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 March 31, 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 001-35238

HORIZON THERAPEUTICS PUBLIC LIMITED COMPANY

(Exact name of registrant as specified in its charter)

Ireland	**Not Applicable**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
Connaught House, 1st Floor 1 Burlington Road, Dublin 4, D04 C5Y6, Ireland	**Not Applicable**
(Address of principal executive offices)	**(Zip Code)**

011 353 1 772 2100
(Registrant's telephone number, including area code)

Not applicable
(Former name, former address and former fiscal year, if changed since last report)

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

Title of each class	Trading Symbol	Name of each exchange on which registered
Ordinary shares, nominal value $0.0001 per share	HZNP	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, smaller reporting company, or an emerging growth company. See the definitions of ''large accelerated filer,'' ''accelerated filer,'' ''smaller reporting company,'' and ''emerging growth company'' in Rule 12b–2 of the Exchange Act.

Large accelerated filer	☒	Accelerated filer	☐
Non-accelerated filer	☐	Smaller reporting company	☐
Emerging growth company	☐		

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

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

Number of registrant's ordinary shares, nominal value $0.0001, outstanding as of April 29, 2021: 224,768,551.

HORIZON THERAPEUTICS PLC

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

HORIZON THERAPEUTICS PLC
CONDENSED CONSOLIDATED BALANCE SHEETS
(UNAUDITED)
(In thousands, except nominal value and share data)

	As of March 31, 2021	As of December 31, 2020
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 811,609	$ 2,079,906
Restricted cash	3,839	3,573
Accounts receivable, net	443,172	659,701
Inventories, net	238,306	75,283
Prepaid expenses and other current assets	334,442	251,945
Total current assets	**1,831,368**	**3,070,408**
Property and equipment, net	201,857	189,037
Developed technology and other intangible assets, net	3,210,221	1,782,962
In-process research and development	880,000	—
Goodwill	1,076,388	413,669
Deferred tax assets, net	589,618	560,841
Other assets	57,158	55,699
Total assets	**$ 7,846,610**	**$ 6,072,616**
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 42,986	$ 37,710
Accrued expenses	389,626	485,567
Accrued trade discounts and rebates	325,232	352,463
Long-term debt—current portion	16,000	—
Total current liabilities	**773,844**	**875,740**
LONG-TERM LIABILITIES:		
Long-term debt, net	2,562,517	1,003,379
Deferred tax liabilities, net	524,407	66,474
Other long-term liabilities	131,072	101,672
Total long-term liabilities	**3,217,996**	**1,171,525**
COMMITMENTS AND CONTINGENCIES		
SHAREHOLDERS' EQUITY:		
Ordinary shares, $0.0001 nominal value; 600,000,000 shares authorized at March 31, 2021 and December 31, 2020; 225,027,621 and 221,721,674 shares issued at March 31, 2021 and December 31, 2020, respectively; and 224,643,255 and 221,337,308 shares outstanding at March 31, 2021 and December 31, 2020, respectively	22	22
Treasury stock, 384,366 ordinary shares at March 31, 2021 and December 31, 2020	(4,585)	(4,585)
Additional paid-in capital	4,199,823	4,245,945
Accumulated other comprehensive loss	(1,253)	(145)
Accumulated deficit	(339,237)	(215,886)
Total shareholders' equity	**3,854,770**	**4,025,351**
Total liabilities and shareholders' equity	**$ 7,846,610**	**$ 6,072,616**

The accompanying notes are an integral part of these condensed consolidated financial statements.

HORIZON THERAPEUTICS PLC
CONDENSED CONSOLIDATED STATEMENTS OF COMPREHENSIVE LOSS
(UNAUDITED)
(In thousands, except share and per share data)

	For the Three Months Ended March 31,	
	2021	**2020**
Net sales	$ 342,406	$ 355,909
Cost of goods sold	100,368	97,416
Gross profit	**242,038**	**258,493**
OPERATING EXPENSES:		
Research and development	57,693	27,209
Selling, general and administrative	331,992	247,775
Impairment of long-lived assets	12,371	—
Total operating expenses	**402,056**	**274,984**
Operating loss	**(160,018)**	**(16,491)**
OTHER EXPENSE, NET:		
Interest expense, net	(13,460)	(17,344)
Foreign exchange (loss) gain	(848)	776
Other income, net	3,224	442
Total other expense, net	**(11,084)**	**(16,126)**
Loss before benefit for income taxes	**(171,102)**	**(32,617)**
Benefit for income taxes	(47,751)	(19,026)
Net loss	**$ (123,351)**	**$ (13,591)**
Net loss per ordinary share—basic and diluted	$ (0.55)	$ (0.07)
Weighted average ordinary shares outstanding—basic and diluted	223,920,768	190,072,112
OTHER COMPREHENSIVE LOSS, NET OF TAX		
Foreign currency translation adjustments	$ (821)	$ (325)
Pension remeasurements	(287)	—
Other comprehensive loss	**(1,108)**	**(325)**
Comprehensive loss	**$ (124,459)**	**$ (13,916)**

The accompanying notes are an integral part of these condensed consolidated financial statements.

HORIZON THERAPEUTICS PLC
CONDENSED CONSOLIDATED STATEMENTS OF SHAREHOLDERS' EQUITY
(UNAUDITED)
(In thousands, except share data)

	Ordinary Shares		Treasury Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Shareholders'
	Shares	Amount	Shares	Amount	Capital	Loss	Deficit	Equity
Balances at December 31, 2020	**221,721,674**	**$ 22**	**384,366**	**$ (4,585)**	**$ 4,245,945**	**$ (145)**	**$ (215,886)**	**$ 4,025,351**
Issuance of ordinary shares in conjunction with the exercise of stock options and the vesting of restricted stock and performance stock units	3,305,947	—	—	—	19,843	—	—	19,843
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(128,261)	—	—	(128,261)
Share-based compensation	—	—	—	—	62,296	—	—	62,296
Currency translation adjustment	—	—	—	—	—	(821)	—	(821)
Pension remeasurements	—	—	—	—	—	(287)	—	(287)
Net loss	—	—	—	—	—	—	(123,351)	(123,351)
Balances at March 31, 2021	**225,027,621**	**$ 22**	**384,366**	**$ (4,585)**	**$ 4,199,823**	**$ (1,253)**	**$ (339,237)**	**$ 3,854,770**

	Ordinary Shares		Treasury Stock		Additional Paid-in	Accumulated Other Comprehensive	Accumulated	Total Shareholders'
	Shares	Amount	Shares	Amount	Capital	Loss	Deficit	Equity
Balances at December 31, 2019	**188,402,040**	**$ 19**	**384,366**	**$ (4,585)**	**$ 2,797,602**	**$ (1,905)**	**$ (605,682)**	**$ 2,185,449**
Issuance of ordinary shares in conjunction with vesting of restricted stock units, performance stock units and stock option exercises	2,560,573	—	—	—	7,049	—	—	7,049
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(46,664)	—	—	(46,664)
Share-based compensation	—	—	—	—	56,421	—	—	56,421
Currency translation adjustment	—	—	—	—	—	(325)	—	(325)
Net loss	—	—	—	—	—	—	(13,591)	(13,591)
Balances at March 31, 2020	**190,962,613**	**$ 19**	**384,366**	**$ (4,585)**	**$ 2,814,408**	**$ (2,230)**	**$ (619,273)**	**$ 2,188,339**

The accompanying notes are an integral part of these condensed consolidated financial statements.

HORIZON THERAPEUTICS PLC
CONDENSED CONSOLIDATED STATEMENTS OF CASH FLOWS
(UNAUDITED)
(In thousands)

	For the Three Months Ended March 31,	
	2021	2020
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (123,351)	$ (13,591)
Adjustments to reconcile net loss to net cash used in operating activities:		
Depreciation and amortization expense	70,820	65,741
Equity-settled share-based compensation	61,166	56,421
Impairment of long-lived assets	12,371	—
Amortization of debt discount and deferred financing costs	773	5,569
Deferred income taxes	(28,771)	(2,082)
Foreign exchange and other adjustments	(5,440)	(190)
Changes in operating assets and liabilities:		
Accounts receivable	224,575	(16,869)
Inventories	(13,660)	(14,444)
Prepaid expenses and other current assets	(65,575)	(24,953)
Accounts payable	993	28,551
Accrued trade discounts and rebates	(28,736)	(129,940)
Accrued expenses	(111,963)	(28,087)
Other non-current assets and liabilities	3,070	11,281
Net cash used in operating activities	**(3,728)**	**(62,593)**
CASH FLOWS FROM INVESTING ACTIVITIES:		
Payments for acquisition, net of cash acquired	(2,707,358)	(105,200)
Purchases of property and equipment	(18,333)	(119,004)
Payments for long-term investments, net	(3,808)	—
Change in escrow deposit for property purchase	—	6,000
Net cash used in investing activities	**(2,729,499)**	**(218,204)**
CASH FLOWS FROM FINANCING ACTIVITIES:		
Net proceeds from term loans	1,577,612	—
Proceeds from the issuance of ordinary shares in connection with stock option exercises	19,843	7,050
Payment of employee withholding taxes relating to share-based awards	(128,261)	(46,664)
Net cash provided by (used in) financing activities	**1,469,194**	**(39,614)**
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	(3,998)	(1,366)
Net decrease in cash, cash equivalents and restricted cash	**(1,268,031)**	**(321,777)**
Cash, cash equivalents and restricted cash, beginning of the period	2,083,479	1,080,039
Cash, cash equivalents and restricted cash, end of the period	**$ 815,448**	**$ 758,262**
SUPPLEMENTAL CASH FLOW INFORMATION:		
Cash paid for interest	$ 18,988	$ 26,636
Cash paid for income taxes, net of refunds received	1,201	266
Cash paid for amounts included in the measurement of lease liabilities	2,084	1,812
SUPPLEMENTAL NON-CASH FLOW INFORMATION:		
Milestone payments for TEPEZZA intangible asset included in accrued expenses as of March 31, 2021 and March 31, 2020, respectively	$ 69,962	$ —
Purchases of property and equipment included in accounts payable and accrued expenses as of March 31, 2021 and March 31, 2020, respectively	10,523	539

The accompanying notes are an integral part of these condensed consolidated financial statements.

NOTE 1 – BASIS OF PRESENTATION AND BUSINESS OVERVIEW

Basis of Presentation

Unless otherwise indicated or the context otherwise requires, references to "Horizon", the "Company", "we", "us" and "our" refer to Horizon Therapeutics plc and its consolidated subsidiaries.

On March 15, 2021, the Company completed its acquisition of Viela Bio, Inc. ("Viela") and acquired all of the issued and outstanding shares of Viela's common stock for $53.00 per share. The total consideration for the acquisition was approximately $3.0 billion, including cash acquired of $342.3 million. Following the completion of the acquisition, Viela became a wholly-owned subsidiary of the Company. The unaudited condensed consolidated financial statements presented herein include the results of operations of the acquired business from the date of acquisition.

The unaudited condensed consolidated financial statements presented herein have been prepared in accordance with accounting principles generally accepted in the United States ("GAAP") for interim financial information and in accordance with the instructions to Form 10-Q and Article 10 of Regulation S-X. Accordingly, the financial statements do not include all of the information and notes required by GAAP for complete financial statements. In the opinion of management, all adjustments, including normal recurring adjustments, considered necessary for a fair statement of the financial statements have been included. Operating results for the three months ended March 31, 2021 are not necessarily indicative of the results that may be expected for the year ending December 31, 2021. The December 31, 2020 condensed consolidated balance sheet was derived from audited financial statements, but does not include all disclosures required by GAAP.

Business Overview

Horizon is focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare, autoimmune and serious inflammatory diseases. The Company's pipeline is purposeful: it applies scientific expertise and courage to bring clinically meaningful therapies to patients. Horizon believes science and compassion must work together to transform lives. The Company has two reportable segments, the orphan segment and the inflammation segment, and its portfolio is currently composed of 12 medicines in the areas of rare diseases, gout, ophthalmology and inflammation.

The Viela acquisition expanded the Company's marketed medicine portfolio by adding an additional rare disease medicine, UPLIZNA®.

As of March 31, 2021, the Company's marketed medicines consisted of the following:

Orphan
TEPEZZA® (teprotumumab-trbw), for intravenous infusion
KRYSTEXXA® (pegloticase injection), for intravenous infusion
RAVICTI® (glycerol phenylbutyrate) oral liquid
PROCYSBI® (cysteamine bitartrate) delayed-release capsules and granules, for oral use
ACTIMMUNE® (interferon gamma-1b) injection, for subcutaneous use
BUPHENYL® (sodium phenylbutyrate) tablets and powder, for oral use
QUINSAIR™ (levofloxacin) solution for inhalation
UPLIZNA (inebilizumab-cdon) injection, for intravenous use
Inflammation
PENNSAID® (diclofenac sodium topical solution) 2% w/w ("PENNSAID 2%"), for topical use
DUEXIS® (ibuprofen/famotidine) tablets, for oral use
RAYOS® (prednisone) delayed-release tablets, for oral use
VIMOVO® (naproxen/esomeprazole magnesium) delayed-release tablets, for oral use

NOTE 2 – SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Recent Accounting Pronouncements

From time to time, the Company adopts new accounting pronouncements issued by the Financial Accounting Standards Board ("FASB") or other standard-setting bodies.

In December 2019, the FASB issued Accounting Standards Update No. 2019-12, *Income Taxes (Topic 740): Simplification and reduce the cost of accounting for income taxes* ("ASU 2019-12"), which was effective for the Company as of January 1, 2021. The adoption of ASU 2019-12 did not have a material impact on the Company's condensed consolidated financial statements and related disclosures.

Other recent authoritative guidance issued by the FASB (including technical corrections to the Accounting Standards Codification ("ASC")), the American Institute of Certified Public Accountants and the Securities and Exchange Commission ("SEC") did not, or are not expected to, have a material impact on the Company's condensed consolidated financial statements and related disclosures.

Significant Accounting Policies

The Company's significant accounting policies have not changed from those previously described in the Company's Annual Report on Form 10-K for the year ended December 31, 2020. The following accounting policy relating to intangible assets is disclosed in connection with the Viela acquisition.

Intangible Assets

Indefinite-lived intangible assets consist of capitalized in-process research and development ("IPR&D"). IPR&D assets represent capitalized incomplete research projects that the Company acquired through business combinations. Such assets are initially measured at their acquisition date fair values and are tested for impairment, until completion or abandonment of research and development efforts associated with the projects. An IPR&D asset is considered abandoned when research and development efforts associated with the asset have ceased, and there are no plans to sell or license the asset or derive value from the asset. At that point, the asset is considered to be impaired and is written off. Upon successful completion of each project, the Company will make a determination about the then remaining useful life of the intangible asset and begin amortization. The Company tests its indefinite-lived intangibles, including IPR&D assets, for impairment annually during the fourth quarter and more frequently if events or changes in circumstances indicate that it is more likely than not that the asset is impaired.

