BioMarin Announces Fourth Quarter and Full Year 2021 Financial Results and Corporate Updates

- Full-year 2021 Total Revenues of $1.85 Billion; Revenues Excluding Kuvan Increased 11% Year-Over-Year

- Company Provides Full-Year 2022 Total Revenue Guidance of $2.05 Billion to $2.15 Billion, Representing 14% Growth Year-Over-Year, Based on Mid-point of Range; Transitions to GAAP Profitability

- Strong Commercial Launch of VOXZOGO™ for the Treatment of Children with Achondroplasia Underway across Europe, the U.S. and other Regions Following 2021 Approvals; Full-year 2022 Guidance for VOXZOGO™ Net Product Revenues Increased to Between $90 Million to $115 Million

- Announced Positive 2-year Efficacy Data for Valoctocogene Roxaparvovec for the Treatment of Severe Hemophilia A to Support U.S. and European Regulatory Health Authority Reviews in 2022

SAN RAFAEL, Calif., Feb. 23, 2022 /PRNewswire/ --

Financial Highlights (in millions of U.S. dollars, except per share data, unaudited)

	Three Months Ended December 31,			Twelve Months Ended December 31,		
	2021	2020	% Change	2021	2020	% Change
Total Revenues	$ 449.8	$ 452.1	(1)%	$ 1,846.3	$ 1,860.5	(1)%
Net Product Revenues Marketed by BioMarin [1]	$ 414.9	$ 435.8	(5)%	$ 1,660.7	$ 1,675.8	(1)%
Vimizim Net Product Revenues	$ 156.3	$ 142.5	10%	$ 623.1	$ 544.4	14%
Naglazyme Net Product Revenues	$ 83.1	$ 119.7	(31)%	$ 380.4	$ 391.3	(3)%
Kuvan Net Product Revenues	$ 68.5	$ 89.0	(23)%	$ 285.8	$ 457.7	(38)%
Palynziq Net Product Revenues	$ 63.8	$ 49.6	29%	$ 237.5	$ 171.0	39%
Brineura Net Product Revenues	$ 37.4	$ 35.0	7%	$ 128.0	$ 110.2	16%
Voxzogo Net Product Revenues	$ 5.8	$ —	n/a	$ 5.9	$ —	n/a
Aldurazyme Net Product Revenues	$ 20.3	$ 1.2	nm[2]	$ 122.8	$ 130.1	(6)%
GAAP Net Income (Loss)	$ (57.9)	$ 22.1		$ (64.1)	$ 859.1	
GAAP Net Income (Loss) per Share – Basic	$ (0.32)	$ 0.12		$ (0.35)	$ 4.75	
GAAP Net Income (Loss) per Share – Diluted	$ (0.32)	$ 0.12		$ (0.35)	$ 4.53	
Non-GAAP Income [3]	$ 7.1	$ 39.5		$ 242.8	$ 312.2	

	December 31, 2021	December 31, 2020
Cash, cash equivalents and investments	$ 1,521.7	$ 1,350.9

(1) Net Product Revenues Marketed by BioMarin is the sum of revenues from Vimizim, Naglazyme, Kuvan, Palynziq, Brineura and Voxzogo (formerly known as vosoritide) for the three and twelve months ended December 31, 2021, each calculated in accordance with Generally Accepted Accounting Principles in the United States (U.S. GAAP). Sanofi (formally known as Sanofi Genzyme) is BioMarin's sole customer for Aldurazyme and is responsible for marketing and selling Aldurazyme to third parties. Refer to page 10 for a table showing Net Product Revenues by product. In January 2020, BioMarin divested the Firdapse assets to a third party in a sale transaction. The sale is reflected in the Company's consolidated financial statements for the twelve months ended December 30, 2020; as a result of the transaction BioMarin no longer recognizes Net Product Revenues from Firdapse.

(2) Not meaningful

(3) Non-GAAP Income is defined by the Company as reported GAAP Net Income/Loss, excluding net interest expense, provision for (benefit from) income taxes, depreciation expense, amortization expense, stock-based compensation expense, contingent consideration expense and, in certain periods, certain other specified items. Refer to Non-GAAP Information beginning on page 11 of this press release for a complete discussion of the Company's Non-GAAP financial information and reconciliations to the comparable information reported under U.S. GAAP.

