be increased. Accordingly, we continue to expend significant time, money and effort in all areas of regulatory compliance, including manufacturing, production, product surveillance, post-marketing studies and quality control.

To obtain regulatory approval to market our products, preclinical studies and costly and lengthy clinical trials are required and the results of the studies and trials are highly uncertain. Likewise, preliminary, initial or interim data from clinical trials should be considered carefully and with caution because the final data may be materially different from the preliminary, initial or interim data, particularly as more patient data become available.

As part of the drug development process we must conduct, at our own expense, preclinical studies in the laboratory, including studies in animals, and clinical trials on humans for each product candidate. The number of preclinical studies and clinical trials that regulatory authorities require varies depending on the product candidate, the disease or condition the drug is being developed to address and regulations applicable to the particular drug. Generally, new drugs for diseases or conditions that affect larger patient populations, are less severe, or are treatable by alternative strategies must be validated through additional preclinical and clinical trials and/or clinical trials with higher enrollments. With respect to our early stage product candidates, we may need to perform multiple preclinical studies using various doses and formulations before we can begin clinical trials, which could result in delays to our development timeline. Furthermore, even if we obtain favorable results in preclinical studies, the results in humans may be significantly different. After we have conducted preclinical studies, we must demonstrate that our product candidates are safe and efficacious for use in the targeted human patients in order to receive regulatory approval for commercial sale. Clinical testing is expensive and can take many years to complete, and its outcome is inherently uncertain. Failure can occur at any time during the clinical trial process. The results of preclinical studies and early clinical trials of our product candidates may not be predictive of the results of later-stage clinical trials, and favorable data from interim analyses do not ensure the final results of a trial will be favorable. From time to time, we have and may in the future publish or report preliminary, initial or interim data from our clinical trials, such as the data we have announced from the GENE-8-1 study for valoctocogene roxaparvovec. Preliminary, initial or interim data from our clinical trials may not be indicative of the final results of the trial and are subject to the risk that one or more of the clinical outcomes may materially change as patient enrollment continues and/or more patient data become available. In this regard, such data may show initial evidence of clinical benefit, but as patients continue to be followed and more patient data become available, there is a risk that any therapeutic effects will not be durable in patients and/or will decrease over time or cease entirely. Preliminary, initial or interim data also remain subject to audit and verification procedures that may result in the final data being materially different from such preliminary, initial or interim data. As a result, preliminary, initial or interim data should be considered carefully and with caution until the final data are available.

Product candidates may fail to show the desired safety and efficacy traits despite having progressed through preclinical studies and initial clinical trials, or despite having favorable data in connection with an interim analysis. A number of companies in the biopharmaceutical industry have suffered significant setbacks in advanced clinical trials due to lack of efficacy or adverse safety profiles, notwithstanding promising results in earlier trials. Also, as noted above, we do not always follow the advice of regulatory authorities or comply with all of their requests regarding the design of our clinical programs. In those cases, we may choose a

development program that is inconsistent with the advice of regulatory authorities, which may limit the jurisdictions where we conduct clinical trials and/or adversely affect our ability to obtain approval in those jurisdictions where we do not follow the regulatory advice.

Adverse or inconclusive clinical results could stop us from obtaining regulatory approval of our product candidates. Additional factors that can cause delay or termination of our clinical trials include:

- slow or insufficient patient enrollment;
- slow recruitment of, and completion of necessary institutional approvals at, clinical sites;
- budgetary constraints or prohibitively high clinical trial costs;
- longer treatment time required to demonstrate efficacy;
- lack of sufficient supplies of the product candidate;
- adverse medical events or side effects in treated patients, including immune reactions;
- lack of effectiveness of the product candidate being tested;
- availability of competitive therapies to treat the same indication as our product candidates;
- regulatory requests for additional clinical trials or preclinical studies;
- deviations in standards for Good Clinical Practice (GCP); and
- disputes with or disruptions in our relationships with clinical trial partners, including CROs, clinical laboratories, clinical sites, and principal investigators.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services reportable to the FDA or other regulatory authority. If the FDA or other regulatory authority concludes that a financial relationship between us and a principal investigator has created a conflict of interest, the FDA or other regulatory authority may question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized.

Similar rules governing clinical trials to those in place in the United States apply in the EU and the U.K. Following the U.K.'s exit from the EU, commonly referred to as Brexit, and the end of the transition period that was in place until the end of 2020, clinical trials that take place in the U.K. are seen as trials that have taken place in a "third country" and will only be considered during the course of a marketing authorization application if they are carried out on a basis that is in line with the regulations governing clinical trials in the EU. Clinical trials in the EU must be conducted in accordance with the requirements of the EU Clinical Trials Directive, as implemented in national law by individual member states, and applicable good clinical practice standards. The EU Clinical Trials Directive is due to be replaced with the new EU Clinical Trials Regulation (EU CTR), which will become effective on January 31, 2022. Should the U.K. not seek to align its regulations governing clinical trials with the EU CTR then trials that take place in the U.K. may carry less weight than they currently do when applying for a marketing authorization in the EU.

Government price controls or other changes in pricing regulation could restrict the amount that we are able to charge for our current and future products, which would adversely affect our revenues and results of operations.

We expect that coverage and reimbursement may be increasingly restricted in all the markets in which we sell our products. The escalating cost of healthcare has led to increased pressure on the healthcare industry to reduce costs. In particular, drug pricing by pharmaceutical companies has recently come under increased scrutiny and continues to be subject to intense political and public debate in the U.S. and abroad. Governmental and private third-party payers have proposed healthcare reforms and cost reductions. A number of federal and state proposals to control the cost of healthcare, including the cost of drug treatments, have been made in the U.S. Specifically, there have been several recent U.S. congressional inquiries and proposed bills and enacted legislation designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for drugs. Further, Congress and the executive branch have each indicated that they will continue to seek new legislative and/or administrative measures to control drug costs. In some international markets, the government controls the pricing, which can affect the profitability of drugs. Current government regulations and possible future legislation regarding healthcare may affect coverage and reimbursement for medical treatment by third-party payers, which may render our products not commercially viable or may adversely affect our future revenues and gross margins.

International operations are also generally subject to extensive price and market regulations, and there are many proposals for additional cost-containment measures, including proposals that would directly or indirectly impose additional price controls or mandatory price cuts or reduce the value of our intellectual property portfolio. As part of these cost containment measures, some countries have imposed and continue to propose revenue caps limiting the annual volume of sales of our

products. Some of these caps are significantly below the actual demand in certain countries, and if the trend regarding revenue caps continues, our future revenues and gross margins may be adversely affected.

We cannot predict the extent to which our business may be affected by these or other potential future legislative or regulatory developments. However, future price controls or other changes in pricing regulation or negative publicity related to our product pricing or the pricing of pharmaceutical drugs generally could restrict the amount that we are able to charge for our current and future products or our sales volume, which would adversely affect our revenues and results of operations.

***Government healthcare reform could increase our costs and adversely affect our revenues and results of operations.**

Our industry is highly regulated and changes in law may adversely impact our business, operations or financial results. In the U.S., there have been and continue to be a number of legislative initiatives to contain healthcare costs. For example, the Patient Protection and Affordable Care Act of 2010, as amended by the Health Care and Education Reconciliation Act of 2010 (collectively, the PPACA) is a sweeping measure intended to, among other things, expand healthcare coverage within the U.S., primarily through the imposition of health insurance mandates on employers and individuals and expansion of the Medicaid program. Several provisions of the law have affected us and increased certain of our costs. Since its enactment, there have been executive, judicial and congressional challenges to certain aspects of the PPACA. Although the PPACA has generally been upheld thus far, it is unclear how continued challenges to the law may impact the PPACA and our business. In addition, other legislative changes have been adopted since the PPACA was enacted. Some of these changes have resulted in additional reductions in Medicare and other healthcare funding, which could have a material adverse effect on our customers and, accordingly, our financial operations.

We anticipate that the PPACA, as well as other healthcare reform measures that may be adopted in the future in the U.S. or abroad, may result in more rigorous coverage criteria and an additional downward pressure on the reimbursement our customers may receive for our products. Recently there has been heightened governmental scrutiny in countries worldwide over the manner in which manufacturers set prices for their marketed products.

In the U.S., there have been several recent congressional inquiries, proposed and enacted federal and state legislation, and executive action designed to, among other things, bring more transparency to drug pricing, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies for drug products. Any reduction in reimbursement from Medicare and other government programs may result in a similar reduction in payments from private payers. In addition, individual states in the U.S. have also increasingly passed legislation and implemented regulations designed to control pharmaceutical 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. Moreover, regional healthcare authorities and individual hospitals are increasingly using bidding procedures to determine what pharmaceutical products and which suppliers will be included in their prescription drug and other healthcare programs. Further, it is possible that additional governmental action is taken in response to the COVID-19 pandemic.

Likewise, in many EU countries, legislators and other policymakers continue to propose and implement healthcare cost-containing measures in response to the increased attention being paid to healthcare costs in the EU. Certain of these changes could impose limitations on the prices we will be able to charge for our products and any approved product candidates or the amounts of reimbursement available for these products from governmental and private third-party payers, may increase the tax obligations on pharmaceutical companies or may facilitate the introduction of generic competition with respect to our products. Further, an increasing number of EU countries and other non-U.S. countries use prices for medicinal products established in other countries as “reference prices” to help determine the price of the product in their own territory. If the price of one of our products decreases substantially in a reference price country, it could impact the price for that product in other countries. Consequently, a downward trend in prices of our products in some countries could contribute to similar downward trends elsewhere, which would have a material adverse effect on our revenues and results of operations. Moreover, in order to obtain reimbursement for our products in some countries, we may be required to conduct clinical trials that compare the cost-effectiveness of our products to other available therapies.

Legally mandated price controls on payment amounts by governmental and private third-party payers or other restrictions could harm our business, results of operations, financial condition and prospects. The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability or commercialize our products.

For more information regarding government healthcare reform, see “Government Regulation - Health Reform” in Part I, Item 1 of our Annual Report on Form 10-K for the year ended December 31, 2020, filed with the SEC on February 26, 2021.

If we fail to obtain or maintain orphan drug exclusivity for some of our products, our competitors may obtain approval to sell the same drugs to treat the same conditions and our revenues will be reduced.