NOTE 3 – NET LOSS PER SHARE

The following table presents basic and diluted net loss per share for the three months ended March 31, 2021 and 2020 (in thousands, except share and per share data):

	For the Three Months Ended March 31,	
	2021	2020
Basic and diluted net loss per share calculation:		
Numerator - net loss	$ (123,351)	$ (13,591)
Denominator - weighted average of ordinary shares outstanding	223,920,768	190,072,112
Basic and diluted net loss per share	**$ (0.55)**	**$ (0.07)**

Basic net loss per share is computed by dividing net loss by the weighted-average number of ordinary shares outstanding during the period. Diluted net loss per share reflects the potential dilution that could occur if securities or other contracts to issue ordinary shares were exercised, converted into ordinary shares or resulted in the issuance of ordinary shares that would have shared in the Company's earnings.

The computation of diluted net loss per share for the three months ended March 31, 2021 excluded 13.4 million shares subject to equity awards because their inclusion would have had an anti-dilutive effect on diluted net loss per share.

The computation of diluted net loss per share for the three months ended March 31, 2020 excluded 9.3 million shares subject to equity awards and 14.0 million shares (based on the if-converted method) related to the Company's 2.50% Exchangeable Senior Notes due 2022 (the "Exchangeable Senior Notes") because their inclusion would have had an anti-dilutive effect on diluted net loss per share. On August 3, 2020, the Exchangeable Senior Notes were fully extinguished through exchanges for ordinary shares or cash redemption.

NOTE 4 – ACQUISITIONS, DIVESTITURES AND OTHER ARRANGEMENTS

Acquisition of Viela

On March 15, 2021, the Company completed its acquisition of Viela and acquired all of the issued and outstanding shares of Viela's common stock for $53.00 per share. The acquisition added an additional rare disease medicine, UPLIZNA, to the Company's medicine portfolio. The Viela acquisition provides multiple opportunities to drive long-term growth and solidify the Company's future as an innovation-driven biotech company. Viela's mid-stage biologics pipeline, research and development ("R&D") team and on-market medicine UPLIZNA, make it a complementary strategic fit with the Company's pipeline, commercial portfolio and therapeutic areas of focus. Following completion of the acquisition, Viela became a wholly-owned subsidiary of the Company. The Company financed the transaction through cash on hand and $1.6 billion of aggregate principal amount of term loans pursuant to Company's existing credit agreement, as described in Note 13.

The total consideration for the acquisition was approximately $3.0 billion, including cash acquired of $342.3 million, and was composed of the following (in thousands):

Equity value (54,988,820 shares at $53.00 per share)	$	2,914,407
Net settlements on the exercise of stock options		78,554
Consideration for exchange of Viela stock options		1,130
Total consideration	**$**	**2,994,091**

During the three months ended March 31, 2021, the Company incurred $28.0 million in Viela transaction costs, including advisory, legal, accounting, valuation and other professional and consulting fees, which were accounted for as "Selling, General and Administrative Expenses" in the condensed consolidated statement of comprehensive loss.

Pursuant to ASC 805, Business Combinations ("ASC 805"), the Company accounted for the Viela acquisition as a business combination using the acquisition method of accounting. Identifiable assets and liabilities of Viela, including identifiable intangible assets, were recorded based on their estimated fair values as of the date of the closing of the acquisition. The excess of the purchase price over the fair value of the net assets acquired was recorded as goodwill. The valuation of assets acquired and liabilities assumed has not yet been finalized as of March 31, 2021. While all amounts remain subject to adjustments, the areas subject to the most significant potential adjustments are inventory, intangible assets, IPR&D and deferred income taxes. As a result, the Company recorded preliminary estimates for the fair value of assets acquired and liabilities assumed as of the acquisition date. Such preliminary valuation required estimates and assumptions including, but not limited to, estimating future cash flows and direct costs in addition to developing the appropriate discount rates and current market profit margins. Accordingly, the purchase price adjustments are preliminary and are subject to further adjustments as additional information becomes available and as additional analyses are performed, and such further adjustments may be material. The Company's management believes the fair values recognized for the assets acquired and the liabilities assumed are based on reasonable estimates and assumptions.

The following table summarizes the preliminary fair values assigned to the assets acquired and the liabilities assumed by the Company along with the resulting goodwill (in thousands):

		Allocation
Deferred tax liabilities, net	$	(457,928)
Accrued expenses		(73,401)
Other long-term liabilities		(22,631)
Accounts payable		(4,768)
Accrued trade discounts and rebates		(1,492)
Marketable securities		400
Property, plant and equipment		1,747
Other assets		3,253
Accounts receivable		8,053
Prepaid expenses and other current assets		16,444
Inventories		149,348
Cash and cash equivalents		342,347
In-process research and development		910,000
Developed technology		1,460,000
(Liabilities assumed) and assets acquired		**2,331,372**
Goodwill		662,719
Fair value of consideration paid	**$**	**2,994,091**

Inventories acquired included raw materials, work in process and finished goods for UPLIZNA. Inventories were recorded at their preliminary estimated fair values. The fair value of finished goods has been determined based on the estimated selling price, net of selling costs and a margin on the selling activities. The fair value of work in process has been determined based on estimated selling price, net of selling costs and costs to complete the manufacturing, and a margin on the selling and manufacturing activities. The fair value of raw materials was estimated to equal the replacement cost. A step-up in the value of inventory of $149.3 million was recorded in connection with the acquisition, which was composed of $10.1 million for raw materials, $119.0 million for work-in-process and $20.2 million for finished goods. During the three months ended March 31, 2021, the Company recorded inventory step-up expense of $0.9 million related to UPLIZNA based on the acquired units sold during the period.

Other tangible assets and liabilities were valued at their respective carrying amounts as management believes that these amounts approximated their acquisition-date fair values.

Developed technology is an intangible asset that reflects the estimated fair value of Viela's rights to its currently marketed medicine, UPLIZNA. The preliminary estimated fair values of the developed technology represent preliminary valuations performed with the assistance of an independent appraisal firm based on management's estimates, forecasted financial information and reasonable and supportable assumptions. The preliminary fair value of developed technology was determined using an income approach. The income approach explicitly recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on current sales projections and estimated direct costs for UPLIZNA. Indications of value were developed by discounting these benefits to their acquisition-date fair value at a discount rate of 11.5% that reflects the return requirements of the market. Some of the most significant assumptions inherent in the development of the asset valuation include the estimated net cash flows for each year (including net sales, cost of goods sold, sales and marketing costs and R&D costs) and the discount rate. The fair value of the UPLIZNA developed technology was capitalized as of the Viela acquisition date and is subsequently being amortized over approximately 14 years.

IPR&D is related to R&D projects including:

(i) Potential regulatory approval of UPLIZNA for neuromyelitis optica spectrum disorder outside of the United States and certain other indications worldwide. As of the date of the acquisition, UPLIZNA had not been granted regulatory approval in any territory outside the United States. On March 24, 2021, the Company announced that its strategic partner Mitsubishi Tanabe Pharma Corporation, had received manufacturing and marketing approval for UPLIZNA in Japan. Refer to Note 8 for further details.

(ii) HZN-7734, an investigational human monoclonal antibody designed to deplete plasmacytoid dendritic cells (pDCs), a cell type believed to be critical to the pathogenesis of multiple autoimmune diseases.

(iii) HZN-4920, an investigational fusion protein designed to block a key co-stimulatory pathway involved in many autoimmune and inflammatory diseases.

Each IPR&D asset is considered separable from the business as each project could be sold to a third party. The fair value of each IPR&D asset was determined using an income approach. The income approach explicitly recognizes that the fair value of an asset is premised upon the expected receipt of future economic benefits such as earnings and cash inflows based on sales projections and estimated direct costs. Indications of value are developed by discounting these benefits to their present value at a discount rate of 12.5% that reflects the return requirements of the market. Some of the most significant assumptions inherent in the development of the asset valuations include the estimated net cash flows for each year (including net sales, cost of goods sold, sales and marketing costs and R&D costs), the discount rate, the assessment of each asset's life cycle and the potential regulatory and commercial success risk. The fair value of the various IPR&D assets was recorded as an indefinite-lived intangible asset and will be tested for impairment until completion or abandonment of R&D efforts associated with the project. The Company reviews amounts capitalized as acquired IPR&D for impairment annually and whenever events or changes in circumstances indicate that the carrying value of the assets might not be recoverable.

Deferred tax assets and liabilities arise from acquisition accounting adjustments where book values of certain assets and liabilities differ from their tax bases. Deferred tax assets and liabilities are recorded at the currently enacted rates which will be in effect at the time when the temporary differences are expected to reverse in the country where the underlying assets and liabilities are located. The developed technology, IPR&D assets and inventory acquired through the Viela acquisition were located in the United States, as of the acquisition date, where a U.S. tax rate of 24.1% is being utilized and a significant deferred tax liability of $457.9 million was recorded.

Goodwill represents the excess of the total consideration over the estimated fair value of net assets acquired and was recorded in the consolidated balance sheet as of the acquisition date. The goodwill was primarily attributable to the establishment of a deferred tax liability for the developed technology intangible asset and the IPR&D intangible assets. Viela's mid-stage biologics pipeline, R&D team and on-market medicine UPLIZNA, make it a complementary strategic fit with the Company's pipeline, commercial portfolio and therapeutic areas of focus. The Company does not expect any portion of this goodwill to be deductible for tax purposes.

The following table presents the pro forma combined results of the Company and Viela for the three months ended March 31, 2021 and 2020 as if the acquisition of Viela had occurred on January 1, 2020:

	For the Three Months Ended March 31,					
	2021			2020		
	As reported	Pro forma adjustments	Pro forma	As reported	Pro forma adjustments	Pro forma
Net sales	$ 342,406	$ 10,588	$ 352,994	$ 355,909	$ —	$ 355,909
Net loss	(123,351)	(43,556)	(166,907)	(13,591)	(120,002)	(133,593)

The pro forma combined financial information was prepared using the acquisition method of accounting and was based on the historical financial information of Horizon and Viela. In order to reflect the pro forma information as if the acquisition occurred on January 1, 2020 as required, the pro forma financial information includes adjustments to reflect incremental amortization expense to be incurred based on the current preliminary fair values of the identifiable intangible assets acquired; the incremental cost of products sold related to the fair value adjustments associated with acquisition date inventory; the additional interest expense associated with the issuance of debt to finance the acquisition; and the reclassification of transaction costs incurred during the three months ended March 31, 2021 to the three months ended March 31, 2020. Significant non-recurring pro forma adjustments include transaction costs of $86.1 million which were assumed to have been incurred on January 1, 2020 and were recognized as if incurred in the first quarter of 2020. The pro forma financial information is not necessarily indicative of what the consolidated results of operations would have been had the acquisition actually been completed on January 1, 2020. In addition, the pro forma financial information is not a projection of future results of operations of the combined company nor does it reflect the expected realization of any synergies or cost savings associated with the acquisition.

Acquisition of Curzion Pharmaceuticals, Inc.

On April 1, 2020, the Company acquired Curzion Pharmaceuticals, Inc. ("Curzion"), a privately held development-stage biopharma company, and its development-stage oral selective lysophosphatidic acid 1 receptor ($LPAR_1$) antagonist, CZN001 (renamed HZN-825).

Under the terms of the acquisition agreement, the Company acquired Curzion for a $45.0 million upfront payment with additional payments contingent on the achievement of development and regulatory milestones. Pursuant to ASC 805, the Company accounted for the Curzion acquisition as the purchase of an in-process research and development asset and, pursuant to ASC Topic 730, *Research and Development* ("ASC 730"), recorded the purchase price as research and development expense during the year ended December 31, 2020. HZN-825 was originally discovered and developed by Sanofi-Aventis U.S. LLC ("Sanofi-Aventis U.S."), which is eligible to receive contingent payments upon the achievement of development and commercialization milestones and royalties based on revenue thresholds. A member of the Company's board of directors was also a member of the board of directors of, and held a beneficial interest in, Curzion. This related party transaction was conducted in the normal course of business on an arm's length basis.

Refer to Note 15 for further detail on HZN-825 milestone payments.

Sale of RAVICTI and BUPHENYL Rights in Japan

On October 27, 2020, the Company sold its rights to develop and commercialize RAVICTI and BUPHENYL in Japan to Medical Need Europe AB, part of the Immedica Group, for $5.4 million and recorded a gain of $4.9 million on the sale in the fourth quarter of 2020. The Company has retained the rights to RAVICTI and BUPHENYL in North America.

Acquisition of River Vision

On May 8, 2017, the Company acquired 100% of the equity interests in River Vision Development Corp. ("River Vision") for upfront cash payments totaling approximately $150.3 million, including cash acquired of $6.3 million, with additional potential future milestone and royalty payments contingent on the satisfaction of certain regulatory milestones and sales thresholds.

Under the acquisition agreement for River Vision, the Company agreed to pay up to $325.0 million upon the attainment of various milestones, composed of $100.0 million related to U.S. Food and Drug Administration ("FDA") approval and $225.0 million related to net sales thresholds for TEPEZZA. The agreement also includes a royalty payment of 3 percent of the portion of annual worldwide net sales exceeding $300.0 million (if any). The Company made the milestone payment of $100.0 million related to FDA approval during the first quarter of 2020 which is now capitalized as a finite-lived intangible asset representing the developed technology for TEPEZZA.

Additionally, under the Company's license agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc. (together referred to as "Roche"), the Company made a milestone payment of CHF5.0 million ($5.2 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.0382), during the first quarter of 2020 which the Company also capitalized as a finite-lived intangible asset representing the developed technology for TEPEZZA.

In April 2020, a subsidiary of the Company entered into an agreement with S.R. One, Limited ("S.R. One") and an agreement with Lundbeckfond Invest A/S ("Lundbeckfond") pursuant to which the Company acquired all of S.R. One's and Lundbeckfond's beneficial rights to proceeds from certain contingent future TEPEZZA milestone and royalty payments in exchange for a one-time payment of $55.0 million to each of the respective parties. The total payments of $110.0 million were capitalized as a finite-lived intangible asset representing the developed technology for TEPEZZA during the second quarter of 2020.

In addition, during the year ended December 31, 2020, the Company recorded $120.8 million as a finite-lived intangible asset representing the developed technology for TEPEZZA, composed of $67.0 million in relation to the expected future attainment of various net sales milestones payable under the acquisition agreement for River Vision and CHF50.0 million ($53.8 million when converted using a CHF-to-Dollar exchange rate as of the date the intangible asset was recorded) in relation to the expected future attainment of various net sales milestones payable to Roche. The liabilities relating to these net sales milestones were recorded in accrued expenses on the consolidated balance sheet as of December 31, 2020. The Company paid the milestones to Roche in February 2021 and paid the applicable milestones to the former River Vision stockholders in April 2021. There are no further TEPEZZA net sales milestone obligations remaining to Roche and the former River Vision stockholders.

Licensing Agreement

On November 21, 2020, the Company entered into a global collaboration and license agreement with Halozyme Therapeutics, Inc. ("Halozyme") that gives the Company exclusive access to Halozyme's ENHANZE® drug delivery technology for subcutaneous ("SC") formulation of medicines targeting IGF-1R. The Company intends to use ENHANZE to develop a SC formulation of TEPEZZA, indicated for the treatment of thyroid eye disease, a serious, progressive and vision-threatening rare autoimmune disease, potentially shortening drug administration time, reducing healthcare practitioner time and offering additional flexibility and convenience for patients. Under the terms of the agreement, the Company paid Halozyme an upfront cash payment of $30.0 million in December 2020, with additional potential future milestone payments of up to $160.0 million contingent on the satisfaction of certain development and sales thresholds. The $30.0 million upfront payment was accounted for as the acquisition of an IPR&D asset and was recorded as a "research and development" expense in the consolidated statement of comprehensive income (loss) during the year ended December 31, 2020.