BioMarin Pharmaceutical Inc. (NASDAQ: BMRN) (BioMarin or the Company) today announced financial results for the fourth quarter and full-year ended December 31, 2021.

BioMarin Announces Fourth Quarter and Full-year 2021 Results

"During 2021, we established the foundation for a return to double-digit revenue growth and profitability in 2022," said Jean-Jacques Bienaimé, Chairman and Chief Executive Officer of BioMarin. "We are pleased with 2021 full-year results, which demonstrated solid performance despite the impact of the loss of exclusivity of Kuvan in the U.S. Following the 2021 global approvals of Voxzogo in the U.S., Europe and Brazil, the enthusiasm from families seeking treatment for their children with achondroplasia has been very encouraging. We are pleased that families now have an approved treatment option, and we look forward to increasing access to Voxzogo as the launch rolls out over the coming quarters."

Mr. Bienaimé continued, "With Voxzogo in launch mode in many countries across the globe, the regulatory team is focused on our next significant potential approval with valoctocogene roxaparvovec gene therapy for the treatment of severe hemophilia A. The two-year data from the 134-participant Phase 3 study, shared in January 2022, met all primary and secondary efficacy endpoints. The results are clinically meaningful, demonstrating superiority to standard of care and an 85% reduction in annualized bleeding rates compared to baseline. We anticipate resubmitting the U.S. application in the second quarter of 2022 and continue to anticipate the European opinion in the second quarter of 2022. With the potential approvals of valoctocogene roxaparvovec in Europe and US, and the continued strong launch of Voxzogo, we expect 2022 to be a transformational year for BioMarin and the patients we seek to serve."

Financial Highlights:

- **Total Revenues** for the fourth quarter of 2021 were $449.8 million, essentially flat compared to the same period in 2020 despite continued erosion of the U.S. Kuvan market. Significant product level revenue fluctuations were as follows:
    - Higher Aldurazyme product revenues due to timing of product fulfillment to Sanofi. BioMarin Aldurazyme revenues are driven by the timing of when the product is released and control is transferred to Sanofi. Revenues for the fourth quarter of 2021 were comparatively higher than 2020 due to such timing.
    - Higher 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. The commercial launch of Palynziq in BioMarin's European, Middle East and African (EMEA) region continues to progress through individual country level pricing and reimbursement negotiations.
    - Higher Vimizim product revenues primarily driven by timing of orders in the Middle East and Latin America.
    - Voxzogo received approval from European Medicines Agency (EMA) and the U.S. Food and Drug Administration (FDA) in the third and fourth quarters of 2021 with commercial sales launching regionally in the same period as approval.

  These factors were more than offset by the following:

    - Lower Naglazyme product revenues primarily driven by timing of orders from Latin America, the Middle East and Europe. High patient compliance rates and year-over-year patient growth reflect strong underlying demand.
    - Lower Kuvan product revenues primarily due to generic competition as a result of the loss of exclusivity in the U.S., which was consistent with expectations.

- **GAAP Net Loss** increased to $57.9 million for the fourth quarter of 2021 compared to GAAP Net Income of $22.1 million for the same period in 2020 primarily due to the following:
    - Higher tax benefit in 2020 due to the change in the jurisdictional mix of earnings and the related tax impact from the completion of an intra-entity transfer of certain intellectual property rights to an Irish subsidiary. There was no similar transaction in 2021.
    - Higher selling, general and administrative (SG&A) expenses primarily due to higher commercialization activities to support the commercial launch of Voxzogo, as well as an increase in administrative costs.

- **Non-GAAP Income** for the fourth quarter of 2021 decreased to $7.1 million compared to Non-GAAP Income of $39.5 million for the same period in 2020. The decrease in Non-GAAP Income for the quarter compared to the same period in 2020 was primarily attributable to higher SG&A and research and development (R&D) expenses.