As part of our business strategy, we have developed and may in the future develop some drugs that may be eligible for FDA and EU orphan drug designation. Under the Orphan Drug Act, the FDA may designate a product as an orphan drug if it is intended to treat a rare disease or condition, defined as a patient population of fewer than 200,000 in the U.S. In the EU, orphan drug designation is available if a sponsor can establish that: (1) the medicine is intended for the diagnosis, prevention or treatment of a life-threatening or chronically debilitating condition, (2) such condition affects no more than five in 10,000 people in the EU or without incentives it is unlikely that the marketing of the medicine in the EU would generate sufficient return to justify the necessary investment and (3) the applicant must demonstrate that there exists no satisfactory method of diagnosis, prevention or treatment of the condition in question that has been authorized in the EU or, if such method exists, the medicine will be of significant benefit to those affected by that condition. The company that first obtains FDA approval for a designated orphan drug for a given rare disease receives marketing exclusivity for use of that drug for the stated condition for a period of seven years. Orphan drug exclusive marketing rights may be lost if the FDA later determines that the request for designation was materially defective or if the manufacturer is unable to assure sufficient quantity of the drug. In addition, the FDA may approve another drug during a period of orphan drug exclusivity if the second drug is found to be clinically superior to the first drug. In the EU, a ten-year period of market exclusivity (extendable to twelve years for orphan drugs that have complied with an agreed pediatric investigation plan pursuant to Regulation 1901/2006), during which similar medicines for the same indication cannot be placed on the market, is available. Orphan drug marketing exclusivity may be lost in the EU if a manufacturer is unable to supply sufficient quantities and marketing authorization may also be granted to a similar medicinal product with the same orphan indication if this medicinal product is safer, more effective or otherwise clinically superior to the original orphan medicinal product. The period of market exclusivity may, in addition, be reduced to six years if, at the end of the fifth year, it can be demonstrated on the basis of available evidence that the criteria for its designation as an orphan medicine are no longer satisfied, for example if the original orphan medicinal product has become sufficiently profitable not to justify maintenance of market exclusivity. Because the extent and scope of patent protection for some of our products is limited, orphan drug designation is especially important for our products that are eligible for orphan drug designation. For eligible products, we plan to rely on the exclusivity period under the Orphan Drug Act to maintain a competitive position. If we do not obtain orphan drug exclusivity for our products that do not have broad patent protection, our competitors may then sell the same drug to treat the same condition and our revenues will be reduced.

Even though we have obtained orphan drug designation for certain of our product candidates and even if we obtain orphan drug designation for our future product candidates, due to the uncertainties associated with developing biopharmaceutical products, we may not be the first to obtain marketing approval for any particular orphan indication, which means that we may not obtain orphan drug exclusivity and could also potentially be blocked from approval of certain product candidates until the competitor product's orphan drug exclusivity period expires. Moreover, with respect to certain biologics and gene therapies, it is uncertain how similarity between product candidates designed to treat the same rare disease or condition may affect such product candidates' orphan drug exclusivities. Further, even if we obtain orphan drug exclusivity for a product, that exclusivity may not effectively protect the product from competition because different drugs can be approved for the same condition and the same drug can be approved for different conditions and potentially used off-label in the orphan indication. Even after an orphan drug is approved and granted orphan drug exclusivity, the FDA can subsequently approve the same drug for the same condition if the FDA concludes that the later drug is safer or more effective or makes a major contribution to patient care. Orphan drug designation neither shortens the development time or regulatory review time of a drug, nor gives the drug any advantage in the regulatory review or approval process.

We may face competition from biosimilars approved through an abbreviated regulatory pathway.

Our Aldurazyme, Brineura, Naglazyme, Palynziq and Vimizim products are regulated by the FDA as biologics under the Federal Food, Drug, and Cosmetic Act (the FDC Act) and the Public Health Service Act (the PHS Act). Biologics require the submission of a BLA and approval by the FDA prior to being marketed in the U.S. The Biologics Price Competition and Innovation Act of 2009 (BPCIA) created a regulatory pathway under the PHS Act for the abbreviated approval of biological products that are demonstrated to be "biosimilar" or "interchangeable" with an FDA-approved biological product. A similar abridged marketing authorization process is available to biosimilar products in the EU. In order to meet the standard of interchangeability, a sponsor must demonstrate that the biosimilar product can be expected to produce the same clinical result as the reference product, and for a product that is administered more than once, that the risk of switching between the reference product and biosimilar product is not greater than the risk of maintaining the patient on the reference product. The BPCIA establishes a period of 12 years of exclusivity for reference products. In the EU, a medicinal product containing a new active substance benefits from eight years of data exclusivity, during which biosimilar applications referring to the data of that product may not be accepted by the regulatory authorities, and a further two years of market exclusivity, during which such biosimilar products may not be placed on the market. The two-year period may be extended to three years if during the first eight years a new therapeutic indication with significant clinical benefit over existing therapies is approved. Our products approved under BLAs in the U.S. or Marketing Authorization

Applications (MAAs) in the EU, as well as products in development that may be approved under those regimes in the future, could be reference products for biosimilar marketing applications.

Changes in funding for the FDA, the EMA and other government agencies or government shutdowns could hinder the ability of such agencies to hire and retain key leadership and other personnel or otherwise prevent those agencies from performing normal functions on which the operation of our business may rely, which could negatively impact our business.

Changes in funding levels of government agencies can affect their ability to hire and retain key personnel and carry out their normal functions that support our business. For example, the ability of the FDA to timely review and approve INDs or marketing authorizations for our product candidates may be hindered by a lack of resources and qualified personnel. In addition, funding of other government agencies on which our operations rely, including those that fund research and development activities, is subject to the political budget process, which is inherently fluid and unpredictable.

Government shutdowns could also impact the ability of government agencies to function normally and support our operations. For example, the U.S. federal government has shut down repeatedly since 1980, including for a period of 35 days beginning on December 22, 2018. During a shutdown, certain regulatory agencies, such as the FDA, have had to furlough key personnel and stop critical activities. If a prolonged government shutdown occurs, it could significantly impact the ability of the FDA to timely review and process our regulatory submissions, which could have a material adverse effect on our business.

Risks Related to Valoctocogene Roxaparovec

Our valoctocogene roxaparovec program is based on a gene therapy approach, which, as a novel technology, presents additional development and treatment risks in relation to our other, more traditional drug development programs.

In addition to the risks set forth in this Risk Factors section associated with developing more traditional pharmaceutical drugs, there are additional, unique development and treatment risks associated with gene therapy products like our product candidate valoctocogene roxaparovec. The goal of gene therapy is to be able to correct an inborn genetic defect through one-time administration of therapeutic genetic material containing non-defective gene copies. The gene copies are designed to reside permanently in a patient, allowing the patient to produce an essential protein or ribonucleic acid (RNA) molecule that a healthy person would normally produce. There is a risk, however, that the new gene copies will produce too little or too much of the desired protein or RNA. Although a one-time administration of a gene therapy product like our product candidate valoctocogene roxaparovec is intended to correct an inborn genetic defect for the entire lifetime of a patient, there is a risk that the therapeutic effect will not be durable and production of the desired protein or RNA will decrease over time or cease entirely. Because the treatment is irreversible, there may be challenges in managing side effects, particularly those caused by potential overproduction of the desired protein. Adverse effects would not be able to be reversed or relieved by stopping dosing, and we may have to develop additional clinical safety procedures. Furthermore, because the new gene copies are designed to reside permanently in a patient, there is a risk that they will disrupt other normal biological molecules and processes, including other healthy genes, and we may not learn the nature and magnitude of these side effects until long after clinical trials have been completed.

As compared to our other, more traditional products, our gene therapy product candidate valoctocogene roxaparovec, if approved, may present additional problems with respect to the pricing, coverage, and reimbursement and acceptance of the product candidate.

In addition to the risks set forth in this Risk Factors section associated with commercializing more traditional pharmaceutical drugs, there are additional, unique commercial risks associated with gene therapy products like our product candidate valoctocogene roxaparovec. Due to the relative novelty of gene therapy and the potential to provide extended duration therapeutic treatment with a one-time administration, we face uncertainty with respect to the pricing, coverage and reimbursement of valoctocogene roxaparovec, if approved. In order to recover our research and development costs and commercialize this one-time treatment on a profitable basis, we expect the cost of a single administration of valoctocogene roxaparovec to be substantial. Therefore, we expect that coverage and reimbursement by governments and other third-party payers will be essential for the vast majority of patients to be able to afford valoctocogene roxaparovec. Accordingly, sales of valoctocogene roxaparovec, if approved, will depend substantially, both domestically and internationally, on the extent to which its cost will be paid by third-party payers. Even if coverage is provided, the reimbursement amounts approved by third-party payers may not be high enough to allow us to realize sufficient revenues from our investment in the development of valoctocogene roxaparovec.

We also face uncertainty as to whether gene therapy will gain the acceptance of the public or the medical community. Even if we obtain regulatory approval for valoctocogene roxaparovec, the commercial success of valoctocogene roxaparovec will depend, in part, on the acceptance of physicians, patients and third-party payers of gene therapy products in general, and our product candidate in particular, as medically necessary, cost-effective and safe. In particular, our success will depend upon physicians prescribing our product candidate in lieu of existing treatments they are already familiar with and for which greater clinical data may be available. Moreover, physicians and patients may delay acceptance of valoctocogene roxaparovec until the

product candidate has been on the market for a certain amount of time. Negative public opinion or more restrictive government regulations could have a negative effect on our business and financial condition and may delay or impair the successful commercialization of, and demand for, valoctocogene roxaparvovec

We have implemented a data access plan for valoctocogene roxaparvovec, which restricts our management's review of emerging data from these trials. Without access to ongoing data, management does not have the ability to adjust the trials based on such emerging data, which could adversely impact the ultimate outcome of these trials.

In order to preserve the scientific integrity of the valoctocogene roxaparvovec trials and to allow us to only report on data at intervals that we believe will be meaningful to investors, we have implemented a data access plan related to the ongoing open label trials, which is designed to significantly mirror blinded trials. Pursuant to this plan, the ongoing emerging data are generally not collected by us, with the exception that certain specific data points are collected and reviewed by a small group of medical personnel monitoring and managing the trial, and then, only to the extent necessary to allow them to perform their monitoring responsibilities. As we disclose and publicly discuss prior data from these trials, such discussions do not incorporate any of the currently emerging data that are being collected and reviewed by personnel monitoring the trial and, accordingly, this prior data may differ significantly from more recent data that are only available to such personnel. Further, because our management does not have access to any of the ongoing data and does not have the ability to adjust the trials based on such emerging data, the data access plan could adversely impact the ultimate outcome of the trials.

Financial and Financing Risks

If we continue to incur operating losses or are unable to sustain positive cash flows for a period longer than anticipated, we may be unable to continue our operations at planned levels and be forced to reduce our operations.

Since we began operations in March 1997, we have been engaged in substantial research and development and capital investments, and we have operated at a net loss for each year since our inception, with the exception of 2008, 2010 and 2020. Our future profitability and cash flows depend on our marketing and selling of our products, the receipt of regulatory approval of our product candidates, our ability to successfully manufacture and market any products, either by ourselves or jointly with others, our spending on our development programs, the impact of any possible future business development transactions and other risks set forth in this Risk Factors section. The extent of our future losses and the timing of profitability and positive cash flows are highly uncertain. If we fail to become profitable or are unable to sustain profitability and positive cash flows on a continuing basis, then we may be unable to continue our operations at planned levels and be forced to reduce our operations.

***If we fail to obtain the capital necessary to fund our operations, our financial results and financial condition will be adversely affected and we will have to delay or terminate some or all of our product development programs.**

As of September 30, 2021, we had cash, cash equivalents and investments totaling \$1.55 billion and debt obligations of \$1.1 billion (undiscounted), which consisted of our 0.599% senior subordinated convertible notes due in 2024 (the 2024 Notes) and our 1.25% senior subordinated convertible notes due in 2027 (the 2027 Notes). The 2024 Notes and the 2027 Notes (collectively, the Notes), if not converted, will be required to be repaid in cash at maturity in August 2024 and May 2027, respectively. We will need cash not only to pay the ongoing interest due on the Notes during their term, but also to repay the principal amount of the Notes if not converted.