Other Arrangements

On January 3, 2019, the Company entered into a collaboration agreement with HemoShear Therapeutics, LLC ("HemoShear"), a biotechnology company, to discover novel therapeutic targets for gout. The collaboration provides the Company with an opportunity to address unmet treatment needs for people with gout by evaluating new targets for the control of serum uric acid levels. Under the terms of the agreement, the Company paid HemoShear an upfront cash payment of $2.0 million with additional potential future milestone payments upon commencement of new stages of development, contingent on the Company's approval at each stage. In June 2019, the Company incurred a $4.0 million progress payment, which was subsequently paid in July 2019. In June 2020, a $3.0 million progress payment became due, which the Company subsequently paid in July 2020. In February 2021, a $3.0 million progress payment became due and was paid during the first quarter of 2021.

NOTE 5 – INVENTORIES

Inventories are stated at the lower of cost or net realizable value. Inventories consist of raw materials, work-in-process and finished goods. The Company has entered into manufacturing and supply agreements for the manufacture of drug substance and finished goods inventories, and the purchase of raw materials and production supplies. The Company's inventories include the direct purchase cost of materials and supplies and manufacturing overhead costs.

The components of inventories as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Raw materials	$ 29,861	$ 11,760
Work-in-process	140,813	33,167
Finished goods	67,632	30,356
Inventories, net	**$ 238,306**	**$ 75,283**

Raw materials, work-in-process, and finished goods at March 31, 2021 included $10.1 million, $119.0 million, and $19.3 million, respectively, of stepped-up UPLIZNA inventory. The Company recorded $0.9 million of UPLIZNA inventory step-up expense during the three months ended March 31, 2021.

Because inventory step-up expense is related to an acquisition, will not continue indefinitely and has a significant effect on the Company's gross profit, gross margin percentage and net loss for all affected periods, the Company discloses balance sheet and income statement amounts related to inventory step-up within the notes to the condensed consolidated financial statements.

NOTE 6 – PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Advance payments for inventory	$ 167,753	$ 137,680
Deferred charge for taxes on intercompany profit	58,617	52,306
Prepaid income taxes and income tax receivable	23,456	102
Rabbi trust assets	21,709	18,423
Other prepaid expenses and other current assets	62,907	43,434
Prepaid expenses and other current assets	**$ 334,442**	**$ 251,945**

Advance payments for inventory as of March 31, 2021 and December 31, 2020, primarily represented payments made to the contract manufacturer of TEPEZZA drug substance.

NOTE 7 – PROPERTY AND EQUIPMENT

Property and equipment as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Buildings	$ 128,268	$ 80,341
Land and land improvements	38,880	38,076
Machinery and equipment	16,910	4,695
Software	14,487	14,618
Furniture and fixtures	12,017	5,973
Leasehold improvements	9,558	26,323
Construction in process	7,370	63,656
Other	4,917	3,146
	232,407	**236,828**
Less accumulated depreciation	(30,550)	(47,791)
Property and equipment, net	**$ 201,857**	**$ 189,037**

Depreciation expense was $4.5 million and $7.2 million for the three months ended March 31, 2021 and 2020, respectively.

In February 2020, the Company purchased a three-building campus in Deerfield, Illinois for total consideration and directly attributable transaction costs of $118.5 million. The Deerfield campus totals 70 acres and consists of approximately 650,000 square feet of office space. In February 2021, the Company's Lake Forest office employees moved to the Deerfield campus and the Company is marketing its Lake Forest office space for sublease. The increase in amount classified as buildings and the decrease in amount classified as construction in process is primarily due to the Deerfield campus becoming operational in February 2021. The decreases in leasehold improvements and accumulated depreciation amounts are primarily due to the Company vacating the Lake Forest office building in February 2021.

NOTE 8 – GOODWILL AND INTANGIBLE ASSETS

Goodwill

The gross carrying amount of goodwill as of March 31, 2021 and December 31, 2020 was $1,076.4 million and $413.7 million, respectively.

The table below presents goodwill for the Company's reportable segments as of March 31, 2021 (in thousands):

	Orphan	Inflammation	Total
Balance at December 31, 2020	$ 357,498	$ 56,171	$ 413,669
Acquired during the period	662,719	—	662,719
Balance at March 31, 2021	**$ 1,020,217**	**$ 56,171**	**$ 1,076,388**

In March 2021, the Company recognized goodwill with a preliminary value of $662.7 million in connection with the Viela acquisition, which represented the excess of the purchase price over the fair value of the net assets acquired. See Note 4 for further details.

As of March 31, 2021, there were no accumulated goodwill impairment losses.

Intangible Assets

As of March 31, 2021, the Company's finite-lived intangible assets consisted of developed technology related to ACTIMMUNE, BUPHENYL, KRYSTEXXA, PROCYSBI, RAVICTI, RAYOS, TEPEZZA and UPLIZNA as well as customer relationships for ACTIMMUNE. The intangible assets related to PENNSAID 2%, and VIMOVO developed technology were fully amortized as of December 31, 2020.

On March 15, 2021, in connection with the acquisition of Viela, the Company capitalized $1,460.0 million of developed technology related to UPLIZNA. See Note 4 for further details.

In connection with the acquisition of River Vision, the Company capitalized payments of $336.0 million related to TEPEZZA developed technology during the year ended December 31, 2020. See Note 4 for further details on the River Vision acquisition.

Intangible assets as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021			December 31, 2020		
	Cost Basis	Accumulated Amortization	Net Book Value	Cost Basis	Accumulated Amortization	Net Book Value
Developed technology	$ 4,587,515	$ (1,380,104)	$ 3,207,411	$ 3,093,886	$ (1,313,934)	$ 1,779,952
In-process research and development (1)	880,000	—	880,000	—	—	—
Customer relationships	8,100	(5,290)	2,810	8,100	(5,090)	3,010
Total intangible assets	**$ 5,475,615**	**$ (1,385,394)**	**$ 4,090,221**	**$ 3,101,986**	**$ (1,319,024)**	**$ 1,782,962**

(1) The Company acquired IPR&D of $910.0 million relating to Viela. On March 24, 2021, the Company announced that its strategic partner, Mitsubishi Tanabe Pharma Corporation, had received manufacturing and marketing approval of UPLIZNA in Japan. As a result, the Company transferred $30.0 million of IPR&D to developed technology. As of March 31, 2021, the remaining IPR&D relating to the Viela acquisition was $880.0 million.

Amortization expense for the three months ended March 31, 2021 and 2020 was $66.4 million and $58.6 million, respectively. IPR&D is not amortized until successful completion of a project. As of March 31, 2021, estimated future amortization expense was as follows (in thousands):

2021 (April to December)	$ 268,242
2022	355,047
2023	354,582
2024	353,102
2025	350,861
Thereafter	1,528,387
Total	**$ 3,210,221**

NOTE 9 – ACCRUED EXPENSES

Accrued expenses as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Payroll-related expenses	$ 72,906	$ 121,577
Accrued milestone payments	69,962	123,442
Consulting and professional services	50,635	21,893
Allowances for returns	38,089	40,918
R&D and manufacturing programs	31,376	17,289
Accrued royalties	23,839	68,006
Advertising and marketing	17,468	12,428
Pricing review liability	17,169	16,046
Accrued interest	7,784	14,207
Accrued other	60,398	49,761
Accrued expenses	**$ 389,626**	**$ 485,567**

As of March 31, 2021, accrued milestone payments represented the attainment in 2020 of a TEPEZZA net sales milestone payable under the acquisition agreement for River Vision. The Company paid the milestone to the former River Vision stockholders in April 2021. Refer to Note 4 for further detail.

NOTE 10 – ACCRUED TRADE DISCOUNTS AND REBATES

Accrued trade discounts and rebates as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Accrued government rebates and chargebacks	$ 177,758	$ 172,893
Accrued co-pay and other patient assistance	80,449	96,924
Accrued commercial rebates and wholesaler fees	67,025	82,646
Accrued trade discounts and rebates	**$ 325,232**	**$ 352,463**
Invoiced commercial rebates and wholesaler fees, co-pay and other patient assistance costs, and government rebates and chargebacks in accounts payable	2,608	1,452
Total customer-related accruals and allowances	**$ 327,840**	**$ 353,915**

The following table summarizes changes in the Company's customer-related accruals and allowances from December 31, 2020 to March 31, 2021 (in thousands):

	Government Rebates and Chargebacks	Co-Pay and Other Patient Assistance	Wholesaler Fees and Commercial Rebates	Total
Balance at December 31, 2020	$ 172,893	$ 96,924	$ 84,098	$ 353,915
Current provisions relating to sales during the three months ended March 31, 2021	146,491	199,031	63,971	409,493
Adjustments relating to prior-year sales	(3,716)	(52)	(758)	(4,526)
Payments relating to sales during the three months ended March 31, 2021	(31,764)	(124,234)	(10,799)	(166,797)
Payments relating to prior-year sales	(107,557)	(90,728)	(67,452)	(265,737)
Viela acquisition on March 15, 2021	1,411	11	70	1,492
Balance at March 31, 2021	**$ 177,758**	**$ 80,952**	**$ 69,130**	**$ 327,840**

NOTE 11 – SEGMENT AND OTHER INFORMATION

The Company has two reportable segments, the orphan segment and the inflammation segment, and the Company reports net sales and segment operating income for each segment.

On March 15, 2021, the Company completed its acquisition of Viela. The acquisition expanded the Company's medicine portfolio by adding an additional rare disease medicine, UPLIZNA.

The orphan segment includes the medicines TEPEZZA, KRYSTEXXA, RAVICTI, PROCYSBI, ACTIMMUNE, BUPHENYL, QUINSAIR, UPLIZNA and also the Company's R&D programs. The inflammation segment includes the medicines PENNSAID 2%, DUEXIS, RAYOS and VIMOVO.

The Company's chief operating decision maker ("CODM") evaluates the financial performance of the Company's segments based upon segment operating income. Segment operating income is defined as loss before benefit for income taxes adjusted for the items set forth in the reconciliation below. Items below income from operations are not reported by segment, since they are excluded from the measure of segment profitability reviewed by the Company's CODM. Additionally, certain expenses are not allocated to a segment. The Company does not report balance sheet information by segment as no balance sheet by segment is reviewed by the Company's CODM.

The following table reflects net sales by medicine for the Company's reportable segments for the three months ended March 31, 2021 and 2020 (in thousands):

	Three Months Ended March 31	
	2021	2020
KRYSTEXXA	$ 106,757	$ 93,248
RAVICTI	72,817	61,189
PROCYSBI	43,363	38,343
ACTIMMUNE	28,763	26,541
TEPEZZA	2,065	23,452
UPLIZNA	1,873	—
BUPHENYL	1,660	2,313
QUINSAIR	209	277
Orphan segment net sales	**$ 257,507**	**$ 245,363**
PENNSAID 2%	45,817	41,563
DUEXIS	19,465	31,346
RAYOS	15,272	18,209
VIMOVO	4,345	19,428
Inflammation segment net sales	**$ 84,899**	**$ 110,546**
Total net sales	**$ 342,406**	**$ 355,909**

The table below provides reconciliations of the Company's segment operating income to the Company's total loss before benefit for income taxes for the three months ended March 31, 2021 and 2020 (in thousands):

	For the Three Months Ended March 31,	
	2021	2020
Segment operating income:		
Orphan	$ 1,054	$ 54,356
Inflammation	42,680	51,942
Reconciling items:		
Amortization and step-up:		
Intangible amortization expense	(66,369)	(58,575)
Inventory step-up expense	(911)	—
Share-based compensation	(61,166)	(56,421)
Acquisition/divestiture-related costs	(49,391)	(284)
Interest expense, net	(13,460)	(17,344)
Impairment of long-lived assets	(12,371)	—
Depreciation	(4,451)	(7,165)
Restructuring and realignment costs	(6,093)	—
Upfront, progress and milestone payments related to license and collaboration agreements	(3,000)	—
Foreign exchange (loss) gain	(848)	776
Drug substance harmonization costs	—	(290)
Fees related to refinancing activities	—	(54)
Other income, net	3,224	442
Loss before benefit for income taxes	**$ (171,102)**	**$ (32,617)**

The following table presents the amount and percentage of gross sales to customers that represented more than 10% of the Company's gross sales included in its two reportable segments and all other customers as a group for the three months ended March 31, 2021 and 2020 (in thousands, except percentages):

	For the Three Months Ended March 31,			
	2021		2020	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Customer A	$ 248,740	33%	$ 246,775	31%
Customer B	184,687	24%	207,277	26%
Customer C	118,037	15%	133,876	17%
Customer D	90,619	12%	84,788	10%
Other Customers	119,449	16%	130,806	16%
Gross Sales	**$ 761,532**	**100%**	**$ 803,522**	**100%**

Geographic revenues are determined based on the country in which the Company's customers are located. The following table presents a summary of net sales attributed to geographic sources for the three months ended March 31, 2021 and 2020 (in thousands, except percentages):

	Three Months Ended March 31, 2021		Three Months Ended March 31, 2020	
	Amount	% of Total Net Sales	Amount	% of Total Net Sales
United States	$ 340,330	99%	$ 354,016	100%
Rest of world	2,076	1%	1,893	*
Net sales	**$ 342,406**		**$ 355,909**	

***Less than 1%**

NOTE 12 – FAIR VALUE MEASUREMENTS

The following tables and paragraphs set forth the Company's financial instruments that are measured at fair value on a recurring basis within the fair value hierarchy. Assets and liabilities measured at fair value are classified in their entirety based on the lowest level of input that is significant to the fair value measurement. The Company's assessment of the significance of a particular input to the fair value measurement in its entirety requires management to make judgments and consider factors specific to the asset or liability. The following describes three levels of inputs that may be used to measure fair value:

Level 1—Observable inputs such as quoted prices in active markets for identical assets or liabilities;

Level 2—Observable inputs other than Level 1 prices such as quoted prices for similar assets or liabilities, quoted prices in markets that are not active, or other inputs that are observable or can be corroborated by observable market data for substantially the full term of the assets or liabilities; and

Level 3—Unobservable inputs that are supported by little or no market activity and that are significant to the fair value of the assets or liabilities.

The Company utilizes the market approach to measure fair value for its money market funds. The market approach uses prices and other relevant information generated by market transactions involving identical or comparable assets or liabilities.

Other current assets and other long-term liabilities recorded at fair value on a recurring basis are composed of investments held in a rabbi trust and the related deferred liability for deferred compensation arrangements. Quoted prices for this investment, primarily in mutual funds, are available in active markets. Thus, the Company's investments related to deferred compensation arrangements and the related long-term liability are classified as Level 1 measurements in the fair value hierarchy.