Late-stage Regulatory Portfolio (Voxzogo and valoctocogene roxaparvovec)

- In August 2021, the European Commission approved Voxzogo for the treatment of children, ages 2 years and older. Regulatory approvals were also received in Brazil and the U.S. in November 2021, for children ages five and older with open growth plates. The launch is actively underway, with market access and reimbursement progressing as anticipated. By February 15, 2022, an estimated 210 children were being treated with commercial Voxzogo globally, with an estimated additional 54 children in process in the U.S.
- Marketing authorization reviews of Voxzogo are in process in Japan and Australia, with potential approvals in those countries in 2022. At the end of 2021, there were seven active markets contributing to Voxzogo sales.
- Today, the Company announced an update from the Phase 2 randomized, double-blind, placebo-controlled Voxzogo study in infants and

young children up to five years of age with achondroplasia. 52-week results trended in favor of Voxzogo compared to placebo on height Z-score, annualized growth velocity, with no worsening in proportionality in the overall study population. Height Z-score measures height adjusted for age and sex. The safety profile was generally consistent with older subjects from the Phase 3 Voxzogo 301 study and current label population. Serious Adverse Events (SAEs) were higher in the placebo group (18%) compared to Voxzogo treated children (7%). All SAEs, including a fatal event of SIDS in the treatment group, were deemed by the investigators to be unrelated to treatment. A small increase in events of sleep apnea were reported in the treatment group that were mild or moderate in severity and did not require treatment discontinuation. These events will be fully assessed when sleep study and MRI data are available. BioMarin intends to initiate discussions with regulatory health authorities to discuss next steps regarding efforts to expand access to Voxzogo treatment for this younger age group.

- The European Medicines Agency (EMA) validated BioMarin's Marketing Authorization Applications (MAA) for valoctocogene roxaparvovec resulting in an anticipated Committee for Medicinal Products for Human Use (CHMP) opinion in the second quarter of 2022. BioMarin has provided the EMA with two-year follow-up safety and efficacy data from the GENEr8-1 study.
- Based on the favorable results from the two-year follow-up safety and efficacy data from the GENEr8-1 study, BioMarin is targeting a Biologics License Application (BLA) resubmission for valoctocogene roxaparvovec in the second quarter of 2022. If the resubmission satisfies FDA's response to the Complete Response Letter received in August 2020, BioMarin expects resubmission will be followed by a 6-month review procedure by the FDA.

Earlier-stage Development Portfolio (BMN 307, BMN 255, BMN 331, BMN 351, BMN 349, DiNA-001)

- BMN 307 gene therapy product candidate for PKU: In September 2021, the FDA placed a clinical hold on PHEarless, the Phase 1/2 study evaluating BMN 307, an investigational AAV5-phenylalanine hydroxylase (PAH) gene therapy, in adults with phenylketonuria (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. In February 2022, the FDA requested data from additional non-clinical studies to assess theoretical oncogenic risk to human study participants, which is expected to take several quarters. The Company will communicate next steps for the program when available.
- BMN 255 for primary hyperoxaluria type 1, a subset of chronic renal disease: The Investigational New Drug application (IND) for BMN 255 is active and the Company is dosing subjects with dose selection for advanced studies expected in the second half of 2022. BioMarin believes 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 gene therapy product candidate for Hereditary Angioedema (HAE): The Company announced that its Phase 1/2 HAERMONY study to evaluate BMN 331, an investigational AAV5-mediated gene therapy for people living with hereditary angioedema (HAE), is open for enrollment. In addition, the FDA granted Orphan Disease Designation status to BMN 331.
- BMN 351 for Duchenne Muscular Dystrophy (DMD): IND-enabling studies continue with BMN 351, an antisense oligonucleotide therapy for individuals with 51-skip-amenable DMD. 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. BioMarin expects to file an IND for BMN 351 in the first half of 2022, and anticipates treating clinical trial participants with Duchenne muscular dystrophy in the fourth quarter of 2022.
- BMN 349 for alpha-1 antitrypsin deficiency: Preclinical studies have demonstrated that BMN 349 is an orally bioavailable, small molecule that is titratable with rapid onset and high potency and efficacy. Preclinical results have strong implications for potential improvement of current management, particularly around burden of treatment, particularly for severe cases requiring rapid action. BioMarin's goal is to file the IND in the second half of 2023.
- DiNA-001 for MYBPC3 hypertrophic cardiomyopathy (HCM): Preclinical studies are underway with DiNA-001 following a collaboration announced in 2020 with DiNAQOR, a gene therapy platform company, to develop novel gene therapies to treat rare genetic cardiomyopathies. Mutations in MYBPC3 are the most common cause of inherited HCM. Early investigations suggest that gene therapy-mediated gene transfer can lead to widespread expression of the gene product, cardiac myosin-binding protein C (MyBP-C), in cardiac tissue, which can normalize relaxation kinetics and potentially ameliorate the disease phenotype in individuals suffering from cardiomyopathy. BioMarin's goal is to file the IND in 2023.