In January 2016, we terminated our License and Commercialization Agreement with Ares Trading, S.A. (Merck Serono). Pursuant to the Termination and Transition Agreement related to Kuvan and the Termination Agreement related to Palylnziq, we are obligated to make certain payments to Merck Serono if sales and development milestones are achieved. The remaining milestone payments that may become payable include up to a maximum of €60 million, in cash, if future sales milestones are met with respect to Kuvan and Palylnziq.

We may require additional financing to fund the repayment of the Notes, future milestone payments and our future operations, including the commercialization of our products and product candidates currently under development, preclinical studies and clinical trials, and potential licenses and acquisitions. We may be unable to raise additional financing due to a variety of factors, including our financial condition, the status of our product programs, and the general condition of the financial markets. If we fail to raise any necessary additional financing we may have to delay or terminate some or all of our product development programs and our financial condition and operating results will be adversely affected.

We expect to continue to spend substantial amounts of capital for our operations for the foreseeable future. The amount of capital we will need depends on many factors, including:

- our ability to successfully market and sell our products;

- the time and cost necessary to develop commercial manufacturing processes, including quality systems, and to build or acquire manufacturing capabilities the progress and success of our preclinical studies and clinical trials (including studies and the manufacture of materials);
- the timing, number, size and scope of our preclinical studies and clinical trials;
- the time and cost necessary to obtain regulatory approvals and the costs of post-marketing studies which may be required by regulatory authorities;
- the progress of research programs carried out by us;
- our possible achievement of development and commercial milestones under agreements with third parties, such as the Kuvan and Palynziq milestones under the termination agreements with Merck Serono;
- any changes made to, or new developments in, our existing collaborative, licensing and other commercial relationships or any new collaborative, licensing and other commercial relationships that we may establish;
- Sanofi Genzyme's (Genzyme) ability to continue to successfully commercialize Aldurazyme; and
- whether our convertible debt is converted to common stock in the future.

Moreover, our fixed expenses such as rent, license payments, interest expense and other contractual commitments are substantial and may increase in the future. These fixed expenses may increase because we may enter into:

- additional licenses and collaborative agreements;
- additional contracts for product manufacturing; and
- additional financing facilities or arrangements.

We will need to raise additional funds from equity or debt securities, loans or collaborative agreements if we are unable to satisfy our liquidity requirements. The sale of additional equity and/or equity-linked securities will result in additional dilution to our stockholders. Furthermore, additional financing may not be available in amounts or on terms satisfactory to us or at all. This could result in the delay, reduction or termination of our research, which could harm our business.

***We have incurred substantial indebtedness that may decrease our business flexibility, access to capital, and/or increase our borrowing costs, which may adversely affect our operations and financial results.**

As of September 30, 2021, we had \$1.1 billion (undiscounted) principal amount of indebtedness, including \$495.0 million (undiscounted) principal amount of indebtedness under the 2024 Notes and \$600.0 million (undiscounted) principal amount of indebtedness under the 2027 Notes. In October 2018, we also entered into an unsecured credit agreement (the 2018 Credit Facility) with Bank of America, N.A., as the administrative agent, swingline lender and a lender, Citibank N.A. as letter of credit issuer and each of Merrill Lynch, Pierce, Fenner & Smith Incorporated, Citibank, N.A. and Wells Fargo Securities, LLC as joint lead arrangers and joint bookrunners, providing up to \$200.0 million in revolving loan commitments. In May 2021, we amended the 2018 Credit Agreement to, among other things, extend the maturity date of the revolving credit facility from October 18, 2021 to May 28, 2024. Our indebtedness may:

- limit our ability to borrow additional funds for working capital, capital expenditures, acquisitions or other general business purposes;
- limit our ability to use our cash flow or obtain additional financing for future working capital, capital expenditures, acquisitions or other general business purposes;
- require us to use a substantial portion of our cash flow from operations to make debt service payments;
- limit our flexibility to plan for, or react to, changes in our business and industry;
- place us at a competitive disadvantage compared to our less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

In addition, the 2018 Credit Facility contains, and any future indebtedness that we may incur may contain, financial and other restrictive covenants that limit our ability to operate our business, raise capital or make payments under our other indebtedness. If we fail to comply with these covenants or to make payments under our indebtedness when due, then we would be in default under that indebtedness, which could, in turn, result in that and our other indebtedness becoming immediately payable in full. If we default under the 2018 Credit Facility, the outstanding borrowings thereunder could become immediately due and payable, the 2018 Credit Facility lenders could refuse to permit additional borrowings under the facility, or it could lead to defaults under agreements governing our current or future indebtedness, including the indentures governing the Notes. If we default under any of the Notes, such Notes could become immediately due and payable and it could lead to defaults under the other Notes and/or the 2018 Credit Facility.

***In addition, our ability to refinance our indebtedness will depend on the capital markets and our financial condition at such time.**

Our outstanding indebtedness consists primarily of the 2024 Notes and 2027 Notes, which, if not converted, will be required to be repaid in cash at maturity in August 2024 and May 2027, respectively. While we could seek to obtain additional third-party financing to pay for any amounts due in cash upon maturity of the Notes, we cannot be sure that such third-party financing will be available on commercially reasonable terms, if at all.

In addition, we also may borrow up to \$200.0 million in revolving loans under the 2018 Credit Facility, which would be required to be repaid in cash at maturity on May 28, 2024.

Manufacturing Risks

***If we fail to comply with manufacturing regulations, our financial results and financial condition will be adversely affected.**

Before we can begin commercial manufacture of our products, regulatory authorities must approve marketing applications that identify manufacturing facilities operated by us or our contract manufacturers that have passed regulatory inspection and manufacturing processes that are acceptable to the regulatory authorities. In addition, our pharmaceutical manufacturing facilities are continuously subject to scheduled and unannounced inspection by the FDA and international regulatory authorities, before and after product approval, to monitor and ensure compliance with cGMP and other regulations. Our manufacturing facility in the U.S. has been approved by the FDA and the European Commission (EC) for the manufacture of Palynziq, by the EC for the manufacture of Voxzogo, and it has been approved by the FDA, the EC, and health agencies in other countries for the manufacture of Aldurazyme, Brineura, Naglazyme and Vimizim. Our manufacturing facility in Shanbally, Cork, Ireland has been approved by the FDA, the EC, and health agencies in other countries for the manufacture of Vimizim, and it has been approved by the FDA and the EMA as a formulated bulk drug substance manufacturing and quality control facility for Brineura. In addition, our third-party manufacturers' facilities involved with the manufacture of our products have also been inspected and approved by various regulatory authorities. Although we are not involved in the day-to-day operations of our contract manufacturers, we are ultimately responsible for ensuring that our products are manufactured in accordance with cGMP regulations.

Due to the complexity of the processes used to manufacture our products and product candidates, we may be unable to continue to pass or initially pass federal or international regulatory inspections in a cost-effective manner. For the same reason, any potential third-party manufacturer of our products or our product candidates may be unable to comply with cGMP regulations in a cost-effective manner and may be unable to initially or continue to pass a federal or international regulatory inspection.

If we, or third-party manufacturers with whom we contract, are unable to comply with manufacturing regulations, we may be subject to delay of approval of our product candidates, warning or untitled letters, fines, unanticipated compliance expenses, recall or seizure of our products, total or partial suspension of production and/or enforcement actions, including injunctions, and criminal or civil prosecution. These possible sanctions would adversely affect our financial results and financial condition.

If we are unable to successfully develop and maintain manufacturing processes for our product candidates to produce sufficient quantities at acceptable costs, we may be unable to support a clinical trial or be forced to terminate a program, or if we are unable to produce sufficient quantities of our products at acceptable costs, we may be unable to meet commercial demand, lose potential revenue, have reduced margins or be forced to terminate a program.

Due to the complexity of manufacturing our product candidates and products, we may not be able to manufacture sufficient quantities. Our inability to produce enough of our product candidate at acceptable costs may result in the delay or termination of development programs. With respect to our commercial portfolio, we may not be able to manufacture our products successfully with a commercially viable process or at a scale large enough to support their respective commercial markets or at acceptable margins.

The development of commercially viable manufacturing processes typically is very difficult to achieve and is often very expensive and may require extended periods of time. Changes in manufacturing processes (including manufacturing cell lines),

equipment or facilities (including moving manufacturing from one of our facilities to another one of our facilities or a third-party facility, or from a third-party facility to one of our facilities) may require us to complete clinical trials to receive regulatory approval of any manufacturing modifications.

With respect to valoctocogene roxaparvovec, gene therapy products are relatively novel and complex and have only in limited cases been manufactured at scales sufficient for pivotal trials and commercialization. Few pharmaceutical contract manufacturers specialize in gene therapy products and those that do are still developing appropriate processes and facilities for large-scale production. We invested a considerable amount of capital building our own commercial gene therapy manufacturing facility, which may be subject to significant impairment if our gene therapy programs are unsuccessful. As we develop, seek to optimize and operate the valoctocogene roxaparvovec manufacturing process, we will likely face technical and scientific challenges, considerable capital costs, and potential difficulty in recruiting and hiring experienced, qualified personnel. There may also be unexpected technical or operational issues during clinical or commercial manufacturing campaigns. As a result, we could experience manufacturing delays that prevent us from completing our clinical studies in a timely manner, if at all, or commercializing valoctocogene roxaparvovec on a profitable basis, if at all.

Also, we may be required to demonstrate product comparability between a biological product made after a manufacturing change and the product made before implementation of the change through additional types of analytical and functional testing or may have to complete additional clinical studies. If we contract for manufacturing services with an unproven process, our contractor is subject to the same uncertainties, high standards and regulatory controls, and may therefore experience difficulty if further process development is necessary.

Even a developed manufacturing process can encounter difficulties. Problems may arise during manufacturing for a variety of reasons, including human error, mechanical breakdowns, problems with raw materials and cell banks, malfunctions of internal information technology systems, and other events that cannot always be prevented or anticipated. Many of the processes include biological systems, which add significant complexity, as compared to chemical synthesis. We expect that, from time to time, consistent with biotechnology industry expectations, certain production lots will fail to produce product that meets our quality control release acceptance criteria. To date, our historical failure rates for all of our product programs have been within our expectations, which are based on industry norms. If the failure rate increased substantially, we could experience increased costs, lost revenue, damage to customer relations, time and expense investigating the cause and, depending upon the cause, similar losses with respect to other lots or products. If problems are not discovered before the product is released to the market, recall and product liability costs may also be incurred.

In order to produce product within our time and cost parameters, we must continue to produce product within our expected success rate and yield expectations. Because of the complexity of our manufacturing processes, it may be difficult or impossible for us to determine the cause of any particular lot failure and we must effectively take corrective action in response to any failure in a timely manner.

We currently rely on third parties for portions of the manufacture of each of our commercial products. If those manufacturers are unwilling or unable to fulfill their contractual obligations or satisfy demand outside of or in excess of the contractual obligations, we may be unable to meet demand for these products or sell these products at all and we may lose potential revenue. Further, the availability of suitable contract manufacturing capacity at scheduled or optimum times is not certain.

In addition, our manufacturing processes subject us to a variety of federal, state and local laws and regulations governing the use, generation, manufacture, storage, handling and disposal of hazardous materials and wastes resulting from their use. We incur significant costs in complying with these laws and regulations.

Supply interruptions may disrupt our inventory levels and the availability of our products and product candidates and cause delays in obtaining regulatory approval for our product candidates, or harm our business by reducing our revenues.