Assets and liabilities measured at fair value on a recurring basis

The following tables set forth the Company's financial assets and liabilities at fair value on a recurring basis as of March 31, 2021 and December 31, 2020 (in thousands):

	March 31, 2021			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 521,000	$ —	$ —	$ 521,000
Other current assets	21,695	—	—	21,695
Total assets at fair value	**$ 542,695**	**$ —**	**$ —**	**$ 542,695**
Liabilities:				
Other long-term liabilities	(21,695)	—	—	(21,695)
Total liabilities at fair value	**$ (21,695)**	**$ —**	**$ —**	**$ (21,695)**

	December 31, 2020			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 1,906,000	—	—	$ 1,906,000
Other current assets	18,423	—	—	18,423
Total assets at fair value	**$ 1,924,423**	**$ —**	**$ —**	**$ 1,924,423**
Liabilities:				
Other long-term liabilities	(18,423)	—	—	(18,423)
Total liabilities at fair value	**$ (18,423)**	**$ —**	**$ —**	**$ (18,423)**

NOTE 13 – DEBT AGREEMENTS

The Company's outstanding debt balances as of March 31, 2021 and December 31, 2020 consisted of the following (in thousands):

	March 31, 2021	December 31, 2020
Term Loan Facility due 2028	$ 1,600,000	—
Term Loan Facility due 2026	418,026	418,026
Senior Notes due 2027	600,000	600,000
Total face value	**2,618,026**	**1,018,026**
Debt discount	(13,675)	(10,061)
Deferred financing fees	(25,834)	(4,586)
Total long-term debt	**2,578,517**	**1,003,379**
Less: current maturities	16,000	—
Long-term debt, net of current maturities	**$ 2,562,517**	**$ 1,003,379**

Term Loan Facility and Revolving Credit Facility

On March 15, 2021, Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc.) (the "Borrower" or "HTUSA"), a wholly-owned subsidiary of the Company, borrowed approximately $1.6 billion aggregate principal amount of loans (the "Incremental Loans") pursuant to an amendment (the "March 2021 Amendment") to the credit agreement, dated as of May 7, 2015, by and among the Borrower, the Company and certain of its subsidiaries as guarantors, the lenders party thereto from time to time and Citibank, N.A., as administrative agent and collateral agent, as amended by Amendment No. 1, dated as of October 25, 2016, Amendment No. 2, dated March 29, 2017, Amendment No. 3, dated October 23, 2017, Amendment No. 4, dated October 19, 2018, Amendment No. 5, dated March 11, 2019, Amendment No. 6, dated May 22, 2019, Amendment No. 7, dated December 18, 2019 and the Incremental Amendment and Joinder Agreement, dated August 17, 2020 (the "Term Loan Facility"). Pursuant to Amendment No. 7, the Borrower borrowed approximately $418.0 million aggregate principal amount of loans (the "December 2019 Refinancing Loans"). Pursuant to Amendment No. 5, the Borrower received $200.0 million aggregate principal amount of revolving commitments, which was increased to $275.0 million aggregate amount of revolving commitments (the "Incremental Revolving Commitments") pursuant to the Incremental Amendment and Joinder Agreement. The Incremental Revolving Commitments were established pursuant to an incremental facility (the "Revolving Credit Facility") and includes a $50.0 million letter of credit sub-facility. The Incremental Revolving Commitments will terminate in March 2024. Borrowings under the Revolving Credit Facility are available for general corporate purposes. As of March 31, 2021, the Revolving Credit Facility was undrawn. As used herein, all references to the "Credit Agreement" are references to the original credit agreement, dated as of May 7, 2015, as amended through the March 2021 Amendment.

The Incremental Loans were incurred as a separate class of term loans under the Credit Agreement with substantially the same terms of the December 2019 Refinancing Loans. The Borrower used the proceeds of the Incremental Loans to fund a portion of the consideration payable in the acquisition of Viela. The Incremental Loans bear interest at a rate, at Borrower's option, equal to the London Inter-Bank Offered Rate ("LIBOR"), plus 2.00% per annum (subject to a 0.50% LIBOR floor) or the adjusted base rate plus 1.00% per annum, with a step-down to LIBOR plus 1.75% per annum or the adjusted base rate plus 0.75% per annum at the time the Company's leverage ratio is less than or equal to 2.00 to 1.00. The adjusted base rate is defined as the greatest of (a) LIBOR (using one-month interest period) plus 1.00%, (b) the prime rate, (c) the federal funds rate plus 0.50%, and (d) 1.00%.

The December 2019 Refinancing Loans were incurred as a separate new class of term loans under the Credit Agreement with substantially the same terms as the previously outstanding senior secured term loans incurred on May 22, 2019 (the "Refinanced Loans") to effectuate a repricing of the Refinanced Loans. The Borrower used the proceeds of the December 2019 Refinancing Loans to repay the Refinanced Loans, which totaled approximately $418.0 million. The December 2019 Refinancing Loans bear interest at a rate, at the Borrower's option, equal to LIBOR plus 2.25% per annum (subject to a 0.00% LIBOR floor) or the adjusted base rate plus 1.25% per annum, with a step-down to LIBOR plus 2.00% per annum or the adjusted base rate plus 1.00% per annum at the time the Company's leverage ratio is less than or equal to 2.00 to 1.00.

The loans under the Revolving Credit Facility bear interest, at the Borrower's option, at a rate equal to either LIBOR plus an applicable margin of 2.25% per annum (subject to a LIBOR floor of 0.00%), or the adjusted base rate plus 1.25% per annum, with a step-down to LIBOR plus 2.00% per annum or the adjusted base rate plus 1.00% per annum at the time the Company's leverage ratio is less than or equal to 2.00 to 1.00. The Credit Agreement provides for (i) the Incremental Loans, (ii) the December 2019 Refinancing Loans, (iii) the Revolving Credit Facility, (iv) one or more uncommitted additional incremental loan facilities subject to the satisfaction of certain financial and other conditions, and (v) one or more uncommitted refinancing loan facilities with respect to loans thereunder. The Credit Agreement allows for the Company and certain of its subsidiaries to become additional borrowers under incremental or refinancing facilities.

The obligations under the Credit Agreement (including obligations in respect of the Incremental Loans, December 2019 Refinancing Loans and the Revolving Credit Facility) and any swap obligations and cash management obligations owing to a lender (or an affiliate of a lender) are guaranteed by the Company and each of the Company's existing and subsequently acquired or formed direct and indirect subsidiaries (other than certain immaterial subsidiaries, subsidiaries whose guarantee would result in material adverse tax consequences and subsidiaries whose guarantee is prohibited by applicable law). The obligations under the Credit Agreement (including obligations in respect of the Incremental Loans, December 2019 Refinancing Loans and the Revolving Credit Facility) and any related swap and cash management obligations are secured, subject to customary permitted liens and other agreed upon exceptions, by a perfected security interest in (i) all tangible and intangible assets of the Borrower and the guarantors, except for certain customary excluded assets, and (ii) all of the capital stock owned by the Borrower and guarantors thereunder (limited, in the case of the stock of certain non-U.S. subsidiaries of the Borrower, to 65% of the capital stock of such subsidiaries). The Borrower and the guarantors under the Credit Agreement are individually and collectively referred to herein as a "Loan Party" and the "Loan Parties," as applicable.

The Borrower is permitted to make voluntary prepayments of the loans under the Credit Agreement at any time without payment of a premium, except that with respect to the Incremental Loans, a 1% premium will apply to a repayment of the Incremental Loans in connection with a repricing of, or any amendment to the Credit Agreement in a repricing of, such loans effected on or prior to September 15, 2021. The Borrower is required to make mandatory prepayments of loans under the Credit Agreement (without payment of a premium) with (a) net cash proceeds from certain non-ordinary course asset sales (subject to reinvestment rights and other exceptions), (b) casualty proceeds and condemnation awards (subject to reinvestment rights and other exceptions), (c) net cash proceeds from issuances of debt (other than certain permitted debt), and (d) 50% of the Company's excess cash flow (subject to decrease to 25% or 0% if the Company's first lien leverage ratio is less than 2.25:1 or 1.75:1, respectively). The Incremental Loans will amortize in equal quarterly installments in an aggregate annual amount equal to 1% of the original principal amount thereof, with any remaining balance payable on March 15, 2028, the final maturity date of the Incremental Loans. The principal amount of the December 2019 Refinancing Loans are due and payable on May 22, 2026, the final maturity date of the December 2019 Refinancing Loans.

The Credit Agreement contains customary representations and warranties and customary affirmative and negative covenants, including, among other things, restrictions on indebtedness, liens, investments, mergers, dispositions, prepayment of other indebtedness and dividends and other distributions. The Credit Agreement also contains a springing financial maintenance covenant, which requires that the Company maintain a specified leverage ratio at the end of each fiscal quarter. The covenant is tested if both the outstanding loans and letters of credit under the Revolving Credit Facility, subject to certain exceptions, exceed 25% of the total commitments under the Revolving Credit Facility as of the last day of any fiscal quarter. If the Company fails to meet this covenant, the commitments under the Revolving Credit Facility could be terminated and any outstanding borrowings, together with accrued interest, under the Revolving Credit Facility could be declared immediately due and payable.

Other events of default under the Credit Agreement include: (i) the failure by the Borrower to timely make payments due under the Credit Agreement; (ii) material misrepresentations or misstatements in any representation or warranty by any Loan Party when made; (iii) failure by any Loan Party to comply with the covenants under the Credit Agreement and other related agreements; (iv) certain defaults under a specified amount of other indebtedness of the Company or its subsidiaries; (v) insolvency or bankruptcy-related events with respect to the Company or any of its material subsidiaries; (vi) certain undischarged judgments against the Company or any of its restricted subsidiaries; (vii) certain ERISA-related events reasonably expected to have a material adverse effect on the Company and its restricted subsidiaries taken as a whole; (viii) certain security interests or liens under the loan documents ceasing to be, or being asserted by the Company or its restricted subsidiaries not to be, in full force and effect; (ix) any loan document or material provision thereof ceasing to be, or any challenge or assertion by any Loan Party that such loan document or material provision is not, in full force and effect; and (x) the occurrence of a change of control. If one or more events of default occurs and continues beyond any applicable cure period, the administrative agent may, with the consent of the lenders holding a majority of the loans and commitments under the facilities, or will, at the request of such lenders, terminate the commitments of the lenders to make further loans and declare all of the obligations of the Loan Parties under the Credit Agreement to be immediately due and payable.

The interest on the Incremental Loans is variable and, as of March 31, 2021 the interest rate on the Incremental Loans was 2.50% and the effective interest rate was 2.76%.

The interest on the December 2019 Refinancing Loans is variable and as of March 31, 2021 the interest rate on the December 2019 Refinancing Loans was 2.13% and the effective interest rate was 2.42%.

As of March 31, 2021, the fair value of the amounts outstanding under the Incremental Loans and the December 2019 Refinancing Loans were approximately $1,596.0 million and $415.9 million, respectively, categorized as a Level 2 instrument, as defined in Note 12.

2027 Senior Notes

On July 16, 2019, HTUSA completed a private placement of $600.0 million aggregate principal amount of 5.5% Senior Notes due 2027 (the "2027 Senior Notes") to several investment banks acting as initial purchasers, who subsequently resold the 2027 Senior Notes to persons reasonably believed to be qualified institutional buyers.

The Company used the net proceeds from the offering of the 2027 Senior Notes, together with approximately $65.0 million in cash on hand, to redeem or prepay $625.0 million of its outstanding debt, consisting of (i) the outstanding $225.0 million principal amount of its 6.625% Senior Notes due 2023, (ii) the outstanding $300.0 million principal amount of its 8.750% Senior Notes due 2024 and (iii) $100.0 million of the outstanding principal amount of senior secured term loans under the Credit Agreement, as well as to pay the related premiums and fees and expenses, excluding accrued interest, associated with such redemption and prepayment.

The 2027 Senior Notes are HTUSA's general unsecured senior obligations, rank equally in right of payment with all existing and future senior debt of HTUSA and rank senior in right of payment to any existing and future subordinated debt of HTUSA. The 2027 Senior Notes are effectively subordinate to all of the existing and future secured debt of HTUSA to the extent of the value of the collateral securing such debt.

The 2027 Senior Notes are unconditionally guaranteed on a senior basis by the Company and all of the Company's restricted subsidiaries, other than HTUSA and certain immaterial subsidiaries, that guarantee the Credit Agreement. The guarantees are each guarantor's senior unsecured obligations and rank equally in right of payment with such guarantor's existing and future senior debt and senior in right of payment to any existing and future subordinated debt of such guarantor. The guarantees are effectively subordinated to all of the existing and future secured debt of each guarantor, including such guarantor's guarantee under the Credit Agreement, to the extent of the value of the collateral securing such debt. The guarantees of a guarantor may be released under certain circumstances. The 2027 Senior Notes are structurally subordinated to all of the liabilities of the Company's subsidiaries that do not guarantee the 2027 Senior Notes.

The 2027 Senior Notes accrue interest at an annual rate of 5.5% payable semiannually in arrears on February 1 and August 1 of each year, beginning on February 1, 2020. The 2027 Senior Notes will mature on August 1, 2027, unless earlier exchanged, repurchased or redeemed.

Except as described below, the 2027 Senior Notes may not be redeemed before August 1, 2022. Thereafter, some or all of the 2027 Senior Notes may be redeemed at any time at specified redemption prices, plus accrued and unpaid interest to the redemption date. At any time prior to August 1, 2022, some or all of the 2027 Senior Notes may be redeemed at a price equal to 100% of the aggregate principal amount thereof, plus a make-whole premium and accrued and unpaid interest to the redemption date. Also prior to August 1, 2022, up to 40% of the aggregate principal amount of the 2027 Senior Notes may be redeemed at a redemption price of 105.5% of the aggregate principal amount thereof, plus accrued and unpaid interest, with the net proceeds of certain equity offerings. In addition, the 2027 Senior Notes may be redeemed in whole but not in part at a redemption price equal to 100% of the principal amount plus accrued and unpaid interest and additional amounts, if any, to, but excluding, the redemption date, if on the next date on which any amount would be payable in respect of the 2027 Senior Notes, HTUSA or any guarantor is or would be required to pay additional amounts as a result of certain tax related events.

If the Company undergoes a change of control, HTUSA will be required to make an offer to purchase all of the 2027 Senior Notes at a price in cash equal to 101% of the aggregate principal amount thereof plus accrued and unpaid interest to, but not including, the repurchase date, subject to certain exceptions. If the Company or certain of its subsidiaries engages in certain asset sales, HTUSA will be required under certain circumstances to make an offer to purchase the 2027 Senior Notes at 100% of the principal amount thereof, plus accrued and unpaid interest to the repurchase date.

The indenture governing the 2027 Senior Notes contains covenants that limit the ability of the Company and its restricted subsidiaries to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales, merge, consolidate with or merge or sell all or substantially all of their assets, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries, and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to the Company. Certain of the covenants will be suspended during any period in which the 2027 Senior Notes receive investment grade ratings. The indenture governing the 2027 Senior Notes also includes customary events of default.

As of March 31, 2021, the interest rate on the 2027 Senior Notes was 5.50% and the effective interest rate was 5.76%.

As of March 31, 2021, the fair value of the 2027 Senior Notes was approximately $640.5 million, categorized as a Level 2 instrument, as defined in Note 12.