2022 Full-Year Financial Guidance (in millions, except %)

Item	2022 Guidance		
Total Revenues	$2,050	to	$2,150
Vimizim Net Product Revenues	$650	to	$700
Naglazyme Net Product Revenues	$400	to	$440
Palynziq Net Product Revenues	$280	to	$310
Kuvan Net Product Revenues	$225	to	$250
Brineura Net Product Revenues	$145	to	$160

Voxzogo Net Product Revenues	$90	to	$115
Cost of Sales (% of Total Revenues)	23%	to	25%
Research and Development Expense	$665	to	$715
Selling, General and Administrative Expense	$790	to	$840
GAAP Net Income	$95	to	$135
Non-GAAP Income [(1)]	$350	to	$390

(1) All Financial Guidance items are calculated based on U.S. GAAP with the exception of Non-GAAP Income. Refer to Non-GAAP Information beginning on page 11 of this press release for a complete discussion of the Company's Non-GAAP financial information and reconciliations to the corresponding GAAP reported information.

BioMarin will host a conference call and webcast to discuss fourth quarter and year to date 2021 financial results today, Wednesday, February 23, 2022 at 4:30 p.m. ET. This event can be accessed on the investor section of the BioMarin website at www.biomarin.com.

U.S./Canada Dial-in Number: 866.502.9859	Replay Dial-in Number: 855.859.2056
International Dial-in Number: 574.990.1362	Replay International Dial-in Number: 404.537.3406
Conference ID: 6284849	Conference ID: 6284849

About BioMarin

BioMarin 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 seven commercial products and multiple clinical and preclinical product candidates for the treatment of various diseases.

For additional information, please visit www.biomarin.com.

Forward-Looking Statements

This press release and the associated conference call and webcast contain forward-looking statements about the business prospects of BioMarin Pharmaceutical Inc. (BioMarin), including, without limitation, statements about: the expectations of Total Revenues, Net Product Revenues, Research and Development Expense, Selling, General and Administrative Expense, Cost of Sales, GAAP Net Loss, Non-GAAP Income, and other specified income statement guidance for the full-year 2022; cash flows from operating activities; the timing of orders for commercial products; the timing of BioMarin's clinical development and commercial prospects, including announcements of data from clinical studies and trials; the clinical development and commercialization of BioMarin's product candidates and commercial products, including (i) BioMarin's plans to re-submit a BLA for valoctocogene roxaparvovec to the FDA with two-year follow-up results from all the subjects from the Phase 3 GENEr8-1 study in the second quarter of 2022, (ii) BioMarin's anticipated IND submission for BMN 351 in the first half of 2022, (iii) BioMarin's anticipated IND submission for BMN 349 in the second half of 2023, (iv) BioMarin's collaboration with DiNAQOR to create gene therapies including BioMarin's goal to file an IND for DiNA-001 in 2023, (v) BioMarin's plans to initiate discussions with regulatory health authorities to discuss next steps regarding efforts to expand access to Voxzogo for infants and young children up to five years of age with achondroplasia and (vi) the status of the clinical hold and potential further clinical development of BMN 307; the potential approval and commercialization of BioMarin's product candidates, including Voxzogo for the treatment of achondroplasia and valoctocogene roxaparvovec for the treatment of severe hemophilia A and the timing of such approval decisions, including (i) the potential approval of Voxzogo in Japan and Australia in 2022, (ii) the BLA resubmission for valoctocogene roxaparvovec and the expectation of a CHMP opinion on our MAA for valoctocogene roxaparvovec, each in the second quarter of 2022, and (iii) the duration of the FDA's review procedure of our BLA resubmission for valoctocogene roxaparvovec if the resubmission satisfies FDA's response to the Complete Response Letter received in August 2020; and the expected benefits and availability of BioMarin's product candidates; and potential growth opportunities and trends, including that BioMarin expects (i) double-digit growth in revenues and profitability in 2022, (ii) increasing access to Voxzogo as the product launch continues in future quarters, (iii) the commercial launch of Palynziq in BioMarin's EMEA region to continue to progress through individual country level pricing and reimbursement negotiations, and (iv) 2022 to be a transformational year for BioMarin.