We depend on single-source suppliers for critical raw materials and a limited number of manufacturing facilities to manufacture our finished products and product candidates. Numerous factors could cause interruptions in the supply or manufacture of our products and product candidates, including:

- timing, scheduling and prioritization of production by our contract manufacturers or a breach of our agreements by our contract manufacturers;
- labor interruptions;
- changes in our sources for manufacturing;
- the timing and delivery of shipments;

- our failure to locate and obtain replacement suppliers and manufacturers as needed on a timely basis; and
- conditions affecting the cost and availability of raw materials.

If one of our suppliers or manufacturers fails or refuses to supply us with necessary raw materials or finished products or product candidates on a timely basis or at all, it would take a significant amount of time and expense to qualify a new supplier or manufacturer. We may not be able to obtain active ingredients or finished products from new suppliers or manufacturers on acceptable terms and at reasonable prices, or at all.

Any interruption in the supply of finished products could hinder our ability to distribute finished products to meet commercial demand and adversely affect our financial results and financial condition.

With respect to our product candidates, production of product is necessary to perform clinical trials and successful registration batches are necessary to file for approval to commercially market and sell product candidates. Delays in obtaining clinical material or registration batches could adversely impact our clinical trials and delay regulatory approval for our product candidates.

If our Manufacturing, Marketing and Sales Agreement with Genzyme were terminated, we could be prevented from continuing to commercialize Aldurazyme or our ability to successfully commercialize Aldurazyme would be delayed or diminished.

Either party may terminate the Manufacturing, Marketing and Sales Agreement (the MMS Agreement) between Genzyme and us related to Aldurazyme for specified reasons, including if the other party is in material breach of the MMS Agreement, has experienced a change of control, as such term is defined in the MMS Agreement, or has declared bankruptcy and also is in breach of the MMS Agreement. Although we are not currently in breach of the MMS Agreement, there is a risk that either party could breach the MMS Agreement in the future. Either party may also terminate the MMS Agreement upon one-year prior written notice for any reason.

If the MMS Agreement is terminated for breach, the breaching party will transfer its interest in the BioMarin/Genzyme LLC to the non-breaching party, and the non-breaching party will pay a specified buyout amount for the breaching party's interest in Aldurazyme and in the BioMarin/Genzyme LLC. If we are the breaching party, we would lose our rights to Aldurazyme and the related intellectual property and regulatory approvals. If the MMS Agreement is terminated without cause, the non-terminating party would have the option, exercisable for one year, to buy out the terminating party's interest in Aldurazyme and in the BioMarin/Genzyme LLC at a specified buyout amount. If such option is not exercised, all rights to Aldurazyme will be sold and the BioMarin/Genzyme LLC will be dissolved. In the event of termination of the buyout option without exercise by the non-terminating party as described above, all right and title to Aldurazyme is to be sold to the highest bidder, with the proceeds to be split between Genzyme and us in accordance with our percentage interest in the BioMarin/Genzyme LLC.

If the MMS Agreement is terminated by either party because the other party declared bankruptcy, the terminating party would be obligated to buy out the other party and would obtain all rights to Aldurazyme exclusively. If the MMS Agreement is terminated by a party because the other party experienced a change of control, the terminating party shall notify the other party, the offeree, of its intent to buy out the offeree's interest in Aldurazyme and the BioMarin/Genzyme LLC for a stated amount set by the terminating party at its discretion. The offeree must then either accept this offer or agree to buy the terminating party's interest in Aldurazyme and the BioMarin/Genzyme LLC on those same terms. The party who buys out the other party would then have exclusive worldwide rights to Aldurazyme. The Amended and Restated Collaboration Agreement between us and Genzyme will automatically terminate upon the effective date of the termination of the MMS Agreement and may not be terminated independently from the MMS Agreement.

If we were obligated or given the option to buy out Genzyme's interest in Aldurazyme and the BioMarin/Genzyme LLC, and thereby gain exclusive rights to Aldurazyme, we may not have sufficient funds to do so and we may not be able to obtain the financing to do so. If we fail to buy out Genzyme's interest, we may be held in breach of the agreement and may lose any claim to the rights to Aldurazyme and the related intellectual property and regulatory approvals. We would then effectively be prohibited from developing and commercializing Aldurazyme. If this happened, not only would our product revenues decrease, but our share price would also decline.

Risks Related to International Operations

***We conduct a significant amount of our sales and operations outside of the U.S., which subjects us to additional business risks that could adversely affect our revenues and results of operations.**

A significant portion of the sales of Aldurazyme, Brineura, Kuvan, Naglazyme and Vimizim are generated from countries other than the U.S. Similarly, we expect a significant portion of the sales of Palynziq and Voxzogo to be generated from countries

other than the U.S. We have operations in Canada and in several European, Middle Eastern, Asian, and Latin American countries. We expect that we will continue to expand our international operations in the future. International operations inherently subject us to a number of risks and uncertainties, including:

- the increased complexity and costs inherent in managing international operations;
- diverse regulatory and compliance requirements, and changes in those requirements that could restrict our ability to manufacture, market and sell our products;
- political and economic instability;
- diminished protection of intellectual property in some countries outside of the U.S.;
- trade protection measures and import or export licensing requirements;
- difficulty in staffing and managing international operations;
- differing labor regulations and business practices;
- potentially negative consequences from changes in or interpretations of tax laws;
- changes in international medical reimbursement policies and programs;
- financial risks such as longer payment cycles, difficulty collecting accounts receivable, exposure to fluctuations in foreign currency exchange rates and potential currency controls imposed by non-U.S. governments;
- regulatory and compliance risks that relate to maintaining accurate information and control over sales and distributors' and service providers' activities that may fall within the purview of the Foreign Corrupt Practices Act (the FCPA); and
- rapidly evolving global laws and regulations relating to data protection and the privacy and security of commercial and personal information.

Any of these factors may, individually or as a group, have a material adverse effect on our business and results of operations.

As we continue to expand our existing international operations, we may encounter new risks. For example, as we focus on building our international sales and distribution networks in new geographic regions, we must continue to develop relationships with qualified local distributors and trading companies. If we are not successful in developing and maintaining these relationships, we may not be able to grow sales in these geographic regions. These or other similar risks could adversely affect our revenues and profitability.

***A significant portion of our international sales are made based on special access programs, and changes to these programs could adversely affect our product sales and revenues in these countries.**

We make a significant portion of our international sales of Naglazyme and Vimizim through special access or "named patient" programs, which do not require full product approval, and we expect a significant portion of our international sales of Brineura and Voxzogo will also be through such programs. The specifics of the programs vary from country to country. Generally, special approval must be obtained for each patient. The approval normally requires an application or a lawsuit accompanied by evidence of medical need. Generally, the approvals for each patient must be renewed from time to time.

These programs are not well defined in some countries and are subject to changes in requirements and funding levels. Any change to these programs could adversely affect our ability to sell our products in those countries and delay sales. If the programs are not funded by the respective government, there could be insufficient funds to pay for all patients. Further, governments have and may continue to undertake unofficial measures to limit purchases of our products, including initially denying coverage for purchasers, delaying orders and denying or taking excessively long to approve customs clearance. Any such actions could materially delay or reduce our revenues from such countries.

Without the special access programs, we would need to seek full product approval to commercially market and sell our products in certain jurisdictions. This can be an expensive and time-consuming process and may subject our products to additional price controls. Because the number of patients is so small in some countries, it may not be economically feasible to seek and maintain a full product approval, and therefore the sales in such country would be permanently reduced or eliminated. For all of

these reasons, if the special access programs that we are currently using are eliminated or restricted, our revenues could be adversely affected.

U.S. export control and economic sanctions may adversely affect our business, financial condition and operating results. Moreover, compliance with such regulatory requirements may increase our costs and negatively impact our ability to sell our products and collect cash from customers.

Our products are subject to U.S. export control laws and regulations, including the U.S. Export Administration Regulations and various economic and trade sanctions regulations administered by the U.S. Treasury Department's Office of Foreign Assets Control (OFAC). Exports of our products and solutions must be made in compliance with these laws and regulations. Changes to these laws and regulations, or to the countries, governments, persons or activities targeted by such laws, could result in decreased use of our products, or hinder our ability to export or sell our products to existing or potential customers, which would likely adversely affect our results of operations, financial condition or strategic objectives. If we fail to comply with these laws and regulations, we could be subject to substantial civil or criminal penalties, including the possible loss of export or import privileges and fines.

We rely on a general license from OFAC to sell our medicines for eventual use by hospital and clinic end-users in Iran. The use of this OFAC general license requires us to observe strict conditions with respect to products sold, end-user limitations and payment requirements. Although we believe we have maintained compliance with the general license requirements, there can be no assurance that the general license will not be revoked, be renewed in the future or that we will remain in compliance. A violation of the OFAC general license could result in substantial fines, sanctions, civil or criminal penalties, competitive or reputational harm, litigation or regulatory action and other consequences that might adversely affect our results of operations, financial condition or strategic objectives.

Moreover, U.S. export control and economic sanctions may make operating in certain countries more difficult and expensive. For example, we may be unable to find distributors or financial institutions willing to facilitate the sale of our products and collection of cash from such sales in a cost-effective manner, if at all.

Failure to comply with applicable anti-corruption legislation could result in fines, criminal penalties and materially adversely affect our business, financial condition and results of operations.

We are required to comply with anti-corruption and anti-bribery laws in the jurisdictions in which we operate, including the FCPA in the U.S., the United Kingdom (U.K.) Bribery Act 2010 and other similar laws in other countries in which we do business. We operate in a number of countries that are recognized to have a reputation for corruption and pose an increased risk of corrupt practices. We also regularly interact with government regulators in many countries, including those that are considered higher risk for corruption, in order to secure regulatory approval to manufacture and distribute our products. The anti-corruption and anti-bribery laws to which we are subject generally prohibit companies and their intermediaries from making improper payments to non-U.S. officials or other persons for the purposes of influencing official decisions or obtaining or retaining business and/or other benefits. These laws also require us to make and keep books and records that accurately and fairly reflect our transactions and to devise and maintain an adequate system of internal accounting controls. As part of our business, we deal with state-owned business enterprises, the employees and representatives of which may be considered non-U.S. officials for purposes of applicable anti-corruption laws.

Although we have adopted policies and procedures designed to ensure that we, our employees and third-party agents will comply with such laws, there can be no assurance that such policies or procedures will work effectively at all times or protect us against liability under these or other laws for actions taken by our employees, partners and other third parties with respect to our business. If we are not in compliance with anti-corruption laws and other laws governing the conduct of business with government entities and/or officials (including local laws), we may be subject to criminal and civil penalties and other remedial measures, which could harm our business, financial condition, results of operations, cash flows and prospects. Investigations of any actual or alleged violations of such laws or policies related to us could harm our business, financial condition, results of operations, cash flows and prospects.

Moreover, there has been enhanced scrutiny of company-sponsored patient assistance programs, including insurance premium and co-pay assistance programs and donations to third-party charities that provide such assistance. There has also been enhanced scrutiny by governments on reimbursement support offerings, clinical education programs and promotional speaker programs. If we, our third-party agents or donation recipients are deemed to have failed to comply with laws, regulations or government guidance in any of these areas, we could be subject to criminal or civil sanctions. Any similar violations by our competitors could also negatively impact our industry reputation and increase scrutiny over our business and our products.

Our international operations pose currency risks, which may adversely affect our operating results and net income.