NOTE 14 – LEASE OBLIGATIONS

As of March 31, 2021, the Company had the following office space lease agreements in place for real properties:

Location	Approximate Square Feet	Lease Expiry Date
Dublin, Ireland	18,900	November 4, 2029
Lake Forest, Illinois	160,000	March 31, 2031
Novato, California	61,000	August 31, 2021
South San Francisco, California	20,000	January 31, 2030
Rockville, Maryland (1)	17,300	August 31, 2023 and February 28, 2025
Chicago, Illinois	9,200	December 31, 2028
Gaithersburg, Maryland (1)	7,200	June 30, 2022
Mannheim, Germany	4,800	December 31, 2022
Washington, D.C.	6,000	September 15, 2022

(1) On March 15, 2021, the Company completed its acquisition of Viela. As part of the acquisition, the Company assumed two leases in Rockville, Maryland for both office and laboratory space and a lease in Gaithersburg, Maryland for office space.

The above table does not include details of an agreement for lease entered into on October 14, 2019, relating to approximately 63,000 square feet of office space under construction in Dublin, Ireland. Lease commencement will begin when construction of the offices is completed by the lessor and the Company has access to begin the construction of leasehold improvements. The Company expects to receive access to the office space and commence the related lease in the second quarter of 2021 and incur leasehold improvement costs during 2021 in order to prepare the building for occupancy.

As of March 31, 2021 and December 31, 2020, the Company had right-of-use lease assets included in other assets of $24.2 million and $34.4 million, respectively; current lease liabilities included in accrued expenses of $4.7 million and $4.1 million, respectively; and non-current lease liabilities included in other long-term liabilities of $43.9 million and $43.2 million, respectively, in its condensed consolidated balance sheets.

In February 2021, the Company vacated the Lake Forest leased office building which represented a triggering event for impairment consideration of the right-of-use asset relating to this building. As a result of the Company vacating the Lake Forest office, the Company recorded an impairment charge of $12.4 million during the three months ended March 31, 2021, using an income approach based on market prices for similar properties provided by a third-party. This charge was reported within impairment of long-lived assets in the condensed consolidated statement of comprehensive loss.

The Company recognizes rent expense on a monthly basis over the lease term based on a straight-line method. Rent expense was $1.6 million for the three months ended March 31, 2021 and 2020.

The table below reconciles the undiscounted cash flows for each of the first five years and total of the remaining years to the lease liabilities recorded on the Company's condensed consolidated balance sheet as of March 31, 2021 (in thousands):

2021 (April to December)	$	6,098
2022		7,063
2023		6,595
2024		6,936
2025		6,913
Thereafter		33,063
Total lease payments		66,668
Imputed interest		(18,041)
Total lease liabilities	**$**	**48,627**

The weighted-average discount rate and remaining lease term for leases as of March 31, 2021 was 7.03% and 9.31 years, respectively.

NOTE 15 – COMMITMENTS AND CONTINGENCIES

Purchase Commitments

Under the Company's supply agreement with AGC Biologics A/S (formerly known as CMC Biologics A/S) ("AGC Biologics"), the Company has agreed to purchase certain minimum annual order quantities of TEPEZZA drug substance. In addition, the Company must provide AGC Biologics with rolling forecasts of TEPEZZA drug substance requirements, with a portion of the forecast being a firm and binding order. At March 31, 2021, the Company had binding purchase commitments with AGC Biologics for TEPEZZA drug substance of €76.3 million ($89.5 million converted at a Euro-to-Dollar exchange rate as of March 31, 2021 of 1.1732), to be delivered through December 2023. Under the Company's supply agreement with Catalent Indiana, LLC ("Catalent"), the Company must provide Catalent with rolling forecasts of TEPEZZA drug product requirements, with a portion of the forecast being a firm and binding order. The Company had binding purchase commitments with Catalent for TEPEZZA drug product of $6.4 million, to be delivered through March 2022.

On December 17, 2020, the Company announced that it expected a short-term disruption in TEPEZZA supply as a result of recent U.S. government-mandated COVID-19 vaccine production orders pursuant to the Defense Production Act of 1950 ("DPA") that dramatically restricted capacity available for the production of TEPEZZA at its drug product contract manufacturer, Catalent. Pursuant to the DPA, Catalent was ordered to prioritize certain COVID-19 vaccine manufacturing at Catalent, resulting in the cancellation of previously guaranteed and contracted TEPEZZA drug product manufacturing slots in December 2020, which were required to maintain TEPEZZA supply. To offset the reduced slots allowed by the DPA and Catalent, the Company accelerated plans to increase the production scale of TEPEZZA drug product. In March 2021, the FDA approved a prior approval supplement to the TEPEZZA Biologics Licensing Application (which was previously approved in January 2020), giving the Company authorization to manufacture more TEPEZZA drug product resulting in an increased number of vials with each manufacturing slot. The Company commenced resupply of TEPEZZA to the market in April 2021.

Under the Company's agreement with Bio-Technology General (Israel) Ltd ("BTG Israel"), the Company has agreed to purchase certain minimum annual order quantities and is obligated to purchase at least 80 percent of its annual world-wide bulk product requirements for KRYSTEXXA from BTG Israel. The term of the agreement runs until December 31, 2030, and will automatically renew for successive three-year periods unless earlier terminated by either party upon three years' prior written notice. The agreement may be terminated earlier by either party in the event of a force majeure, liquidation, dissolution, bankruptcy or insolvency of the other party, uncured material breach by the other party or after January 1, 2024, upon three years' prior written notice. Under the agreement, if the manufacture of the bulk product is moved out of Israel, the Company may be required to obtain the approval of the Israel Innovation Authority (formerly known as Israeli Office of the Chief Scientist) ("IIA") because certain KRYSTEXXA intellectual property was initially developed with a grant funded by the IIA. The Company issues eighteen-month forecasts of the volume of KRYSTEXXA that the Company expects to order. The first nine months of the forecast are considered binding firm orders. At March 31, 2021, the Company had a binding purchase commitment with BTG Israel for KRYSTEXXA of $33.0 million, to be delivered through December 2026. Additionally, there were other purchase orders relating to the manufacture of KRYSTEXXA of $1.8 million outstanding at March 31, 2021.

Under an agreement with Boehringer Ingelheim Biopharmaceuticals GmbH ("Boehringer Ingelheim Biopharmaceuticals"), Boehringer Ingelheim Biopharmaceuticals is required to manufacture and supply ACTIMMUNE and IMUKIN to the Company. Following the Company's sale of the rights to IMUKIN in all territories outside of the United States, Canada and Japan to Clinigen Group plc ("Clinigen"), purchases of IMUKIN inventory are expected to be resold to Clinigen. The Company is required to purchase minimum quantities of finished medicine during the term of the agreement, which term extends to at least June 30, 2024. As of March 31, 2021, the minimum purchase commitment to Boehringer Ingelheim Biopharmaceuticals was $15.0 million (converted using a Euro-to-Dollar exchange rate of 1.1732 as of March 31, 2021) through June 2024.

Excluding the above, additional purchase orders and other commitments relating to the manufacture of RAVICTI, BUPHENYL, PROCYSBI, PENNSAID 2%, DUEXIS, RAYOS, QUINSAIR and UPLIZNA of $21.0 million were outstanding at March 31, 2021.

Contingencies

The Company is subject to claims and assessments from time to time in the ordinary course of business. The Company's management does not believe that any such matters, individually or in the aggregate, will have a material adverse effect on the Company's business, financial condition, results of operations or cash flows. In addition, the Company from time to time has billing disputes with vendors in which amounts invoiced are not in accordance with the terms of their contracts.

In November 2015, the Company received a subpoena from the U.S. Attorney's Office for the Southern District of New York requesting documents and information related to its patient assistance programs and other aspects of its marketing and commercialization activities. The Company is unable to predict how long this investigation will continue or its outcome, but it anticipates that it may continue to incur significant costs in connection with the investigation, regardless of the outcome. The Company may also become subject to similar investigations by other governmental agencies. The investigation by the U.S. Attorney's Office and any additional investigations of the Company's patient assistance programs and sales and marketing activities may result in damages, fines, penalties or other administrative sanctions against the Company.

On March 5, 2019, the Company received a civil investigative demand ("CID") from the United States Department of Justice ("DOJ") pursuant to the Federal False Claims Act regarding assertions that certain of the Company's payments to pharmacy benefit managers ("PBMs") were potentially in violation of the Anti-Kickback Statute. The CID requests certain documents and information related to the Company's payments to PBMs, pricing and the Company's patient assistance program regarding DUEXIS, VIMOVO and PENNSAID 2%. The Company is cooperating with the investigation. While the Company believes that its payments and programs are compliant with the Anti-Kickback Statute, no assurance can be given as to the timing or outcome of the DOJ's investigation, or that it will not result in a material adverse effect on the Company's business.

Royalty and Milestone Agreements

TEPEZZA

Under the acquisition agreement for River Vision, the Company agreed to pay up to $325.0 million upon the attainment of various milestones, composed of $100.0 million related to FDA approval and $225.0 million related to net sales thresholds for TEPEZZA. The Company made the $100.0 million milestone payment related to FDA approval during the first quarter of 2020.

The remaining aggregate potential milestone payments of $225.0 million are payable based on certain TEPEZZA worldwide net sales thresholds being achieved as noted in the following table:

TEPEZZA Worldwide Net Sales Threshold	Milestone Payment
>$250 million	$50 million
>$375 million	$75 million
>$500 million	$100 million

The agreement also includes a royalty payment of 3 percent of the portion of annual worldwide net sales exceeding $300.0 million.

S.R. One and Lundbeckfond, as two of the former River Vision stockholders, both held rights to receive approximately 35.66% of any future TEPEZZA payments. As a result of the Company's agreements with S.R. One and Lundbeckfond in April 2020, the Company's remaining net obligations to make TEPEZZA payments for sales milestones and royalties to the former stockholders of River Vision was reduced by approximately 70.25%, after including payments to a third party.

Under the Company's license agreement with Roche, the Company is required to pay Roche up to CHF103.0 million ($109.2 million when converted using a CHF-to-Dollar exchange rate at March 31, 2021 of 1.0598) upon the attainment of various development, regulatory and sales milestones for TEPEZZA. The Company made a milestone payment of CHF5.0 million ($5.2 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.0382) during the first quarter of 2020. The agreement with Roche also includes tiered royalties on annual worldwide net sales between 9 and 12 percent.

During the year ended December 31, 2020, the Company recorded a liability of $123.4 million in accrued expenses representing net sales milestones for TEPEZZA. The timing of the payments was dependent on when the applicable milestone thresholds were attained. In February 2021, under the license agreement with Roche, the Company made a milestone payment of CHF50.0 million ($56.1 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.1228). As of March 31, 2021, a liability of $67.0 million was remaining in accrued expenses which represents the net sales milestones payable to the former River Vision stockholders. The Company paid the milestones to the former River Vision stockholders in April 2021. Following this payment, the Company has no further TEPEZZA net sales milestone obligations remaining to Roche and the former River Vision stockholders.

Under the Company's license agreement with Lundquist Institute (formerly known as Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center) ("Lundquist"), the Company is required to pay Lundquist a royalty payment of less than 1 percent of TEPEZZA net sales. The royalty terminates upon the expiration date of the longest-lived Lundquist patent rights, which is December 2021 for the U.S. rights.

Under the Company's license agreement with Boehringer Ingelheim Biopharmaceuticals, the Company is required to pay Boehringer Ingelheim Biopharmaceuticals milestone payments totaling less than $2.0 million upon the achievement of certain TEPEZZA sales milestones.

Other Agreements

On April 1, 2020, the Company acquired Curzion for an upfront payment of $45.0 million with additional payments of up to $15.0 million contingent on the achievement of certain development and regulatory milestones. Under separate agreements with two additional parties, the Company is also required to make contingent payments upon the achievement of certain development and regulatory milestones and certain net sales thresholds. These separate agreements also include mid to high-single-digit royalty payments based on the portion of annual worldwide net sales.

During the year ended December 31, 2020, the Company committed to invest as a strategic limited partner in four venture capital funds: Forbion Growth Opportunities Fund I C.V., Forbion Capital Fund V C.V., Aisling Capital V, L.P. and RiverVest Venture Fund V, L.P. As of March 31, 2021, the total carrying amount of the Company's investments in these funds was $17.5 million, which is included in other assets in the condensed consolidated balance sheet, and includes $3.8 million in net cash payments for investments made during the first quarter of 2021. As of March 31, 2021, the Company's total future commitments to these funds were $51.7 million. During the three months ended March 31, 2021, the Company recorded investment income of $2.9 million in the other income, net line item of the Company's consolidated statement of comprehensive loss related to these funds.

On November 21, 2020, the Company entered into a global collaboration and license agreement with Halozyme that gives the Company exclusive access to Halozyme's ENHANZE drug delivery technology for SC formulation of medicines targeting IGF-1R. The Company intends to use ENHANZE to develop a SC formulation of TEPEZZA. Under the terms of the agreement, the Company paid Halozyme an upfront cash payment of $30.0 million in December 2020 and agreed to pay additional potential future milestone payments of up to $160.0 million contingent on the satisfaction of certain development and sales thresholds.

As of March 31, 2021, the Company had $32.1 million of non-cancellable advertising commitments due within one year, primarily related to agreements for advertising for TEPEZZA and KRYSTEXXA.

Indemnification

In the normal course of business, the Company enters into contracts and agreements that contain a variety of representations and warranties and provide for general indemnifications. The Company's exposure under these agreements is unknown because it involves claims that may be made against the Company in the future, but have not yet been made. The Company may record charges in the future as a result of these indemnification obligations.

In accordance with its memorandum and articles of association, the Company has indemnification obligations to its officers and directors for certain events or occurrences, subject to certain limits, while they are serving at the Company's request in such capacity. Additionally, the Company has entered into, and intends to continue to enter into, separate indemnification agreements with its directors and executive officers. These agreements, among other things, require the Company to indemnify its directors and executive officers for certain expenses, including attorneys' fees, judgments, fines and settlement amounts incurred by a director or executive officer in any action or proceeding arising out of their services as one of the Company's directors or executive officers, or any of the Company's subsidiaries or any other company or enterprise to which the person provides services at the Company's request. The Company also has a director and officer insurance policy that enables it to recover a portion of any amounts paid for current and future potential claims. All of the Company's officers and directors have also entered into separate indemnification agreements with HTUSA.

NOTE 16 - LEGAL PROCEEDINGS

PENNSAID 2%

On August 18, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Actavis Laboratories UT, Inc. and Actavis plc for patent infringement of four of the Company's newly issued patents covering PENNSAID 2%. All four of such patents are listed in the FDA's Orange Book. On March 3, 2021, the parties stipulated to the dismissal of all remaining litigation involving PENNSAID 2% and the District Court entered an order of dismissal without prejudice.