These forward-looking statements are predictions and involve risks and uncertainties such that actual results may differ materially from these statements. These risks and uncertainties include, among others: BioMarin's success in the commercialization of its commercial products, including BioMarin's projected impact of the COVID-19 pandemic on its global revenue sources, including due to demand interruptions such as missed patient infusions and delayed treatment starts for new patients; results and timing of current and planned preclinical studies and clinical trials, as well as the potential impact of the COVID-19 pandemic on (i) BioMarin's ability to continue such preclinical studies and clinical trials and (ii) the timing of such preclinical studies and clinical trials, and the release of data from those trials; BioMarin's ability to successfully manufacture its commercial products and product candidates; the content and timing of decisions by the FDA, the European Commission and other regulatory authorities concerning each of the described products and product candidates, including the potential impact of the COVID-19

pandemic on the regulatory authorities' abilities to issue such decisions and the timing of such decisions; the market for each of these products; actual sales of BioMarin's commercial products and the impact that the COVID-19 pandemic may have on such sales; the introduction of generic versions of BioMarin's commercial products, in particular generic versions of Kuvan; and those factors detailed in BioMarin's filings with the Securities and Exchange Commission (SEC), including, without limitation, the factors contained under the caption "Risk Factors" in BioMarin's Quarterly Report on Form 10-Q for the quarter ended September 30, 2021 as such factors may be updated by any subsequent reports. Stockholders are urged not to place undue reliance on forward-looking statements, which speak only as of the date hereof. BioMarin is under no obligation, and expressly disclaims any obligation to update or alter any forward-looking statement, whether as a result of new information, future events or otherwise.

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED BALANCE SHEETS
December 31, 2021 and December 31, 2020
(In thousands of U.S. dollars, except per share amounts)

	December 31, 2021	December 31, 2020(1)
ASSETS	(unaudited)	
Current assets:		
Cash and cash equivalents	$ 587,276	$ 649,158
Short-term investments	426,599	416,228
Accounts receivable, net	373,399	448,351
Inventory	776,669	698,548
Other current assets	110,442	129,934
Total current assets	2,274,385	2,342,219
Noncurrent assets:		
Long-term investments	507,793	285,473
Property, plant and equipment, net	1,035,461	1,032,471
Intangible assets, net	388,652	417,271
Goodwill	196,199	196,199
Deferred tax assets	1,449,075	1,432,150
Other assets	151,760	142,237
Total assets	$ 6,003,325	$ 5,848,020
LIABILITIES AND STOCKHOLDERS' EQUITY		
Current liabilities:		
Accounts payable and accrued liabilities	$ 491,590	$ 492,548
Short-term contingent consideration	48,232	—
Total current liabilities	539,822	492,548
Noncurrent liabilities:		
Long-term convertible debt, net	1,079,077	1,075,145
Long-term contingent consideration	15,167	60,130
Other long-term liabilities	98,519	114,195
Total liabilities	$ 1,732,585	$ 1,742,018
Stockholders' equity:		
Common stock, $0.001 par value: 500,000,000 shares authorized; 183,912,514 and 181,740,999 shares issued and outstanding, respectively	184	182
Additional paid-in capital	5,191,502	4,993,407
Company common stock held by Nonqualified Deferred Compensation Plan	(9,689)	(9,839)
Accumulated other comprehensive income (loss)	14,432	(16,139)
Accumulated deficit	(925,689)	(861,609)

Total stockholders' equity	4,270,740	4,106,002
Total liabilities and stockholders' equity	$ 6,003,325	$ 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 U.S. Securities and Exchange Commission (SEC) on February 26, 2021.