A significant and growing portion of our revenues and earnings, as well as our substantial international net assets, are exposed to changes in foreign exchange rates. As we operate in multiple foreign currencies, including the Euro, the Brazilian Real, the Great British Pound, the Canadian Dollar and several other currencies, changes in those currencies relative to the U.S. Dollar (USD) will impact our revenues and expenses. If the USD were to weaken against another currency, assuming all other variables remained constant, our revenues would increase, having a positive impact on earnings, and our overall expenses would increase, having a negative impact on earnings. Conversely, if the USD were to strengthen against another currency, assuming all other variables remained constant, our revenues would decrease, having a negative impact on earnings, and our overall expenses would decrease, having a positive impact on earnings. In addition, because our financial statements are reported in USD, changes in currency exchange rates between the USD and other currencies have had, and will continue to have, an impact on our results of operations. Therefore, significant changes in foreign exchange rates can impact our results and our financial guidance.

We implement currency hedges intended to reduce our exposure to changes in certain foreign currency exchange rates. However, our hedging strategies may not be successful, and any of our unhedged foreign exchange exposures will continue to be subject to market fluctuations. These risks could cause a material adverse effect on our business, financial position and results of operations and could cause the market value of our common stock to decline.

We face credit risks from government-owned or sponsored customers outside of the U.S. that may adversely affect our results of operations.

Our product sales to government-owned or supported customers in various countries outside of the U.S. are subject to significant payment delays due to government funding and reimbursement practices. This has resulted and may continue to result in an increase in days sales outstanding due to the average length of time that we have accounts receivable outstanding. If significant changes were to occur in the reimbursement practices of these governments or if government funding becomes unavailable, we may not be able to collect on amounts due to us from these customers and our results of operations would be adversely affected.

Intellectual Property Risks

If we are unable to protect our intellectual property, we may not be able to compete effectively or preserve our market shares.

Where appropriate, we seek patent protection for certain aspects of our technology. Patent protection may not be available for some of the products we are developing. If we must spend significant time and money protecting or enforcing our patents, designing around patents held by others or licensing, potentially for large fees, patents or other proprietary rights held by others, our business and financial prospects may be harmed.

The patent positions of biopharmaceutical products are complex and uncertain. The scope and extent of patent protection for some of our products and product candidates are particularly uncertain because key information on some of our product candidates has existed in the public domain for many years. The composition and genetic sequences of animal and/or human versions of Aldurazyme, Naglazyme and many of our product candidates have been published and are believed to be in the public domain. The chemical structure of 6R-BH4 (the active ingredient in Kuvan) has also been published. Publication of this information may prevent us from obtaining or enforcing patents relating to our products and product candidates, including without limitation composition-of-matter patents, which are generally believed to offer the strongest patent protection.

We own or have licensed patents and patent applications related to our products. However, these patents and patent applications do not ensure the protection of our intellectual property for a number of reasons, including without limitation the following:

- With respect to pending patent applications, unless and until actually issued, the protective value of these applications is impossible to determine. We do not know whether our patent applications will result in issued patents.
- Patents have limited duration and expire.
- Enforcing patents is expensive and may absorb significant time of our management. Management would spend less time and resources on developing products, which could increase our operating expenses and delay product programs.

- Receipt of a patent may not provide much, if any, practical protection. For example, if we receive a patent with a narrow scope, then it will be easier for competitors to design products that do not infringe on our patent.
- The Leahy-Smith America Invents Act of 2011, which reformed certain patent laws in the U.S., may create additional uncertainty. Among the significant changes are switching from a “first-to-invent” system to a “first-to-file” system, and the implementation of new procedures that permit competitors to challenge our patents in the U.S. Patent and Trademark Office after grant.

It is also unclear whether our trade secrets are adequately protected. Our current and former employees, consultants or contractors may unintentionally or willfully disclose trade secrets to competitors. Enforcing a claim that someone else illegally obtained and is using our trade secrets, as with patent litigation, is expensive and time consuming, requires significant resources and has an unpredictable outcome. In addition, courts outside of the U.S. are sometimes less willing to protect trade secrets. Furthermore, our competitors may independently develop equivalent knowledge, methods and know-how, in which case we would not be able to enforce our trade secret rights against such competitors.

In the EU, clinical trial data submitted to the EMA in MAAs that were traditionally regarded as confidential commercial information are now subject to public disclosure. Subject to our ability to review and redact a narrow sub-set of confidential commercial information, the EU policies have resulted and will continue to result in the EMA's public disclosure of certain of our clinical study reports, clinical trial data summaries and clinical overviews for recently completed and future MAA submissions. The move toward public disclosure of development data could adversely affect our business in many ways, including, for example, resulting in the disclosure of our confidential methodologies for development of our products, preventing us from obtaining intellectual property right protection for innovations, requiring us to allocate significant resources to prevent other companies from violating our intellectual property rights, adding even more complexity to processing health data from clinical trials consistent with applicable data privacy regulations, and enabling competitors to use our data to gain approvals for their own products.

Competitors may interfere with our patent process in a variety of ways. Competitors may claim that they invented the claimed invention prior to us or that they filed their application for a patent on a claimed invention before we did. Competitors may also claim that we are infringing on their patents and therefore we cannot practice our technology. Competitors may also contest our patents by showing the patent examiner or a court that the invention was not original, was not novel or was obvious, for example. In litigation, a competitor could claim that our issued patents are not valid or are unenforceable for a number of reasons. If a court agrees, we would not be able to enforce that patent. Moreover, generic manufacturers may use litigation and regulatory means to obtain approval for generic versions of our products notwithstanding our filed patents or patent applications.

If we are unable to protect our intellectual property, third parties could develop competing products, which could adversely affect our revenues and financial results generally.

Competitors and other third parties may have developed intellectual property that could limit our ability to market and commercialize our products and product candidates, if approved.

Similar to us, competitors continually seek intellectual property protection for their technology. Several of our development programs, such as valoctocogene roxaparvovec, focus on therapeutic areas that have been the subject of extensive research and development by third parties for many years. Due to the amount of intellectual property in our field of technology, we cannot be certain that we do not infringe intellectual property rights of competitors or that we will not infringe intellectual property rights of competitors granted or created in the future. For example, if a patent holder believes our product infringes its patent, the patent holder may sue us even if we have received patent protection for our technology. If someone else claims we infringe its intellectual property, we would face a number of issues, including the following:

- Defending a lawsuit takes significant executive resources and can be very expensive.
- If a court decides that our product infringes a competitor's intellectual property, we may have to pay substantial damages.
- With respect to patents, in addition to requiring us to pay substantial damages, a court may prohibit us from making, selling, offering to sell, importing or using our product unless the patent holder licenses the patent to us. The patent holder is not required to grant us a license. If a license is available, it may not be available on commercially reasonable terms. For example, we may have to pay substantial royalties or grant cross licenses to our patents and patent applications.
- We may need to redesign our product so it does not infringe the intellectual property rights of others.

- Redesigning our product so it does not infringe the intellectual property rights of competitors may not be possible or could require substantial funds and time.

We may also support and collaborate in research conducted by government organizations, hospitals, universities or other educational institutions. These research partners may be unwilling to grant us any exclusive rights to technology or products derived from these collaborations.

If we do not obtain required licenses or rights, we could encounter delays in our product development efforts while we attempt to design around other patents or may be prohibited from making, using, importing, offering to sell or selling products requiring these licenses or rights. There is also a risk that disputes may arise as to the rights to technology or products developed in collaboration with other parties. If we are not able to resolve such disputes and obtain the licenses or rights we need, we may not be able to develop or market our products.

Risks Related to Ownership of Our Securities

Our stock price may be volatile, and an investment in our stock could suffer a decline in value.

Our valuation and stock price may have no meaningful relationship to current or historical earnings, asset values, book value or many other criteria based on conventional measures of stock value. The market price of our common stock will fluctuate due to factors including:

- product sales and profitability of our products;
- manufacturing, supply or distribution of our product candidates and commercial products;
- progress of our product candidates through the regulatory process and our ability to successfully commercialize any such products that receive regulatory approval;
- results of clinical trials, announcements of technological innovations or new products by us or our competitors;
- generic competition to Kuvan tablets and powder relating to our settlements with the two pharmaceutical companies described above in this Risk Factors section or potential generic competition from future competitors;
- government regulatory action affecting our product candidates, our products or our competitors' product candidates and products in both the U.S. and non-U.S. countries;
- developments or disputes concerning patent or proprietary rights;
- general market conditions and fluctuations for the emerging growth and pharmaceutical market sectors;
- economic conditions in the U.S. or abroad;
- negative publicity about us or the pharmaceutical industry;
- changes in the structure of healthcare payment systems;
- cybersecurity incidents experienced by us or others in our industry;
- broad market fluctuations in the U.S., the EU or in other parts of the world;
- actual or anticipated fluctuations in our operating results, including due to timing of large orders for our products, in particular in Latin America, where governments place large periodic orders for Naglazyme and Vimizim;
- changes in company assessments or financial estimates by securities analysts;
- acquisitions of products, businesses, or other assets; and
- sales of our shares of stock by us, our significant stockholders, or members of our management or Board of Directors.

Furthermore, the stock markets have recently experienced extreme price and volume fluctuations that have affected and continue to affect the market prices of equity securities of many companies. In some cases, these fluctuations have been unrelated or disproportionate to the operating performance of those companies. In the past, companies that have experienced volatility in the market price of their stock have been subject to securities class action litigation. For example, in September 2020, after a substantial drop in our stock price that followed an announcement providing a regulatory update regarding valoctocogene roxaparvovec, we and certain of our officers were sued in a putative class action lawsuit alleging violations of the federal securities laws for allegedly making materially false and misleading statements. We may be the target of additional litigation of this type in the future as well. Securities litigation against us could result in substantial costs and divert our management's time and attention from other business concerns, which could harm our business.

In addition, our stock price can be materially adversely affected by factors beyond our control, such as disruptions in global financial markets or negative trends in the biotechnology sector of the economy, even if our business is operating well.

Conversion of the Notes will dilute the ownership interest of existing stockholders, including holders who had previously converted their Notes, or may otherwise depress the price of our common stock.

The conversion of some or all of the Notes will dilute the ownership interests of existing stockholders. Any sales in the public market of the common stock issuable upon such conversion could adversely affect prevailing market prices of our common stock. In addition, the existence of the Notes may encourage short selling by market participants because the conversion of the Notes could be used to satisfy short positions, or anticipated conversion of the Notes into shares of our common stock could depress the price of our common stock.

Anti-takeover provisions in our charter documents and under Delaware law may make an acquisition of us, which may be beneficial to our stockholders, more difficult.

We are incorporated in Delaware. Certain anti-takeover provisions of Delaware law and our charter documents as currently in effect may make a change in control of us more difficult, even if a change in control would be beneficial to the stockholders. Our anti-takeover provisions include provisions in our restated certificate of incorporation and amended and restated bylaws providing that stockholders' meetings may only be called by our Chairman, the lead independent director or the majority of our Board of Directors and that the stockholders may not take action by written consent and requiring that stockholders that desire to nominate any person for election to our Board of Directors or to make any proposal with respect to business to be conducted at a meeting of our stockholders be submitted in appropriate form to our Secretary within a specified period of time in advance of any such meeting. Additionally, our Board of Directors has the authority to issue shares of preferred stock and to determine the terms of those shares of stock without any further action by our stockholders. The rights of holders of our common stock are subject to the rights of the holders of any preferred stock that may be issued. The issuance of preferred stock could make it more difficult for a third party to acquire a majority of our outstanding voting stock. Delaware law also prohibits corporations from engaging in a business combination with any holders of 15% or more of their capital stock until the holder has held the stock for three years unless, among other possibilities, our Board of Directors approves the transaction. Our Board of Directors may use these provisions to prevent changes in the management and control of us. Also, under applicable Delaware law, our Board of Directors may adopt additional anti-takeover measures in the future.