DUEXIS

On May 29, 2018, the Company received notice from Alkem Laboratories, Inc. ("Alkem") that it had filed an Abbreviated New Drug Application ("ANDA") with the FDA seeking approval of a generic version of DUEXIS. The ANDA contained a Paragraph IV Patent Certification alleging that the patents covering DUEXIS are invalid and/or will not be infringed by Alkem's manufacture, use or sale of the medicine for which the ANDA was submitted. The Company filed suit in the United States District Court of Delaware against Alkem on July 9, 2018, seeking an injunction to prevent the approval of Alkem's ANDA and/or to prevent Alkem from selling a generic version of DUEXIS. The litigation went to trial on September 14, 2020. On November 30, 2020, the District Court issued an adverse judgment against the Company, invalidating U.S Patent No. 8,607,033 and finding that Alkem's generic product would not infringe the '033 patent. And following an adverse claim construction ruling, the District Court entered a judgment that the Alkem generic product would not infringe U.S. Patent No. 8,607,451, subject to the Company's right to appeal the District Court's claim construction ruling. On December 23, 2020, the Company initiated an appeal of the adverse judgments on the '033 and '451 patents with the Federal Circuit Court of Appeals.

On September 26, 2018, the Company received notice from Teva Pharmaceuticals USA, Inc. ("Teva USA") that it had filed an ANDA with the FDA seeking approval of a generic version of DUEXIS. The ANDA contained a Paragraph IV Patent Certification alleging that the patents covering DUEXIS are invalid and/or will not be infringed by Teva USA's manufacture, use or sale of the medicine for which the ANDA was submitted. The Company filed suit in the United States District Court of New Jersey against Teva USA on July 2, 2020, seeking to prevent Teva USA from selling a generic version of DUEXIS. The parties are currently engaged in discovery. The court has not yet set a trial date.

VIMOVO

On February 18, 2020, the FDA granted final approval for Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd. (collectively, "Dr. Reddy's") generic version of VIMOVO. On February 27, 2020, Dr. Reddy's launched its generic version of VIMOVO in the United States, and the Company now faces generic competition with respect to VIMOVO. The Company continues to assert claims of infringement against Dr. Reddy's based on U.S. Patent No. 8,858,996 and U.S. Patent No. 9,161,920 in the District Court for the District of New Jersey.

On November 19, 2018, the District Court granted Dr. Reddy's summary judgment ruling that U.S Patent Numbers 9,220,698 and 9,393,208 are invalid, and on January 21, 2019, it entered final judgment against the '698 and '208 patents and U.S. Patent Number 8,945,621. On February 21, 2019, the Company appealed the adverse judgments on the '208 and '698 patents to the Federal Circuit Court of Appeals. On January 6, 2021, the Federal Circuit affirmed the District Court judgments invalidating the '208 and '698 patents.

PROCYSBI

On June 27, 2020, the Company received notice from Lupin Limited ("Lupin") that it had filed an ANDA with the FDA seeking approval of a generic version of PROCYSBI. The ANDA contained a Paragraph IV Patent Certification alleging that the patents covering PROCYSBI are invalid and/or will not be infringed by Lupin's manufacture, use or sale of the medicine for which the ANDA was submitted. The Company filed suit in the United States District Court of New Jersey against Lupin on August 11, 2020, seeking to prevent Lupin from selling a generic version of PROCYSBI.

NOTE 17 – SHARE-BASED AND LONG-TERM INCENTIVE PLANS

The Company's equity incentive plans at March 31, 2021 included its 2011 Equity Incentive Plan, as amended, 2014 Employee Share Purchase Plan, as amended ("2014 ESPP"), Amended and Restated 2014 Equity Incentive Plan ("2014 EIP"), 2014 Non-Employee Equity Plan, as amended ("2014 Non-Employee Plan"), 2020 Employee Share Purchase Plan ("2020 ESPP"), Amended and Restated 2020 Equity Incentive Plan ("2020 EIP") and the Viela Amended and Restated 2018 Equity Incentive Plan ("Viela 2018 EIP"). The Viela 2018 EIP was subsequently renamed the Horizon Therapeutics Public Limited Company Amended and Restated 2018 Equity Incentive Plan on April 28, 2021.

On February 17, 2021, the Compensation Committee of the Company's Board of Directors (the "Compensation Committee") approved amending the 2020 EIP, subject to shareholder approval, including increasing the number of ordinary shares available for the grant of equity awards to the Company's employees by an additional 7,000,000 shares. On April 29, 2021, the shareholders of the Company approved such amendment to the 2020 EIP.

As of March 31, 2021, an aggregate of 2,994,723 ordinary shares were authorized and available for future issuance under the 2014 ESPP and 2020 ESPP combined, an aggregate of 8,759,022 ordinary shares were authorized and available for future grants under the 2020 EIP, an aggregate of 574,193 ordinary shares were authorized and available for future grants under the 2014 Non-Employee Plan and an aggregate of 2,359,550 ordinary shares were authorized and available for future grants under the Viela 2018 EIP.

Stock Options

The following table summarizes stock option activity during the three months ended March 31, 2021:

	Options	Weighted Average Exercise Price	Weighted Average Contractual Term Remaining (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2020	7,129,615	$ 21.24	4.60	$ 370,073
Assumed in acquisition [1]	1,318,053	41.23		
Exercised	(661,780)	30.06	—	—
Forfeited	(268)	17.19	—	—
Expired	(234)	17.32	—	—
Outstanding as of March 31, 2021	**7,785,386**	**23.88**	**4.82**	**530,665**
Exercisable as of March 31, 2021	**6,771,755**	**$ 21.40**	**4.28**	**$ 478,349**

Stock options typically have a contractual term of ten years from grant date.

(1) On March 15, 2021, the Company completed its acquisition of Viela. Under the terms of the merger agreement for Viela, all outstanding Viela stock options assumed by the Company with vesting dates after June 1, 2021, were converted into stock options to purchase the Company's ordinary shares. As of March 15, 2021, options previously exercisable for an aggregate of 2,180,159 shares of Viela's common stock that were converted at a rate of 0.60 to 1 based on the merger agreement, into options to purchase 1,318,053 of the Company's ordinary shares, were outstanding.

Restricted Stock Units

The following table summarizes restricted stock unit activity for the three months ended March 31, 2021:

	Number of Units	Weighted Average Grant-Date Fair Value Per Unit
Outstanding as of December 31, 2020	5,909,120	$ 27.87
Granted	1,851,309	73.82
Vested	(2,350,056)	23.19
Forfeited	(95,177)	56.21
Outstanding as of March 31, 2021	**5,315,196**	**$ 45.44**

The grant-date fair value of restricted stock units is the closing price of the Company's ordinary shares on the date of grant.

Performance Stock Unit Awards

The following table summarizes performance stock unit awards ("PSUs") activity for the three months ended March 31, 2021:

	Number of Units	Weighted Average Grant-Date Fair Value Per Unit	Average Illiquidity Discount	Recorded Weighted Average Fair Value Per Unit
Outstanding as of December 31, 2020	2,610,924			
Granted	450,577	$ 93.73	8.64%	$ 85.64
Forfeited	(24,450)	93.73	9.21%	85.10
Vested	(2,021,657)	21.21	2.66%	20.65
Performance Based Adjustments (1)	512,819	25.42	7.27%	23.57
Outstanding as of March 31, 2021	**1,528,213**			

(1) Represents adjustment based on the net sales performance criteria meeting 162.5% of target as of December 31, 2020 for the 2020 PSUs (as defined below), the net sales performance criteria meeting 200.0% of target as of December 31, 2020 for the TEPEZZA PSUs (as defined below) and meeting total shareholder return ("TSR") performance at 200.0% for the PSUs that were awarded to key executive participants on January 5, 2018.

On January 4, 2021, the Company awarded PSUs to key executive participants ("2021 PSUs"). The 2021 PSUs utilize three long-term performance metrics, a component tied to technical operations milestones for the Company over the next two years, a component tied to research and development milestones for the Company over the next three years and a component tied to relative three-year compounded annual TSR as follows:

- 50% of the granted 2021 PSUs that may vest (such portion of the PSU award, the "2021 Relative TSR PSUs") are determined by reference to the level of the Company's relative TSR over the three-year period ending December 31, 2023, as measured against the TSR of each company included in the Nasdaq Biotechnology Index ("NBI") during such three-year period. Generally, in order to earn any portion of the 2021 Relative TSR PSUs, the participant must also remain in continuous service with the Company through the earlier of January 1, 2024 or the date immediately prior to a change in control. If a change in control occurs prior to December 31, 2023, the level of the Company's relative TSR will be measured through the date of the change in control.

- 25% of the 2021 PSUs that may vest (such portion of the PSU award, the "2021 Tech Ops PSUs") are determined by reference to the Company's achievement of certain performance objectives related to technical operations.

- 25% of the 2021 PSUs that may vest (such portion of the PSU award, the "2021 R&D PSUs") are determined by reference to the Company's achievement of certain performance objectives related to research and development.

On January 3, 2020, the Company awarded PSUs to key executive participants ("2020 PSUs"). The 2020 PSUs utilize two performance metrics, a short-term component tied to business performance and a long-term component tied to relative compounded annual TSR, as follows:

- 30% of the granted 2020 PSUs that may vest (such portion of the PSU award, the "2020 Relative TSR PSUs") are determined by reference to the level of the Company's relative TSR over the three-year period ending December 31, 2022, as measured against the TSR of each company included in the NBI during such three-year period. Generally, in order to earn any portion of the 2020 Relative TSR PSUs, the participant must also remain in continuous service with the Company through the earlier of January 1, 2023 or the date immediately prior to a change in control. If a change in control occurs prior to December 31, 2022, the level of the Company's relative TSR will be measured through the date of the change in control.

- 70% of the 2020 PSUs that may vest (such portion of the PSU award, the "2020 Net Sales PSUs") are determined by reference to the Company's net sales for certain components of its orphan segment.

As a result of the impact of the COVID-19 pandemic on certain aspects of the Company's business in 2020, the performance goals associated with certain of the Company's performance-based equity awards no longer reflected the Company's expectations, causing the awards to lose their incentive to employees. Accordingly, on July 28, 2020 the Compensation Committee approved a modification to 57% of the 2020 Net Sales PSUs awarded on January 3, 2020 that were to vest based on KRYSTEXXA 2020 net sales. Those 2020 Net Sales PSUs related to KRYSTEXXA may now be earned based on net sales of KRYSTEXXA achieved by the end of a modified 18-month performance period ending July 1, 2021 instead of a 12-month performance period ending December 31, 2020. As a result, the first one-third of any 2020 PSUs earned will vest on July 1, 2021 and the vesting of the remaining two-thirds is unchanged and will vest one-third each on January 5, 2022 and on January 5, 2023. There were 12 participants impacted by the modification. The total compensation cost resulting from the modification was approximately $12.0 million and is being recognized over the remaining requisite service period.

All PSUs outstanding at March 31, 2021 may vest in a range of between 0% and 200%, with the exception of the modified KRYSTEXXA 2020 Net Sales PSUs which are capped at 150%, based on the performance metrics described above. The Company accounts for the 2020 PSUs and 2021 PSUs as equity-settled awards in accordance with ASC 718. Because the value of the 2020 Relative TSR PSUs and 2021 Relative TSR PSUs are dependent upon the attainment of a level of TSR, it requires the impact of the market condition to be considered when estimating the fair value of the 2020 Relative TSR PSUs and 2021 Relative TSR PSUs. As a result, the Monte Carlo model is applied and the most significant valuation assumptions used related to the 2021 PSUs during the three months ended March 31, 2021, include:

Valuation date stock price	$	72.54
Expected volatility		45.8%
Risk free rate		0.2%

The value of the 2020 Net Sales PSUs related to KRYSTEXXA and 2021 Tech Ops PSUs and 2021 R&D PSUs is calculated at the end of each quarter based on the expected payout percentage based on estimated full-period performance against targets, and the Company adjusts the expense quarterly.

On January 4, 2019, the Company awarded a company-wide grant of PSUs (the "TEPEZZA PSUs"). Vesting of the TEPEZZA PSUs was contingent upon receiving shareholder approval of amendments to the 2014 EIP, which approval was received on May 2, 2019. The TEPEZZA PSUs were generally eligible to vest contingent upon receiving approval of the TEPEZZA biologics license application from the FDA no later than September 30, 2020 and the employee's continued service with the Company. In January 2020, the Company received TEPEZZA approval from the FDA and the Company started recognizing the expense related to the TEPEZZA PSUs on that date. As of March 31, 2021, there were 68,459 TEPEZZA PSUs outstanding, for members of the executive committee, expected to vest on January 21, 2022, subject to the employees' continued service through the vesting date. For all other participants, one-half of the TEPEZZA PSUs vested on the FDA approval date and one-half vested on the one-year anniversary of the FDA approval date, subject to the employee's continued service through the vesting date.

Share-Based Compensation Expense

The following table summarizes share-based compensation expense included in the Company's condensed consolidated statements of operations for the three months ended March 31, 2021 and 2020 (in thousands):

	For the Three Months Ended March 31,	
	2021	2020
Share-based compensation expense		
Cost of goods sold	$ 1,936	$ 2,689
Research and development	5,616	6,376
Selling, general and administrative	53,614	47,356
Total share-based compensation expense	**$ 61,166**	**$ 56,421**

During the three months ended March 31, 2021 and 2020, the Company recognized $53.7 million and $14.1 million of tax benefit, respectively, related to share-based compensation resulting primarily from the fair value of equity awards at the time of the exercise of stock options and vesting of restricted stock units and PSUs. As of March 31, 2021, the Company estimates that pre-tax unrecognized compensation expense of $341.5 million for all unvested share-based awards, including stock options, restricted stock units and PSUs, will be recognized through the second quarter of 2023. The Company expects to satisfy the exercise of stock options and future distribution of shares for restricted stock units and PSUs by issuing new ordinary shares which have been reserved under the 2020 EIP and the Viela 2018 EIP.

Cash Incentive Program

On January 5, 2018, the Compensation Committee approved a performance cash incentive program for the Company's executive leadership team, including its executive officers (the "Cash Incentive Program"). Participants receiving awards under the Cash Incentive Program are eligible to earn a cash bonus based upon the achievement of specified Company goals, which both performance criteria were met on or before December 31, 2018. The Company determined that the cash bonus award under the Cash Incentive Program is to be paid out at the maximum 150% target level of $14.1 million. The first and second installments were paid in January 2019 and January 2020, respectively, and the remaining installment vested and was paid in January 2021.

The Company accounted for the Cash Incentive Program as a deferred compensation plan under ASC 710 and is recognizing the payout expense using straight-line recognition through the end of the 36-month vesting period. During the three months ended March 31, 2021, the Company did not record an expense related to the Cash Incentive Program as it was fully expensed as of December 31, 2020.

NOTE 18 – INCOME TAXES

The Company accounts for income taxes based upon an asset and liability approach. Deferred tax assets and liabilities represent the future tax consequences of the differences between the financial statement carrying amounts of assets and liabilities versus the tax basis of assets and liabilities. Under this method, deferred tax assets are recognized for deductible temporary differences and operating loss and tax credit carryforwards. Deferred tax liabilities are recognized for taxable temporary differences. Deferred tax assets are reduced by valuation allowances when, in the opinion of management, it is more likely than not that some portion or all of the deferred tax assets will not be realized. Deferred tax assets and liabilities are recorded at the currently enacted rates which will be in effect at the time when the temporary differences are expected to reverse in the country where the underlying assets and liabilities are located. The impact of tax rate changes on deferred tax assets and liabilities is recognized in the period in which the change is enacted.