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS
Three and Twelve Months Ended December 31, 2021 and 2020
(In thousands of U.S. dollars, except per share amounts)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	**2020**	**2021**	**2020**
	(unaudited)	(unaudited)	(unaudited)	
REVENUES:				
Net product revenues	$ 435,219	$ 437,045	$ 1,783,498	$ 1,805,861
Royalty and other revenues	14,591	15,072	62,777	54,594
Total revenues	449,810	452,117	1,846,275	1,860,455
OPERATING EXPENSES:				
Cost of sales	119,750	126,138	470,515	524,272
Research and development	161,092	156,667	628,793	628,116
Selling, general and administrative	217,563	195,512	759,375	737,669
Intangible asset amortization and contingent consideration	17,285	18,640	69,933	66,658
Gain on sale of nonfinancial assets	—	—	—	(59,495)
Total operating expenses	515,690	496,957	1,928,616	1,897,220
LOSS FROM OPERATIONS	(65,880)	(44,840)	(82,341)	(36,765)
Interest income	1,745	3,071	10,482	16,610
Interest expense	(3,846)	(4,749)	(15,337)	(29,309)
Other income, net	1,407	6,333	11,846	7,142
LOSS BEFORE INCOME TAXES	(66,574)	(40,185)	(75,350)	(42,322)
Benefit from income taxes	(8,676)	(62,284)	(11,270)	(901,422)
NET INCOME (LOSS)	$ (57,898)	$ 22,099	$ (64,080)	$ 859,100
NET INCOME (LOSS) PER SHARE, BASIC	$ (0.32)	$ 0.12	$ (0.35)	$ 4.75
NET INCOME (LOSS) PER SHARE, DILUTED	$ (0.32)	$ 0.12	$ (0.35)	$ 4.53
Weighted average common shares outstanding, basic	183,554	181,435	182,852	180,804
Weighted average common shares outstanding, diluted	183,554	184,476	182,852	191,678

BIOMARIN PHARMACEUTICAL INC.
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
Twelve Months Ended December 31, 2021 and 2020
(In thousands of U.S. dollars)

	Twelve Months Ended December 31,	
	2021	**2020**
	(unaudited)	
CASH FLOWS FROM OPERATING ACTIVITIES:		

Net income (loss)	$ (64,080)	$ 859,100
Adjustments to reconcile net income (loss) to net cash used in operating activities:		
Depreciation and amortization	108,039	105,172
Non-cash interest expense	4,146	16,511
Amortization of premium on investments	5,155	567
Stock-based compensation expense	197,263	189,711
Gain on sale of nonfinancial assets	—	(59,495)
Inventory reserves, net of stock-based compensation	—	75,609
Deferred income taxes	(15,608)	(888,907)
Unrealized foreign exchange loss (gain)	(1,810)	8,011
Non-cash changes in the fair value of contingent consideration	8,026	4,500
Other	(2,629)	(997)
Changes in operating assets and liabilities:		
Accounts receivable, net	65,574	(59,035)
Inventory	(35,060)	(61,151)
Other current assets	29,760	18,312
Other assets	(6,593)	(28,647)
Accounts payable and accrued liabilities	15,689	(87,025)
Other long-term liabilities	(3,336)	(6,871)
Net cash provided by operating activities	304,536	85,365
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property, plant and equipment	(95,578)	(114,312)
Maturities and sales of investments	691,049	555,834
Purchase of available-for-sale debt securities	(937,143)	(529,663)
Proceeds from sale of nonfinancial assets	—	67,159
Purchase of intangible assets	(23,647)	(23,207)
Investment in convertible note	—	(8,709)
Other	(994)	(723)
Net cash used in investing activities	(366,313)	(53,621)
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from exercises of awards under equity incentive plans	49,194	71,913
Taxes paid related to net share settlement of equity awards	(45,805)	(44,638)
Repurchase of common stock	—	(50,000)
Proceeds from convertible senior subordinated note offering, net	—	585,752
Repayments of convertible debt	—	(374,991)
Principal repayments of financing leases	(3,039)	(6,918)
Other	(398)	—
Net cash provided by (used in) financing activities	(48)	181,118
Effect of exchange rate changes on cash	(57)	(1,150)
NET INCREASE (DECREASE) IN CASH AND CASH EQUIVALENTS	$ (61,882)	$ 211,712
Cash and cash equivalents:		
Beginning of period	$ 649,158	$ 437,446
End of period	$ 587,276	$ 649,158

The following table presents Net Product Revenues by Product:

Net Product Revenues by Product
(In millions of U.S. dollars)