The fundamental change repurchase feature of the Notes may delay or prevent an otherwise beneficial attempt to take us over.

The terms of the Notes require us to repurchase the Notes in the event of a fundamental change. A takeover of us would trigger options by the respective holders of the applicable Notes to require us to repurchase such Notes. This may have the effect of delaying or preventing a takeover of us that would otherwise be beneficial to our stockholders or investors in the Notes.

Our amended and restated bylaws designate the Court of Chancery of the State of Delaware and the federal district courts of the U.S. as the exclusive forums for the adjudication of certain disputes, which could limit our stockholders' ability to obtain a favorable judicial forum for disputes with us or our directors, officers, or employees.

Our amended and restated bylaws provide that the Court of Chancery of the State of Delaware is the sole and exclusive forum for the following types of actions or proceedings under Delaware statutory or common law:

- any derivative claim or cause of action brought on our behalf;
- any claim or cause of action for breach of a fiduciary duty owed by any director, officer or other employee of BioMarin to us or our stockholders;
- any claim or cause of action against us or any of our directors, officers or other employees arising pursuant to any provision of the General Corporation Law of the State of Delaware, our restated certificate of incorporation

or our amended and restated bylaws; any claim or cause of action seeking to interpret, apply, enforce or determine the validity of our restated certificate of incorporation or our amended and restated bylaws;

- any claim or cause of action as to which the General Corporation Law of the State of Delaware confers jurisdiction to the Court of Chancery of the State of Delaware; and
- any claim or cause of action against us or any of our directors, officers or other employees that is governed by the internal affairs doctrine.

This exclusive-forum provision would not apply to suits brought to enforce a duty or liability created by the Securities Act of 1933, as amended, the Exchange Act or any other claim for which the U.S. federal courts have exclusive jurisdiction. In addition, our amended and restated bylaws provide that the federal district courts of the U.S. of America will be the exclusive forum for resolving any complaint asserting a cause of action arising under the Securities Act.

While the Delaware courts have determined that such choice of forum provisions are facially valid, a stockholder may nevertheless seek to bring a claim in a venue other than those designated in the exclusive forum provisions. In such instance, we would expect to vigorously assert the validity and enforceability of the exclusive forum provisions of our amended and restated bylaws. This may require significant additional costs associated with resolving such action in other jurisdictions and there can be no assurance that the provisions will be enforced by a court in those other jurisdictions.

These exclusive forum provisions may limit a stockholder's ability to bring a claim in a judicial forum that it finds favorable for disputes with us or our directors, officers, or other employees, which may discourage lawsuits against us and our directors, officers, and other employees. If a court were to find either of our exclusive forum provisions to be inapplicable or unenforceable in an action, we may incur further significant additional costs associated with resolving the dispute in other jurisdictions, all of which could seriously harm our business. Our amended and restated bylaws further provide that any person or entity that acquires any interest in shares of our capital stock will be deemed to have notice of and consented to the provisions of such provisions.

General Risk Factors

We depend upon our key personnel and our ability to attract and retain employees.

Our future growth and success will depend in large part on our continued ability to attract, retain, manage and motivate our employees. The loss of the services of any member of our senior management or the inability to hire or retain experienced management personnel could adversely affect our ability to execute our business plan and harm our operating results.

Because of the specialized scientific and managerial nature of our business, we rely heavily on our ability to attract and retain qualified scientific, technical and managerial personnel. In particular, the loss of one or more of our senior executive officers could be detrimental to us if we do not have an adequate succession plan or if we cannot recruit suitable replacements in a timely manner. While our senior executive officers are parties to employment agreements with us, these agreements do not guarantee that they will remain employed with us in the future. In addition, in many cases, these agreements do not restrict our senior executive officers' ability to compete with us after their employment is terminated. The competition for qualified personnel in the pharmaceutical field is intense, and there is a limited pool of qualified potential employees to recruit. Due to this intense competition, we may be unable to continue to attract and retain qualified personnel necessary for the development of our business or to recruit suitable replacement personnel. If we are unsuccessful in our recruitment and retention efforts, our business may be harmed.

Our success depends on our ability to manage our growth.

Product candidates that we are currently developing or may license or acquire in the future may be intended for patient populations that are significantly larger than any of the patient populations we currently target. In order to continue development and marketing of these products, if approved, we will need to significantly expand our operations. To manage expansion effectively, we need to continue to develop and improve our research and development capabilities, manufacturing and quality capacities, sales and marketing capabilities, financial and administrative systems and standard processes for global operations. Our staff, financial resources, systems, procedures or controls may be inadequate to support our operations and may increase our exposure to regulatory and corruption risks and our management may be unable to manage successfully future market opportunities or our relationships with customers and other third parties.

***Changes in tax laws or regulations that are applied adversely to us or our customers may have a material adverse effect on our business and financial condition.**

New tax laws or regulations could be enacted at any time, and existing tax laws or regulations could be interpreted, modified or applied in a manner that is adverse to us or our customers, which could adversely affect our business and financial

condition. For example, legislation enacted in 2017, informally titled the Tax Cuts and Jobs Act (TCJA), enacted many significant changes to the U.S. tax laws, including changes in corporate tax rates, the application of certain tax credits (including a reduction of tax credits under the Orphan Drug Act), the deductibility of expenses, the utilization of net operating losses (NOLs) and other deferred tax assets, and the taxation of non-U.S. earnings. Future guidance from the Internal Revenue Service and other tax authorities with respect to the TCJA may affect us, and certain aspects of the TCJA could be repealed or modified in future legislation. For example, the Coronavirus Aid, Relief, and Economic Security Act, or CARES Act, enacted in 2020, modified certain provisions of the TCJA, including provisions relating to NOL utilization. In addition, it is uncertain if and to what extent various states will conform to the TCJA, the CARES Act, or any newly enacted federal tax legislation. The impact of changes under the TCJA, the CARES Act, or future reform legislation, including certain legislative proposals by the current presidential administration, could increase our future U.S. tax expense and could have a material adverse impact on our business and financial condition.

Moreover, changes in the tax laws of non-U.S. jurisdictions could arise, including as a result of the base erosion and profit shifting (BEPS) project that was undertaken by the Organization for Economic Co-operation and Development (OECD), or other initiatives led by the OECD or the European Commission. The OECD, which represents a coalition of member countries including the U.S. and other countries in which we have operations, made several recommendations with the aim of addressing tax avoidance and ensuring that profits are taxed where economic activities generating the profits are performed and where value is created. These changes, as adopted by countries, may increase tax uncertainty and may adversely affect our provision for income taxes, results of operations and cash flows. It is not uncommon for taxing authorities in different countries to have conflicting views, for instance, with respect to, among other things, the manner in which the arm's length standard is applied for transfer pricing purposes, or with respect to the valuation of intellectual property. If tax authorities successfully challenge our transfer prices as not reflecting arm's length transactions, they could require us to adjust our transfer prices and thereby reallocate our income to reflect these revised transfer prices, resulting in a higher tax liability. In addition, if a country from which income is reallocated does not agree with the reallocation, both that country and the other country to which the income was allocated could tax the same income, potentially resulting in double taxation. If tax authorities were to allocate income to a higher tax jurisdiction, subject our income to double taxation or assess interest and penalties, it would increase our consolidated tax liability, which could adversely affect our business, financial condition, results of operations and cash flows.

If we are found in violation of healthcare laws or privacy and data protection laws, we may be required to pay penalties, be subjected to scrutiny by regulators or governmental entities, or be suspended from participation in government healthcare programs, which may adversely affect our business, financial condition and results of operations.

We are subject to various healthcare laws and regulations in the U.S. and internationally, including anti-kickback laws, false claims laws, data privacy and security laws, and laws related to ensuring compliance. In the U.S., the federal Anti-Kickback Statute makes it illegal for any person or entity, including a pharmaceutical company, to knowingly and willfully offer, solicit, pay or receive any remuneration, directly or indirectly, in exchange for or to induce the referral of business, including the purchase, order or prescription of a particular drug, for which payment may be made under federal healthcare programs, such as Medicare and Medicaid. Under the federal Anti-Kickback Statute and related regulations, certain arrangements are deemed not to violate the federal Anti-Kickback Statute if they fit within a statutory exception or regulatory safe harbor. However, the exceptions and safe harbors are drawn narrowly, and practices that involve remuneration not intended to induce prescribing, purchases or recommendations may be subject to scrutiny if they do not qualify for an exception or safe harbor. Our practices may not in all cases meet all of the criteria for safe harbor protection from Anti-Kickback liability, although we seek to comply with these safe harbors. Many states have adopted laws similar to the federal Anti-Kickback Statute, some of which apply to referral of patients for healthcare services reimbursed by any source, not just governmental payers.

Federal and state false claims laws, including the civil False Claims Act and the Civil Monetary Penalties Law, prohibit any person or entity from knowingly presenting, or causing to be presented, a false claim for payment to the federal government, or knowingly making, or causing to be made, a false statement to have a false claim paid, or knowingly making, using, or causing to be made or used, a false record or statement to avoid, decrease or conceal an obligation to pay money to the federal government. In addition, certain marketing practices, including off-label promotion, may also violate false claims laws.

Under the Health Insurance Portability and Accountability Act of 1996 (HIPAA), we also are prohibited from, among other things, knowingly and willfully executing a scheme to defraud any healthcare benefit program, including private payers, or knowingly and willfully falsifying, concealing or covering up a material fact or making any materially false, fictitious or fraudulent statement in connection with the delivery of or payment for healthcare benefits, items or services.

In addition, recent healthcare reform legislation has strengthened these laws in the U.S. For example, the PPACA, among other things, amends the intent requirement of the federal Anti-Kickback Statute and criminal healthcare fraud statutes. A person or entity no longer needs to have actual knowledge of these statutes or specific intent to violate them in order to commit a violation. Moreover, the PPACA provides that the government may assert that a claim including items or services resulting from a violation of the federal Anti-Kickback Statute constitutes a false or fraudulent claim for purposes of the civil False Claims Act.

HIPAA, as amended by the Health Information Technology for Economic and Clinical Health Act and its implementing regulations, also imposes obligations, including mandatory contractual terms, on certain types of individuals and entities, with

respect to safeguarding the privacy, integrity, availability, security and transmission of individually identifiable health information. Many state and non-U.S. laws also govern the privacy and security of health information. They often differ from each other in significant ways and often are not preempted by HIPAA, thus complicating compliance efforts. The global data protection landscape is rapidly evolving, and implementation standards and enforcement practices are likely to remain uncertain for the foreseeable future. In the United States, California recently enacted the California Consumer Privacy Act (CCPA), which took effect on January 1, 2020. The CCPA gives California consumers expanded rights to access and delete their personal information, opt out of certain personal information sales, and receive detailed information about how their personal information is used. The CCPA provides for civil penalties for violations, as well as a private right of action for data breaches that is expected to increase data breach litigation. The CCPA will be expanded substantially on January 1, 2023 when the California Privacy Rights Act of 2020 (CPRA), becomes fully operative. The CPRA will, among other things, give consumers the ability to limit use of information deemed to be sensitive, increase the maximum penalties for violations concerning consumers under age 16, expand an individual's private right of action and establish the California Privacy Protection Agency to implement and enforce the new law and impose administrative fines. In addition to California, other U.S. states have recently adopted consumer data protection and privacy laws, and more U.S. states may do so in the future. Aspects of the CCPA, CPRA and similar laws in other states and their interpretation and enforcement remain uncertain. The potential effects of these laws are far-reaching and may require us to modify our data processing practices and policies and to incur substantial costs and expenses in an effort to comply.