The following table presents the benefit for income taxes for the three months ended March 31, 2021 and 2020 (in thousands):

	For the Three Months Ended March 31,	
	2021	2020
Loss before benefit for income taxes	$ (171,102)	$ (32,617)
Benefit for income taxes	(47,751)	(19,026)
Net loss	**$ (123,351)**	**$ (13,591)**

During the three months ended March 31, 2021, the Company recorded a benefit for income taxes of $47.8 million. During the three months ended March 31, 2020, the Company recorded a benefit for income taxes of $19.0 million. The increase in benefit for income taxes recorded during the three months ended March 31, 2021 compared to the three months ended March 31, 2020, resulted primarily from the increase in the tax benefits recognized on share-based compensation.

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

The following discussion and analysis should be read in conjunction with our condensed consolidated financial statements and the related notes that appear elsewhere in this report. This discussion contains forward-looking statements reflecting our current expectations that involve risks and uncertainties which are subject to safe harbors under the Securities Act of 1933, as amended, or the Securities Act, and the Securities Exchange Act of 1934, as amended, or the Exchange Act. These forward-looking statements include, but are not limited to, statements concerning our strategy and other aspects of our future operations, future financial position, future revenues, projected costs, expectations regarding demand and acceptance for our medicines, growth opportunities and trends in the market in which we operate, prospects and plans and objectives of management. The words "anticipates", "believes", "estimates", "expects", "intends", "may", "plans", "projects", "will", "would" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions or expectations disclosed in our forward-looking statements and you should not place undue reliance on our forward-looking statements. These forward-looking statements involve risks and uncertainties that could cause our actual results to differ materially from those in the forward-looking statements, including, without limitation, the risks set forth in Part II, Item 1A, "Risk Factors" in this report and in our other filings with the Securities and Exchange Commission, or SEC. We do not assume any obligation to update any forward-looking statements.

Unless otherwise indicated or the context otherwise requires, references to "Horizon", "we", "us" and "our" refer to Horizon Therapeutics plc and its consolidated subsidiaries.

OUR BUSINESS

We are focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare, autoimmune and serious inflammatory diseases. Our pipeline is purposeful: we apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives. We have two reportable segments, the orphan segment and the inflammation segment, and our portfolio is currently composed of 12 medicines in the areas of rare diseases, gout, ophthalmology and inflammation.

On March 15, 2021, we completed the acquisition of Viela Bio, Inc., or Viela. The acquisition expanded our marketed medicine portfolio by adding an additional rare disease medicine, UPLIZNA®. The Viela acquisition provides multiple opportunities to drive long-term growth and solidify our future as an innovation-driven biotech company. Viela's mid-stage biologics pipeline, research and development team and on-market medicine UPLIZNA, make it a complementary strategic fit with our pipeline, commercial portfolio and therapeutic areas of focus.

As of March 31, 2021, our marketed medicines consisted of the following:

Orphan
TEPEZZA® (teprotumumab-trbw), for intravenous infusion
KRYSTEXXA® (pegloticase injection), for intravenous infusion
RAVICTI® (glycerol phenylbutyrate) oral liquid
PROCYSBI® (cysteamine bitartrate) delayed-release capsules and granules, for oral use
ACTIMMUNE® (interferon gamma-1b) injection, for subcutaneous use
BUPHENYL® (sodium phenylbutyrate) tablets and powder, for oral use
QUINSAIR™ (levofloxacin) solution for inhalation
UPLIZNA (inebilizumab-cdon) injection, for intravenous use
Inflammation
PENNSAID® (diclofenac sodium topical solution) 2% w/w, or PENNSAID 2%, for topical use
DUEXIS® (ibuprofen/famotidine) tablets, for oral use
RAYOS® (prednisone) delayed-release tablets, for oral use
VIMOVO® (naproxen/esomeprazole magnesium) delayed-release tablets, for oral use

Acquisitions and Divestitures

Since January 1, 2020, we completed the following acquisitions and divestitures:

- On March 15, 2021, we completed the acquisition of Viela, in which we acquired all of the issued and outstanding shares of Viela's common stock for $53.00 per share in cash. The total consideration for the acquisition was approximately $3.0 billion, including cash acquired of $342.3 million.

- On October 27, 2020, we sold our rights to develop and commercialize RAVICTI and BUPHENYL in Japan to Medical Need Europe AB, part of the Immedica Group. We have retained the rights to RAVICTI and BUPHENYL in North America.

- On April 1, 2020, we acquired Curzion Pharmaceuticals, Inc., or Curzion, a privately held development-stage biopharma company, and its development-stage oral selective lysophosphatidic acid 1 receptor (LPAR1) antagonist, CZN001 (renamed HZN-825), for an upfront cash payment of $45.0 million with additional payments contingent on the achievement of development and regulatory milestones.

Impact of COVID-19

On March 11, 2020, the World Health Organization made the assessment that a novel strain of coronavirus, which causes the COVID-19 disease, had become a pandemic. On March 13, 2020, the President of the United States declared the COVID-19 pandemic a national emergency and many states and municipalities in the United States took aggressive actions to reduce the spread of the disease, including limiting non-essential gatherings of people, ceasing all non-essential travel, ordering certain businesses and government agencies to cease non-essential operations at physical locations and issuing "shelter-in-place" orders which direct individuals to shelter at their places of residence (subject to limited exceptions). Similarly, the Irish government limited gatherings of people and encouraged employees to work from their homes, and may implement more aggressive policies in the future. In mid-March 2020 we implemented work-from-home policies for all employees and moved to a "virtual" model with respect to our physician, patient and partner support activities. As certain U.S. states started to reduce restrictions, we saw physicians' offices beginning to reopen, which reopening varied on a state-by-state basis. As a result, our sales representatives in some areas have transitioned to being back out in the field and are working on ways to re-engage patients and physicians. However, as COVID-19 cases have increased in certain areas, certain U.S. states have reimplemented restrictions and some physician offices re-established limits on in-person visits. While our financial results during the three months ended March 31, 2021 were strong and we continue to have a significant amount of available liquidity, we anticipate the COVID-19 pandemic to continue to have a negative impact on net sales into 2021. In addition, our clinical trials have been and may in the future be affected by the COVID-19 pandemic as referred to below.

Economic and health conditions in the United States and across most of the world are continuing to change rapidly because of the COVID-19 pandemic. Although COVID-19 is a global issue that is altering business and consumer activity, the pharmaceutical industry is considered a critical and essential industry in the United States and many other countries and, therefore, we do not currently expect any significant extended shut downs of suppliers or distribution channels, except for the short-term disruption in TEPEZZA supply described below. In respect of our other medicines, we believe we have sufficient inventory of raw materials and finished goods and we expect patients to be able to continue to receive their medicines at a site of care, for our infused medicines, and from their current pharmacies, alternative pharmacies or, if necessary, by direct shipment from our third-party providers that have such capability, for our other medicines.

TEPEZZA

The launch of our infused medicine for thyroid eye disease, or TED, TEPEZZA, which was approved by the U.S. Food and Drug Administration, or FDA, on January 21, 2020, significantly exceeded our expectations. In early 2019, we initiated our pre-launch disease awareness, market development and market access efforts with multi-functional field-based teams beginning to engage with key stakeholders in July 2019. We believe these pre-launch efforts, the severity and acute nature of TED, and a highly motivated patient population have generated significant demand for the medicine. While we experienced a much higher number of new patients in 2020 than our initial estimates, the impact from COVID-19 slowed the generation of patient enrollment forms for TEPEZZA, which drive new patient starts.

On December 17, 2020, we announced that we expected a short-term disruption in TEPEZZA supply as a result of recent U.S. government-mandated COVID-19 vaccine production orders pursuant to the Defense Production Act of 1950, or DPA, that dramatically restricted capacity available for the production of TEPEZZA at our drug product contract manufacturer, Catalent Indiana, LLC, or Catalent. Pursuant to the DPA, Catalent was ordered to prioritize certain COVID-19 vaccine manufacturing at Catalent, resulting in the cancellation of previously guaranteed and contracted TEPEZZA drug product manufacturing slots in December 2020, which were required to maintain TEPEZZA supply. To offset the reduced slots, we accelerated plans to increase the production scale of TEPEZZA drug product at Catalent.

Prior to the announcement of the short-term supply disruption in TEPEZZA, we were able to meet the significantly higher than initially expected demand for TEPEZZA in 2020. For the year ended December 31, 2020, we recorded TEPEZZA net sales of $820.0 million, which was more than 20 times greater than the expected TEPEZZA full year 2020 net sales of $30.0 million to $40.0 million that we stated in a Form 8-K filing on February 26, 2020.

In March 2021, the FDA approved a prior approval supplement to the TEPEZZA Biologics Licensing Application, or BLA (which was previously approved in January 2020), giving us authorization to manufacture more TEPEZZA drug product resulting in an increased number of vials with each manufacturing slot. We commenced resupply of TEPEZZA to the market in April 2021. In addition, we are making progress with our second drug product manufacturer and we are on track to begin shipping TEPEZZA supply from this manufacturer, assuming FDA approval, by year end. Other than Catalent, we are not aware of any manufacturing facilities that are part of the supply chain for our medicines that are being utilized for the manufacture of vaccines for COVID-19. At this time, we consider our inventories on hand of all our other medicines to be sufficient to meet our commercial requirements.

We have delayed the start of an FDA-required post-marketing study to evaluate safety of TEPEZZA in a larger patient population and retreatment rates relative to how long patients receive the medicine given the supply disruption. We have also delayed the start of our planned TEPEZZA clinical trial in chronic TED and an exploratory trial of TEPEZZA in diffuse cutaneous systemic sclerosis until later in 2021, assuming commercial drug product supplies have normalized by that time.

KRYSTEXXA

KRYSTEXXA is an infused medicine for uncontrolled gout and was also achieving rapid growth prior to the COVID-19 pandemic. While the vast majority of patients on therapy have maintained therapy, many new patients have delayed infusions due to shelter-in-place guidelines and patients voluntarily delaying visits to healthcare providers and infusion centers. Patient visits to physicians substantially declined during 2020, which resulted in a reduction of new patients. Although we cannot predict when healthcare activities will return to normal levels due to the continued uncertainty with respect to the COVID-19 pandemic, patient demand is beginning to return with the return of healthcare activity.

Our other medicines

Our other orphan segment medicines, RAVICTI, PROCYSBI and ACTIMMUNE, treat serious, chronic diseases with serious consequences if left untreated. It is therefore critical for patients to maintain therapy. Patient motivation to continue treatment is high, and therefore net sales for these three medicines were stable during 2020 and the first quarter of 2021, with less impact from COVID-19 compared to our other medicines.

In regard to the inflammation segment, we are experiencing reduced demand given the absence of in-person engagement by our sales representatives with healthcare providers and reduced levels of non-essential patient visits to physicians. This impact has been somewhat mitigated by the virtual engagement efforts of our sales representatives, as well as the use of telemedicine by many physicians, which allows them to continue to see patients and prescribe medicines. In addition, with our HorizonCares program, most patients do not need to physically visit a pharmacy to obtain a prescription because the vast majority of these medicines are delivered to a patient’s home through mail or local courier, depending on the participating pharmacy.

Clinical trials

Our clinical trials have been and may in the future be affected by COVID-19. As referred to above, two of our clinical trials for TEPEZZA have been delayed due to the impact of the TEPEZZA supply disruption at Catalent. In addition, clinical site initiation and patient enrollment may be delayed due to prioritization of hospital and healthcare resources toward COVID-19. Current or potential patients in our ongoing or planned clinical trials may also choose to not enroll, not participate in follow-up clinical visits or drop out of the trial as a result of, or a precaution against, contracting COVID-19. Further, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Some clinical sites in the United States have slowed or stopped further enrollment of new patients in clinical trials, denied access to site monitors or otherwise curtailed certain operations. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted. These events could delay our clinical trials, increase the cost of completing our clinical trials and negatively impact the integrity, reliability or robustness of the data from our clinical trials.

We are continuing to actively monitor the possible impacts from the COVID-19 pandemic and may take further actions to alter our business operations as may be required by federal, state or local authorities or that we determine are in the best interests of patients. There is significant uncertainty about the duration and potential impact of the COVID-19 pandemic. This means that our results could change at any time and the contemplated impact of the COVID-19 pandemic on our business results and outlook represents our estimate based on the information available as of the date of this Quarterly Report on Form 10-Q.

Strategy

Horizon is a leading high-growth innovation-driven profitable biotech company. We are focused on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. Our strategy is to expand our development-stage pipeline for long-term sustainable growth and maximize the benefit and value of our on-market medicines, with particular focus on our current key growth drivers TEPEZZA and KRYSTEXXA, both rare disease medicines. Our vision is to build healthier communities, urgently and responsibly, which we believe generates value for our many stakeholders, including our shareholders.

Our pipeline strategy is to expand our pipeline with early-to late-stage clinical programs for sustainable growth. We are pursuing this strategy by acquiring and developing medicines that address unmet needs in rare, autoimmune and severe inflammatory diseases, with a focus on the therapeutic areas of ophthalmology, rheumatology, nephrology and endocrinology. With the March 2021 acquisition of Viela and the addition of its mid-stage biologics pipeline, at the end of the first quarter of 2021 we had 22 pipeline programs, with more than half of these programs in Phase 1, Phase 2 or Phase 3 clinical trials. Of the 22 programs, we expect to initiate a total of eight clinical trials in 2021, one of which has already initiated. For our on-market rare disease medicines, including our current key growth driver medicines TEPEZZA and KRYSTEXXA, our commercialization strategy includes efforts to increase awareness of the conditions each medicine is designed to treat, enhancing efforts to identify target patients and to maximize the value of the medicines through clinical trials. In addition, we are pursuing a global expansion strategy, which includes bringing TEPEZZA to patients with TED outside of the United States, including Japan where we are engaging with the Pharmaceutical and Medical Devices Agency and the Japanese medical community. Furthermore, we are initiating an investment in our European infrastructure to support the potential approval in the first quarter of 2022 of UPLIZNA for neuromyelitis optica spectrum disorder, which has been granted orphan designation by the European Commission.

RESULTS OF OPERATIONS

Comparison of Three Months Ended March 31, 2021 and 2020

Consolidated Results

The table below should be referenced in connection with a review of the following discussion of our results of operations for the three months ended March 31, 2021, compared to the three months ended March 31, 2020.

	For the Three Months Ended March 31,		
	2021	2020	Change
	(in thousands)		
Net sales	$ 342,406	$ 355,909	$ (13,503)
Cost of goods sold	100,368	97,416	2,952
Gross profit	**242,038**	**258,493**	**(16,455)**
Operating expenses:			
Research and development	57,693	27,209	30,484
Selling, general and administrative	331,992	247,775	84,217
Impairment of long-lived assets	12,371	—	12,371
Total operating expenses	**402,056**	**274,984**	**127,072**
Operating loss	**(160,018)**	**(16,491)**	**(143,527)**
Other expense, net:			
Interest expense, net	(13,460)	(17,344)	3,884
Foreign exchange (loss) gain	(848)	776	(1,624)
Other income, net	3,224	442	2,782
Total other expense, net	**(11,084)**	**(16,126)**	**5,042**
Loss before benefit for income taxes	**(171,102)**	**(32,617)**	**(138,485)**
Benefit for income taxes	(47,751)	(19,026)	(28,725)
Net loss	**$ (123,351)**	**$ (13,591)**	**$ (109,760)**

Net sales. Net sales decreased $13.5 million, or 3.8%, to $342.4 million during the three months ended March 31, 2021, from $355.9 million during the three months ended March 31, 2020. The decrease in net sales during the three months ended March 31, 2021 was primarily due to a decrease in net sales in our inflammation segment of $25.6 million and a decrease in TEPEZZA net sales of $21.4 million due to the short-term supply disruption as described below, partially offset by an increase of $13.5 million in KRYSTEXXA net sales and an increase of $11.6 million in RAVICTI net sales when compared to the three months ended March 31, 2020.