	Three Months Ended	**Twelve Months Ended**

	December 31,			December 31,		
	2021	2020	% Change	2021	2020	% Change
	(unaudited)	(unaudited)		(unaudited)	(unaudited)	
Vimizim	$ 156.3	$ 142.5	10%	$ 623.1	$ 544.4	14%
Naglazyme	83.1	119.7	(31)%	380.4	391.3	(3)%
Kuvan	68.5	89.0	(23)%	285.8	457.7	(38)%
Palynziq	63.8	49.6	29%	237.5	171.0	39%
Brineura	37.4	35.0	7%	128.0	110.2	16%
Voxzogo	5.8	—	n/a	5.9	—	n/a
Firdapse [1]	—	—	—%	—	1.2	(100)%
Net Product Revenues Marketed by BioMarin	$ 414.9	$ 435.8		$ 1,660.7	$ 1,675.8	
Aldurazyme Net Product Revenues Marketed by Sanofi	20.3	1.2	1592%	122.8	130.1	(6)%
Total Net Product Revenues	$ 435.2	$ 437.0		$ 1,783.5	$ 1,805.9	

(1) In January 2020, BioMarin divested the Firdapse assets to a third party in a sale transaction. The sale is reflected in the Company's consolidated financial statements for the twelve months ended December 31, 2020; and as a result of the transaction BioMarin no longer generates Net Product Revenues from Firdapse.

Non-GAAP Information

The results presented in this press release include both GAAP information and Non-GAAP information. As used in this release, Non-GAAP Income is defined by the Company as GAAP Net Income/Loss excluding net interest expense, provision for income taxes, depreciation expense, amortization expense, stock-based compensation expense, contingent consideration expense and, in certain periods, certain other specified items, as detailed below when applicable. In addition, BioMarin includes in this press release the effects of these adjustments on certain components of GAAP Net Income/Loss for each of the periods presented. In this regard, Non-GAAP Income and its components, including Non-GAAP Cost of Sales, Non-GAAP Research and Development expenses, Non-GAAP Selling, General and Administrative expense, Non-GAAP Intangible Asset Amortization and Contingent Consideration, Non-GAAP Gain on the Sale of Intangible Asset and Non-GAAP Benefit From Income Taxes are statement of operations line items prepared on the same basis as, and therefore components of, the overall Non-GAAP measures.

BioMarin regularly uses both GAAP and Non-GAAP results and expectations internally to assess its financial operating performance and evaluate key business decisions related to its principal business activities: the discovery, development, manufacture, marketing and sale of innovative biologic therapies. Because Non-GAAP Income and its components are important internal measurements for BioMarin, the Company believes that providing this information in conjunction with BioMarin's GAAP information enhances investors' and analysts' ability to meaningfully compare the Company's results from period to period and to its forward-looking guidance, and to identify operating trends in the Company's principal business. BioMarin also uses Non-GAAP Income internally to understand, manage and evaluate its business and to make operating decisions, and compensation of executives is based in part on this measure.

Non-GAAP Income and its components are not meant to be considered in isolation, as a substitute for, or superior to comparable GAAP measures and should be read in conjunction with the consolidated financial information prepared in accordance with GAAP. Investors should note that the Non-GAAP information is not prepared under any comprehensive set of accounting rules or principles and does not reflect all of the amounts associated with the Company's results of operations as determined in accordance with GAAP. Investors should also note that these Non-GAAP measures have no standardized meaning prescribed by GAAP and, therefore, have limits in their usefulness to investors. In addition, from time to time in the future there may be other items that the Company may exclude for purposes of its Non-GAAP measures; likewise, the Company may in the future cease to exclude items that it has historically excluded for purposes of its Non-GAAP measures. Because of the non-standardized definitions, the Non-GAAP measure as used by BioMarin in this press release and the accompanying tables may be calculated differently from, and therefore may not be directly comparable to, similarly titled measures used by other companies.

The following table presents the reconciliation of GAAP Net Income (Loss) to Non-GAAP Income:

Reconciliation of GAAP Net Income (Loss) to Non-GAAP Income
(In millions of U.S. dollars)
(unaudited)

Three Months Ended December 31,		Twelve Months Ended December 31,		Guidance [3] Year Ending
2021	2020	2021	2020	December 31, 2022

GAAP Net Income (Loss)	**$ (57.9)**	**$ 22.1**	**$ (64.1)**	**$ 859.1**	**$ 95.0 — $ 135.0**	
Interest expense, net	2.1	1.7	4.9	12.7		9.0
Benefit from income taxes	(8.7)	(62.3)	(11.3)	(901.4)		47.0
Depreciation expense	10.4	11.9	46.1	43.0		44.0
Amortization expense	15.6	15.4	61.9	62.2		63.0
Stock-based compensation expense	43.9	47.5	197.3	189.7		195.0
Contingent consideration expense	1.7	3.2	8.0	4.5		5.0
Gain on sale of nonfinancial assets	—	—	—	(59.5)		(108.0)
Provision for inventory reserve, net [1]	—	—	—	75.6		—
Licensed In-Process R&D [2]	—	—	—	26.3		—
Non-GAAP Income	$ 7.1	$ 39.5	$ 242.8	$ 312.2	$ 350.0 — $ 390.0	

(1) Represents a $81.2 million charge related to pre-launch valoctocogene roxaparvovec inventory, net of stock-based compensation, as a result of the unexpected delays in anticipated regulatory approvals.