The European Regulation 2016/679, known as the General Data Protection Regulation (GDPR), as well as EU Member State implementing legislations, apply to the processing of personal data of individuals located in the EEA, including health-related information, by companies located in the EEA, or in certain circumstances, by companies located outside of the EEA. These laws impose strict obligations on the ability to collect, record, store, disclose, use and transmit personal data, including health-related information. These include several requirements relating to (i) obtaining, in some situations, the consent of the individuals to whom the personal data relates, (ii) the information provided to the individuals about how their personal information is used, (iii) ensuring the security and confidentiality of the personal data, (iv) the obligation to notify regulatory authorities and affected individuals of personal data breaches, (v) extensive internal privacy governance obligations, and (vi) obligations to honor rights of individuals in relation to their personal data (for example, the right to access, correct and delete their data). The GDPR prohibits the transfer of personal data to countries outside of the EEA, such as the United States, which are not considered by the European Commission to provide an adequate level of data protection. Switzerland has adopted similar restrictions. Potential pecuniary fines for noncompliant companies may be up to the greater of €20 million or 4% of annual global revenue. The GDPR has increased our responsibility and liability in relation to personal data that we process and has increased our compliance costs.

The GDPR and other European data protection laws generally restrict the transfer of personal information from Europe, including the EEA and Switzerland, to the U.S. and most other countries unless the parties to the transfer have implemented specific safeguards to protect the transferred personal information. One of the primary safeguards allowing U.S. companies to import personal information from Europe has been the European Commission's Standard Contractual Clauses (SCCs). However, the Court of Justice of the EU issued a decision that called into question whether the SCCs can lawfully be used for transfers of personal information from Europe to the United States or most other countries. At present, there are few, if any, viable alternatives to the SCCs, on which we have relied for personal information transfers from Europe to the United States and other "third countries." The Court of Justice of the EU ruled that subject to their containing "effective mechanisms" to ensure compliance with the protections offered by EU law, namely implementation of transfer impact assessments regarding country surveillance laws, the SCCs were generally upheld. New SCCs were published in June 2021 and will require implementation within 12 months from publication. Compliance with the regulations covering the transfer of personal information from Europe to the U.S. has increased our compliance costs.

Following the U.K.'s withdrawal from the EU on January 31, 2020 and the end of the transitional arrangements agreed to between the U.K. and EU, the GDPR no longer has effect in law in the U.K. However, the data protection obligations of the GDPR continue to apply to U.K.-related processing of personal data in substantially unvaried form under the so-called "UK GDPR" (i.e., the GDPR as it continues to form part of law in the U.K. However, going forward, there will be increasing scope for divergence in application, interpretation and enforcement of the data protection law as between the U.K. and EEA. Furthermore, the relationship between the U.K. and the EEA in relation to certain aspects of data protection law remains unclear, which could expose us to two parallel regimes, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations. Also in the event of a violation of the GDPR affecting data subjects across the U.K. and the EEA, we could potentially be investigated by, and ultimately fined by the U.K. Information Commissioner's Office and the supervisory authority in each and every EEA Member State where data subjects have been affected by such violation.

Substantial new laws and regulations affecting compliance have also been adopted in the U.S. and certain non-U.S. countries, which may require us to modify our business practices with healthcare practitioners. For example, in the U.S., the PPACA, through the Physician Payments Sunshine Act, requires certain drug, biologicals and medical supply manufacturers to collect and report to CMS information on payments or transfers of value to physicians (defined to include doctors, dentists, optometrists, podiatrists and chiropractors) and teaching hospitals, as well as investment and ownership interests held by such physicians and their immediate family members during the preceding calendar year. Effective January 1, 2022, manufacturers will also be required to report on payments or transfers of value during the previous year to physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists, and certified nurse-midwives. In

addition, there has been a recent trend of increased state regulation of payments made to physicians. Certain states and/or local jurisdictions mandate implementation of compliance programs, compliance with the Office of Inspector General Compliance Program Guidance for Pharmaceutical Manufacturers and the Pharmaceutical Research and Manufacturers of America (PhRMA) Code on Interactions with Healthcare Professionals, the registration of pharmaceutical sales representatives and/or the tracking and reporting of gifts, compensation and other remuneration to physicians, marketing expenditures, and drug pricing. Likewise, in many non-U.S. countries there is an increasing focus on the relationship between drug companies and healthcare practitioners. Recently enacted non-U.S. legislation creates reporting obligations on payments, gifts and benefits made to these professionals; however, implementing regulations enacting such laws are still pending and subject to varying interpretations by courts and government agencies. The shifting regulatory environment and the need to implement systems to comply with multiple jurisdictions with different compliance and/or reporting requirements increases the costs of maintaining compliance and the possibility that we may violate one or more of the requirements and be subject to fines or sanctions.

Due to the breadth of the healthcare and privacy and data protection laws described above, the narrowness of available statutory and regulatory exceptions and safe harbors and the increased focus by law enforcement agencies in enforcing such laws, our business activities could be subject to challenge under one or more of such laws. If we are found in violation of one of these laws, we may be subject to significant criminal, civil or administrative sanctions, including damages, fines, disgorgement, imprisonment, contractual damages, reputational harm, diminished profits and future earnings, additional reporting requirements and oversight if we become subject to a corporate integrity agreement or similar agreement to resolve allegations of non-compliance with these laws, curtailment of our operations, and debarment, suspension or exclusion from participation in government healthcare programs, any of which could adversely affect our business, financial condition and results of operations.

If product liability lawsuits are successfully brought against us, we may incur substantial liabilities.

We are exposed to the potential product liability risks inherent in the testing, manufacturing and marketing of human pharmaceuticals. We currently maintain insurance against product liability lawsuits for the commercial sale of our products and for the clinical trials of our product candidates. Pharmaceutical companies must balance the cost of insurance with the level of coverage based on estimates of potential liability. Historically, the potential liability associated with product liability lawsuits for pharmaceutical products has been unpredictable. Although we believe that our current insurance is a reasonable estimate of our potential liability and represents a commercially reasonable balancing of the level of coverage as compared to the cost of the insurance, we may be subject to claims in connection with our clinical trials and commercial use of our products and product candidates for which our insurance coverage may not be adequate and we may be unable to avoid significant liability if any product liability lawsuit is brought against us. If we are the subject of a successful product liability claim that exceeds the limits of any insurance coverage we obtain, we may incur substantial charges that would adversely affect our earnings and require the commitment of capital resources that might otherwise be available for the development and commercialization of our product programs.

We rely significantly on information technology systems and any failure, inadequacy, interruption or security lapse of that technology, including any cybersecurity incidents, could harm our ability to operate our business effectively and have a material adverse effect on our business, reputation, financial condition, and results of operations.

We rely significantly on our information technology systems to effectively manage and maintain our operations, inventory and internal reports, to manufacture and ship products to customers and to timely invoice them. Any failure, inadequacy or interruption of that infrastructure or security lapse of that technology, including cybersecurity incidents or attacks, could harm our ability to operate our business effectively. Our ability to manage and maintain our operations, inventory and internal reports, to manufacture and ship our products to customers and timely invoice them depends significantly on our enterprise resource planning, production management and other information systems. Our technology systems, including our cloud technologies, continue to increase in multitude and complexity, making them potentially vulnerable to breakdown, cyberattack and other disruptions. Potential problems and interruptions associated with the implementation of new or upgraded technology systems or with maintenance or adequate support of existing systems could disrupt or reduce the efficiency of our operations and expose us to greater risk of security breaches. Cybersecurity incidents, including phishing attacks and attempts to misappropriate or compromise confidential or proprietary information or sabotage enterprise IT systems are becoming increasingly frequent and more sophisticated. Cybersecurity incidents resulting in the failure of our enterprise resource planning system, production management or other systems to operate effectively or to integrate with other systems, or a breach in security or other unauthorized access or unavailability of these systems, have occurred in the past and may affect our ability in the future to manage and maintain our operations, inventory and internal reports, and result in delays in product fulfillment and reduced efficiency of our operations.

As part of our business, we collect, store and transmit large amounts of confidential information, proprietary data, intellectual property and personal data. The information and data processed and stored in our technology systems, and those of our research collaborators, CROs, contract manufacturers, suppliers, distributors, or other third parties for which we depend to operate our business, may be vulnerable to loss, damage, denial-of-service, unauthorized access or misappropriation. Data security breaches may be the result of unauthorized or unintended activity (or lack of activity) by our employees or contractors or malware, hacking, business email compromise, phishing or other cyberattacks directed by third parties. These third parties for which we depend on to operate our business have experienced and may continue to experience cybersecurity incidents. While we

have implemented measures to protect our information and data stored in our technology systems and those of the third parties that we rely on, our efforts may not be successful.

We have experienced and may continue to experience cybersecurity incidents. Although to our knowledge we have not experienced any material incident or interruption to date, if such an event were to occur it could result in a material disruption of our development programs and commercial operations, including due to a loss, corruption or unauthorized disclosure of our trade secrets, personal data or other proprietary or sensitive information. Further, these cybersecurity incidents can lead to the public disclosure of personal information (including sensitive personal information) of our employees, clinical trial patients and others and result in demands for ransom or other forms of blackmail. Such attacks are of ever-increasing levels of sophistication and are made by groups and individuals with a wide range of motives (including industrial espionage) and expertise, including by organized criminal groups, “hacktivists”, nation states and others. Moreover, the costs to us to investigate and mitigate cybersecurity incidents could be significant. For example, the loss of clinical trial data could result in delays in our product development or regulatory approval efforts and significantly increase our costs to recover or reproduce the data. Any security breach that results in the unauthorized access, use or disclosure of personal data may require us to notify individuals, governmental authorities, credit reporting agencies, or other parties pursuant to privacy and security laws and regulations or other obligations. Such a security compromise could harm our reputation, erode confidence in our information security measures, and lead to regulatory scrutiny. To the extent that any disruption or security breach resulted in a loss of, or damage to, our data or systems, or inappropriate disclosure of confidential, proprietary or personal information, we could be exposed to a risk of loss, enforcement measures, penalties, fines, indemnification claims, litigation and potential civil or criminal liability, which could materially adversely affect our business, financial condition and results of operations.