(2) Represents the upfront license fee paid to a third party and recognized as R&D expense in the second quarter of 2020.

(3) The adjustments/reconciling items included in the Guidance Year Ending December 31, 2022 column are presented to facilitate the reconciliation of Non-GAAP Income to its closest GAAP financial metric, GAAP Net Income (Loss). The Company notes that the specific amounts included in each reconciling line item above represent approximations of the underlying adjustments from GAAP Net Income (Loss) to Non-GAAP Income, and that actual 2022 results for each reconciling line item may be different, in some cases materially, than the amounts listed above as a result of uncertainty regarding, and the potential variability of, those items.

The following reconciliation of the GAAP reported to the Non-GAAP information provides the details of the effects of the Non-GAAP adjustments on certain components of the Company's operating results for each of the periods presented.

Reconciliation of Certain GAAP Reported Information to Non-GAAP Information
(In millions of U.S. dollars)
(unaudited)

	Three months ended December 31,							
	2021				**2020**			
		Adjustments				**Adjustments**		
	GAAP Reported	**Interest, Taxes, Depreciation and Amortization**	**Stock-Based Compensation, Contingent Consideration and Other Adjustments**	**Non-GAAP**	**GAAP Reported**	**Interest, Taxes, Depreciation and Amortization**	**Stock-Based Compensation, Contingent Consideration and Other Adjustments**	
Cost of sales	**$ 119.8**	$ —	$ (5.5)	$ 114.3	**$ 126.1**	$ —	$ (5.9)	
Research and development	**161.1**	(6.1)	(11.0)	144.0	**156.7**	(6.7)	(16.5)	
Selling, general and administrative	**217.6**	(4.3)	(27.4)	185.9	**195.5**	(5.2)	(25.1)	
Intangible asset amortization and contingent consideration	**17.3**	(15.6)	(1.7)	—	**18.6**	(15.4)	(3.2)	
Interest expense, net	**(2.1)**	2.1	—	—	**(1.7)**	1.7	—	
Benefit from income taxes	**(8.7)**	8.7	—	—	**(62.3)**	62.3	—	
GAAP Net Income (Loss) / Non-GAAP Income	**$ (57.9)**	$ 19.4	$ 45.6	$ 7.1	**$ 22.1**	$ (33.3)	$ 50.7	

	Twelve months ended December 31,							
	2021				2020			
		Adjustments				Adjustments		
	GAAP Reported	Interest, Taxes, Depreciation and Amortization	Stock-Based Compensation, Contingent Consideration and Other Adjustments	Non-GAAP	GAAP Reported	Interest, Taxes, Depreciation and Amortization	Stock-Based Compensation, Contingent Consideration and Other Adjustments
Cost of sales	**$ 470.5**	$ —	$ (22.4)	$ 448.1	**$ 524.3**	$ —	$ (101.9)
Research and development	**628.8**	(27.0)	(67.2)	534.6	**628.1**	(21.9)	(88.2)
Selling, general and administrative	**759.4**	(19.1)	(107.7)	632.6	**737.7**	(21.1)	(101.5)
Intangible asset amortization and contingent consideration	**69.9**	(61.9)	(8.0)	—	**66.7**	(62.2)	(4.5)
Gain on sale of nonfinancial assets	**—**	—	—	—	**(59.5)**	—	59.5
Interest expense, net	**(4.9)**	4.9	—	—	**(12.7)**	12.7	—
Benefit from income taxes	**(11.3)**	11.3	—	—	**(901.4)**	901.4	—
GAAP Net Income (Loss) / Non-GAAP Income	**$ (64.1)**	$ 101.6	$ 205.3	$ 242.8	**$ 859.1**	$ (783.5)	$ 236.6

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