***If a natural disaster, terrorist or criminal activity or other unforeseen event caused significant damage to our facilities or those of our third-party manufacturers and suppliers or significantly disrupted our operations or those of our third-party manufacturers and suppliers, we may be unable to meet demand for our products and lose potential revenue, have reduced margins, or be forced to terminate a program.**

The occurrence of an earthquake or other catastrophic disaster could cause damage to our facility and equipment, or that of our third-party manufacturers or single-source suppliers, which could materially impair the ability for us or our third-party manufacturers to manufacture our products and product candidates. Our Galli Drive facility, located in Novato, California, is currently our only manufacturing facility for Aldurazyme, Naglazyme, Voxzogo and Palyzniq and is one of two manufacturing facilities for Brineura and Vimizim. Our gene therapy manufacturing facility is also located in Novato, California, and it is currently our only manufacturing facility to support valoctocogene roxaparovec clinical development activities and the anticipated commercial demand for valoctocogene roxaparovec, if approved. These facilities are located in the San Francisco Bay Area near known earthquake fault zones and are vulnerable to significant damage from earthquakes. We, the third-party manufacturers with whom we contract and our single-source suppliers of raw materials, which include many of our critical raw materials, are also vulnerable to damage from other types of disasters, including fires, explosions, floods, and similar events. If any disaster were to occur, or any terrorist or criminal activity caused significant damage to our facilities or the facilities of our third-party manufacturers and suppliers, our ability to manufacture our products, or to have our products manufactured, could be seriously, or potentially completely, impaired, and our commercialization efforts and revenues could be seriously impaired.

Moreover, other unforeseen events, such as power outages, could significantly disrupt our operations or those of our third-party manufacturers and suppliers, which could result in significant delays in the manufacture of our products and adversely impact our commercial operations and revenues. Pacific Gas and Electric Company, the electric utility in the San Francisco Bay Area where many of our facilities are located, commenced widespread blackouts during the fall of 2019 to avoid and contain wildfires sparked during strong wind events by downed power lines or equipment failures. While we have not experienced damage to our facilities or material disruption to our operations as a result of these power outages, ongoing blackouts, particularly if prolonged or frequent, could impact our business going forward. The insurance that we carry, the inventory that we maintain and our risk mitigation plans may not be adequate to cover our losses resulting from disasters or other business interruptions.

Our business is affected by macroeconomic conditions.

Various macroeconomic factors could adversely affect our business and the results of our operations and financial condition, including changes in inflation, interest rates and foreign currency exchange rates and overall economic conditions and uncertainties, including those resulting from the current and future conditions in the global financial markets. For instance, if inflation or other factors were to significantly increase our business costs, it may not be feasible to pass price increases on to our customers due to the process by which healthcare providers are reimbursed for our products by the government. Interest rates, the liquidity of the credit markets and the volatility of the capital markets could also affect the value of our investments and our ability to liquidate our investments in order to fund our operations. We purchase or enter into a variety of financial instruments and transactions, including investments in commercial paper, the extension of credit to corporations, institutions and governments and

hedging contracts. If any of the issuers or counter parties to these instruments were to default on their obligations, it could materially reduce the value of the transaction and adversely affect our cash flows.

We sell our products in countries that face economic volatility and weakness. Although we have historically collected receivables from customers in those countries, sustained weakness or further deterioration of the local economies and currencies may cause customers in those countries to be unable to pay for our products. Additionally, if one or more of these countries were unable to purchase our products, our revenues would be adversely affected.

Interest rates and the ability to access credit markets could also adversely affect the ability of our customers/distributors to purchase, pay for and effectively distribute our products. Similarly, these macroeconomic factors could affect the ability of our contract manufacturers, sole-source or single-source suppliers to remain in business or otherwise manufacture or supply product. Failure by any of them to remain a going concern could affect our ability to manufacture products.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

None.

Item 3. Defaults Upon Senior Securities

None.

Item 4. Mine Safety Disclosures

Not applicable.

Item 5. Other Information

None

Item 6. Exhibits

Exhibit Number	Description
2.1	Amended and Restated Termination and Transition Agreement, dated as of December 23, 2015, between BioMarin Pharmaceutical Inc. and Ares Trading S.A., previously filed with the SEC on January 7, 2016 as Exhibit 2.1 to the Company's Current Report on Form 8-K (File No. 000-26727), which is incorporated herein by reference. Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment. Omitted portions have been filed separately with the SEC.
2.2	Termination and Transition Agreement, dated as of October 1, 2015, between BioMarin Pharmaceutical Inc. and Ares Trading S.A., previously filed with the SEC on January 7, 2016 as Exhibit 2.3 to the Company's Current Report on Form 8-K (File No. 000-26727), which is incorporated herein by reference. Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment. Omitted portions have been filed separately with the SEC.
2.3	First Amendment, dated as of December 12, 2016, to the Amended and Restated Termination and Transition Agreement, dated as of December 23, 2015 and effective as of October 1, 2015, between BioMarin Pharmaceutical Inc. and Ares Trading S.A., previously filed with the SEC on February 27, 2017 as Exhibit 2.6 to the Company's Annual Report on Form 10-K (File No. 000-26727), which is incorporated herein by reference. Portions of this exhibit (indicated by asterisks) have been omitted pursuant to a request for confidential treatment. Omitted portions have been filed separately with the SEC.
3.1	Restated Certificate of Incorporation of BioMarin Pharmaceutical Inc., previously filed with the SEC on June 12, 2017 as Exhibit 3.2 to the Company's Current Report on Form 8-K (File No. 000-26727), which is incorporated herein by reference.
3.2	Amended and Restated Bylaws of BioMarin Pharmaceutical Inc., previously filed with the SEC on December 18, 2020 as Exhibit 3.1 to the Company's Current Report on Form 8-K (File No. 000-26727), which is incorporated herein by reference.
31.1*	Certification of Chief Executive Officer pursuant to Rules 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.
31.2*	Certification of Chief Financial Officer pursuant to Rules 13a-14(a)/15d-14(a) of the Securities Exchange Act of 1934, as amended.
32.1*+	Certification of Chief Executive Officer and Chief Financial Officer pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002. This Certification accompanies this report and shall not, except to the extent required by the Sarbanes-Oxley Act of 2002, be deemed filed for purposes of §18 of the Securities Exchange Act of 1934, as amended.
101.INS	XBRL Instance Document - the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document.
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase
101.LAB	Inline XBRL Taxonomy Extension Labels Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Link Document
104	XBRL tags for the cover page from the Company's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021, are embedded within the Inline XBRL document.

* Filed herewith

+ The certifications attached as Exhibit 32.1 accompany this Quarterly Report on Form 10-Q pursuant to 18 U.S.C. Section 1350, as adopted pursuant to Section 906 of the Sarbanes-Oxley Act of 2002, and shall not be deemed "filed" by the Registrant for purposes of Section 18 of the Securities Exchange Act of 1934, as amended, and are not to be incorporated by reference into any of the Registrant's filings under the Securities Act of 1933, as amended, irrespective of any general incorporation language contained in any such filing.

Attached as Exhibit 101 to this report are documents formatted in XBRL (Extensible Business Reporting Language): (i) Condensed Consolidated Balance Sheets as of September 30, 2021 and December 31, 2020, (ii) Condensed Consolidated Statements of Comprehensive Income for the three and nine months ended September 30, 2021 and 2020, (iii) Condensed Consolidated Statement of Stockholders' Equity for the three and nine months ended September 30, 2021 and 2020, (iv) Condensed Consolidated Statements of Cash Flows for the nine months ended September 30, 2021 and 2020, and (v) Notes to Condensed Consolidated Financial Statements.

CERTIFICATION

I, Jean-Jacques Bienaimé, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of BioMarin Pharmaceutical Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - (a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - (b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - (c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - (d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - (a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - (b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: October 29, 2021

/s/ JEAN-JACQUES BIENAIMÉ

Jean-Jacques Bienaimé
Chief Executive Officer

CERTIFICATION

I, Brian R. Mueller, certify that:

1. I have reviewed this Quarterly Report on Form 10-Q of BioMarin Pharmaceutical Inc.;
2. Based on my knowledge, this report does not contain any untrue statement of a material fact or omit to state a material fact necessary to make the statements made, in light of the circumstances under which such statements were made, not misleading with respect to the period covered by this report;
3. Based on my knowledge, the financial statements, and other financial information included in this report, fairly present in all material respects the financial condition, results of operations and cash flows of the registrant as of, and for, the periods presented in this report;
4. The registrant's other certifying officer(s) and I are responsible for establishing and maintaining disclosure controls and procedures (as defined in Exchange Act Rules 13a-15(e) and 15d-15(e)) and internal control over financial reporting (as defined in Exchange Act Rules 13a-15(f) and 15d-15(f)) for the registrant and have:
 - a) Designed such disclosure controls and procedures, or caused such disclosure controls and procedures to be designed under our supervision, to ensure that material information relating to the registrant, including its consolidated subsidiaries, is made known to us by others within those entities, particularly during the period in which this report is being prepared;
 - b) Designed such internal control over financial reporting, or caused such internal control over financial reporting to be designed under our supervision, to provide reasonable assurance regarding the reliability of financial reporting and the preparation of financial statements for external purposes in accordance with generally accepted accounting principles;
 - c) Evaluated the effectiveness of the registrant's disclosure controls and procedures and presented in this report our conclusions about the effectiveness of the disclosure controls and procedures, as of the end of the period covered by this report based on such evaluation; and
 - d) Disclosed in this report any change in the registrant's internal control over financial reporting that occurred during the registrant's most recent fiscal quarter (the registrant's fourth fiscal quarter in the case of an annual report) that has materially affected, or is reasonably likely to materially affect, the registrant's internal control over financial reporting; and
5. The registrant's other certifying officer(s) and I have disclosed, based on our most recent evaluation of internal control over financial reporting, to the registrant's auditors and the audit committee of the registrant's board of directors (or persons performing the equivalent functions):
 - a) All significant deficiencies and material weaknesses in the design or operation of internal control over financial reporting which are reasonably likely to adversely affect the registrant's ability to record, process, summarize and report financial information; and
 - b) Any fraud, whether or not material, that involves management or other employees who have a significant role in the registrant's internal control over financial reporting.

Date: October 29, 2021

/s/ BRIAN R. MUELLER

Brian R. Mueller
Executive Vice President, Finance &
Chief Financial Officer

**CERTIFICATION PURSUANT TO
18 U.S.C. SECTION 1350,
AS ADOPTED PURSUANT TO
SECTION 906 OF THE SARBANES-OXLEY ACT OF 2002**

We, Jean-Jacques Bienaimé and Brian R. Mueller, hereby certify, pursuant to 18 U.S.C. §1350, as adopted pursuant to §906 of the Sarbanes-Oxley Act of 2002, that BioMarin Pharmaceutical Inc.'s Quarterly Report on Form 10-Q for the period ended September 30, 2021, fully complies with the requirements of Section 13(a) or 15(d) of the Securities Exchange Act of 1934 and the information contained in such Form 10-Q fairly presents, in all material respects, the financial condition and results of operations of BioMarin Pharmaceutical Inc.

/s/ JEAN-JACQUES BIENAIMÉ

Jean-Jacques Bienaimé
Chief Executive Officer

Date: October 29, 2021

/s/ BRIAN R. MUELLER

Brian R. Mueller
Executive Vice President, Finance &
Chief Financial Officer

Date: October 29, 2021

This certification accompanies the Quarterly Report on Form 10-Q to which it relates, is not deemed filed with the Securities and Exchange Commission and is not to be incorporated by reference into any filing of BioMarin Pharmaceutical Inc. under the Securities Act of 1933, as amended, or the Securities Exchange Act of 1934, as amended (whether made before or after the date of the Quarterly Report on Form 10-Q), irrespective of any general incorporation language contained in such filing.