The following table reflects net sales by medicine for the three months ended March 31, 2021 and 2020 (in thousands, except percentages):

	Three Months Ended March 31,		Change $	Change %
	2021	2020		
KRYSTEXXA	$ 106,757	$ 93,248	13,509	15%
RAVICTI	72,817	61,189	11,628	19%
PROCYSBI	43,363	38,343	5,020	13%
ACTIMMUNE	28,763	26,541	2,222	8%
TEPEZZA	2,065	23,452	(21,387)	(91)%
UPLIZNA	1,873	—	1,873	100%
BUPHENYL	1,660	2,313	(653)	(28)%
QUINSAIR	209	277	(68)	(25)%
Orphan segment net sales	**$ 257,507**	**$ 245,363**	**$ 12,144**	**5%**
PENNSAID 2%	45,817	41,563	4,254	10%
DUEXIS	19,465	31,346	(11,881)	(38)%
RAYOS	15,272	18,209	(2,937)	(16)%
VIMOVO	4,345	19,428	(15,083)	(78)%
Inflammation segment net sales	**$ 84,899**	**$ 110,546**	**$ (25,647)**	**(23)%**
Total net sales	**$ 342,406**	**$ 355,909**	**$ (13,503)**	**(4)%**

Orphan Segment

KRYSTEXXA. Net sales increased $13.5 million, or 15%, to $106.7 million during the three months ended March 31, 2021, from $93.2 million during the three months ended March 31, 2020. Net sales increased by approximately $8.4 million due to higher net pricing and $5.1 million due to volume growth, despite the ongoing challenges associated with the COVID-19 pandemic.

RAVICTI. Net sales increased $11.6 million, or 19%, to $72.8 million during the three months ended March 31, 2021, from $61.2 million during the three months ended March 31, 2020. Net sales increased by approximately $11.3 million due to volume growth and $0.3 million due to higher net pricing.

PROCYSBI. Net sales increased $5.0 million, or 13%, to $43.3 million during the three months ended March 31, 2021, from $38.3 million during the three months ended March 31, 2020. Net sales increased by approximately $2.8 million due to volume growth and $2.3 million due to higher net pricing.

ACTIMMUNE. Net sales increased $2.2 million, or 8%, to $28.7 million during the three months ended March 31, 2021, from $26.5 million during the three months ended March 31, 2020. Net sales increased by approximately $2.3 million due to higher net pricing, partially offset by a decrease of approximately $0.1 million resulting from lower sales volume.

TEPEZZA. Net sales decreased $21.4 million, or 91%, to $2.1 million during the three months ended March 31, 2021, from $23.5 million during the three months ended March 31, 2020, due to the short-term TEPEZZA supply disruption. On December 17, 2020, we announced that we expected a short-term disruption in TEPEZZA supply as a result of recent U.S. government-mandated COVID-19 vaccine production orders pursuant to the DPA, that dramatically restricted capacity available for the production of TEPEZZA at our drug product contract manufacturer, Catalent. In March 2021, the FDA approved a prior approval supplement to the TEPEZZA BLA (which was previously approved in January 2020), giving us authorization to manufacture more TEPEZZA drug product resulting in an increased number of vials with each manufacturing slot. We commenced resupply of TEPEZZA to the market in April 2021. Refer to the *Impact of COVID-19* section above for further information. Due to the timing of new patients and the restarting of therapy for existing patients following the supply disruption, we expect variability in quarterly net sales of TEPEZZA for the remainder of 2021.

UPLIZNA. Net sales generated for UPLIZNA during the three months ended March 31, 2021 were $1.9 million. We began recognizing UPLIZNA sales following our acquisition of Viela on March 15, 2021.

Inflammation Segment

As a result of the COVID-19 pandemic, sales volumes for our inflammation medicines have been negatively impacted due to reduced demand given the absence of in-person engagement by our sales representatives with health care providers and reduced levels of non-essential patient visits to physicians.

PENNSAID 2%. Net sales increased $4.3 million, or 10%, to $45.8 million during the three months ended March 31, 2021, from $41.5 million during the three months ended March 31, 2020. Net sales increased by approximately $8.9 million resulting from higher net pricing primarily due to lower utilization of our patient assistance programs, partially offset by a decrease of approximately $4.6 million resulting from lower sales volume.

DUEXIS. Net sales decreased $11.9 million, or 38%, to $19.4 million during the three months ended March 31, 2021, from $31.3 million during the three months ended March 31, 2020. Net sales decreased by approximately $11.6 million due to lower net pricing and $0.3 million resulting from lower sales volume.

RAYOS. Net sales decreased $2.9 million, or 16%, to $15.3 million during the three months ended March 31, 2021, from $18.2 million during the three months ended March 31, 2020. Net sales decreased by approximately $2.2 million due to lower net pricing and $0.8 million resulting from lower sales volume.

VIMOVO. Net sales decreased $15.1 million, or 78%, to $4.3 million during the three months ended March 31, 2021, from $19.4 million during the three months ended March 31, 2020. Net sales decreased by approximately $14.8 million due to lower sales volume as a result of generic competition and $0.3 million due to lower net pricing.

The table below reconciles our gross to net sales for the three months ended March 31, 2021 and 2020 (in millions, except percentages):

	Three Months Ended March 31, 2021		Three Months Ended March 31, 2020	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Gross sales	$ 761.5	100.0%	$ 803.5	100.0%
Adjustments to gross sales:				
Prompt pay discounts	(12.0)	(1.6)%	(13.0)	(1.6)%
Medicine returns	(2.1)	(0.3)%	(8.8)	(1.1)%
Co-pay and other patient assistance	(199.1)	(26.1)%	(230.1)	(28.6)%
Commercial rebates and wholesaler fees	(63.1)	(8.3)%	(59.5)	(7.4)%
Government rebates and chargebacks	(142.7)	(18.7)%	(136.2)	(17.0)%
Total adjustments	**(419.0)**	**(55.0)%**	**(447.6)**	**(55.7)%**
Net sales	**$ 342.4**	**45.0%**	**$ 355.9**	**44.3%**

During the three months ended March 31, 2021, co-pay and other patient assistance costs, as a percentage of gross sales, decreased to 26.1% from 28.6% during the three months ended March 31, 2020, primarily due to lower utilization of our patient assistance programs and the reduction of VIMOVO sales as a result of generic competition.

On a quarter-to-quarter basis, our net sales have traditionally been lower in first half of the year, particularly in the first quarter, with the second half of the year representing a greater share of overall net sales each year. This is due to annual managed care plan changes and the re-setting of patients' medical insurance deductibles at the beginning of each year, resulting in higher co-pay and other patient assistance costs as patients meet their annual medical insurance deductibles during the first and second quarters, and higher net sales in the second half of the year after patients meet their deductibles and healthcare plans reimburse a greater portion of the total cost of our medicines. In addition, the TEPEZZA supply disruption as described above negatively impacted sales of TEPEZZA in the first quarter of 2021.

Research and Development Expenses. Research and development expenses increased $30.5 million to $57.7 million during the three months ended March 31, 2021, from $27.2 million during the three months ended March 31, 2020. The increase during the three months ended March 31, 2021 compared to three months ended March 31, 2020, was primarily attributable to a $21.0 million increase in clinical trial and manufacturing development costs reflecting increased activity in our research and development pipeline as well as the addition of Viela's medicine candidates and development programs. In addition, employee-related costs increased by $4.7 million and a progress payment of $3.0 million was paid during the first quarter of 2021, in relation to our collaboration agreement with HemoShear Therapeutics, LLC, or HemoShear.

We expect our research and development expenses to significantly increase in 2021 as a result of our planned additional clinical trials for our pipeline as well as the addition of Viela's medicine candidates and development programs. Refer to Note 4 of the notes to the condensed consolidated financial statements, for further details of this acquisition.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased $84.2 million to $332.0 million during the three months ended March 31, 2021, from $247.8 million during the three months ended March 31, 2020. The increase was primarily attributable to costs associated with the Viela acquisition in March 2021 and an increase in TEPEZZA commercial activities including $28.0 million of transaction costs that were incurred during the first quarter of 2021, an increase of $25.8 million in employee-related costs, an increase of $11.4 million in consulting costs, primarily related to the integration of Viela, and an increase of $8.7 million related to marketing program costs.

We expect our selling, general and administrative expenses to significantly increase in 2021 as a result of the increase in the U.S. commercial and field-based organization for TEPEZZA, the completion and integration of the Viela acquisition and global expansion activities. Refer to Note 4 of the notes to the condensed consolidated financial statements, for further details of the Viela acquisition.

Impairment of long-lived assets. During the three months ended March 31, 2021, we recorded an impairment charge of $12.4 million as a result of vacating the Lake Forest office.

Interest Expense, Net. Interest expense, net, decreased $3.9 million to $13.4 million during the three months ended March 31, 2021, from $17.3 million during the three months ended March 31, 2020. The decrease was primarily due to a decrease in interest expense of $6.9 million, primarily due to the extinguishment of our 2.50% Exchangeable Senior Notes due 2022, or Exchangeable Senior Notes, in August 2020, partially offset by a decrease in interest income of $3.0 million.

We expect our interest expense to increase in 2021 as a result of $1.6 billion of additional debt incurred to fund the Viela acquisition. Refer to Note 13 of the notes to condensed consolidated financial statements, for further details of this additional debt incurred.

Benefit for Income Taxes. During the three months ended March 31, 2021, we recorded a benefit for income taxes of $47.8 million compared to a benefit for income taxes of $19.0 million during the three months ended March 31, 2020. The benefit for income taxes recorded during the three months ended March 31, 2021 resulted primarily from tax benefits recognized on share-based compensation.

Information by Segment

See Note 11, *Segment and Other Information*, of the notes to condensed consolidated financial statements, included in Item 1 of this Quarterly Report on Form 10-Q for a reconciliation of our segment operating income to our total loss before benefit for income taxes for the three months ended March 31, 2021 and 2020.

Orphan Segment

The following table reflects our orphan segment net sales and segment operating income for the three months ended March 31, 2021 and 2020 (in thousands, except percentages).

	For the Three Months Ended March 31,			
	2021	2020	Change	% Change
Net sales	$ 257,507	$ 245,363	$ 12,144	5%
Segment operating income	1,054	54,356	(53,302)	(98%)

The increase in orphan segment net sales during the three months ended March 31, 2021 is described in the *Consolidated Results* section above.

Segment operating income. Orphan segment operating income decreased $53.3 million to $1.1 million during the three months ended March 31, 2021, from $54.4 million during the three months ended March 31, 2020. The decrease was primarily attributable to an increase in selling, general and administrative expenses of $38.7 million and an increase in research and development expenses of $28.2 million, partially offset by an increase in net sales of $12.1 million as described above. The increase in selling, general and administrative expenses and research and development expenses were mainly due to an increase in the commercial and field-based organization for TEPEZZA, as well as incremental net operating expense from Viela after we acquired it on March 15, 2021.

Inflammation Segment

The following table reflects our inflammation segment net sales and segment operating income for the three months ended March 31, 2021 and 2020 (in thousands, except percentages).

	For the Three Months Ended March 31,			
	2021	2020	Change	% Change
Net sales	$ 84,899	$ 110,546	$ (25,647)	(23%)
Segment operating income	42,680	51,942	(9,262)	(18%)

The decrease in inflammation net sales during the three months ended March 31, 2021 is described in the *Consolidated Results* section above.

Segment operating income. Inflammation segment operating income decreased $9.3 million to $42.6 million during the three months ended March 31, 2021, from $51.9 million during the three months ended March 31, 2020. The decrease was primarily attributable to a decrease in net sales of $25.6 million as described above, partially offset by a decrease in sales and marketing expenses of $11.2 million.

NON-GAAP FINANCIAL MEASURES

EBITDA, or earnings before interest, taxes, depreciation and amortization, adjusted EBITDA, non-GAAP net income and non-GAAP earnings per share are used and provided by us as non-GAAP financial measures. These non-GAAP financial measures are intended to provide additional information on our performance, operations and profitability. Adjustments to our GAAP figures as well as EBITDA exclude acquisition/divestiture-related costs, upfront, progress and milestone payments related to license and collaboration agreements, drug substance harmonization costs, fees related to refinancing activities, restructuring and realignment costs and litigation settlements, as well as non-cash items such as share-based compensation, inventory step-up expense, depreciation and amortization, non-cash interest expense, long-lived assets impairment charges, loss on debt extinguishments, (gain) loss on sale of assets and other non-cash adjustments. Certain other special items or substantive events may also be included in the non-GAAP adjustments periodically when their magnitude is significant within the periods incurred. We maintain an established non-GAAP cost policy that guides the determination of what costs will be excluded in non-GAAP measures. We believe that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of our financial and operating performance. The non-GAAP financial measures are included with the intent of providing investors with a more complete understanding of our historical financial results and trends and to facilitate comparisons between periods. In addition, these non-GAAP financial measures are among the indicators our management uses for planning and forecasting purposes and measuring our performance. For example, adjusted EBITDA is used by us as one measure of management performance under certain incentive compensation arrangements. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, financial measures calculated in accordance with GAAP. The non-GAAP financial measures used by us may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies.

Reconciliations of reported GAAP net loss to EBITDA, adjusted EBITDA and non-GAAP net income, and the related per share amounts, were as follows (in thousands, except share and per share amounts):

	For the Three Months Ended March 31,	
	2021	2020
GAAP net loss	**$ (123,351)**	**$ (13,591)**
Depreciation (1)	4,451	7,165
Amortization and step-up:		
Intangible amortization expense (2)	66,369	58,575
Inventory step-up expense (3)	911	—
Interest expense, net (including amortization of debt discount and deferred financing costs)	13,460	17,344
Benefit for income taxes	(47,751)	(19,026)
EBITDA	**(85,911)**	**50,467**
Other non-GAAP adjustments:		
Share-based compensation (4)	61,166	56,421
Acquisition/divestiture-related costs (5)	49,108	(6)
Impairment of long-lived assets (6)	12,371	—
Restructuring and realignment costs (7)	6,093	—
Upfront, progress and milestone payments related to license and collaboration agreements (8)	3,000	—
Drug substance harmonization costs (9)	—	290
Fees related to refinancing activities (10)	—	54
Total of other non-GAAP adjustments	**131,738**	**56,759**
Adjusted EBITDA	**$ 45,827**	**$ 107,226**

	For the Three Months Ended March 31,	
	2021	2020
GAAP net loss	**$ (123,351)**	**$ (13,591)**
Non-GAAP adjustments:		
Depreciation (1)	4,451	7,165
Amortization and step-up:		
Intangible amortization expense (2)	66,369	58,575
Amortization of debt discount and deferred financing costs (11)	773	5,569
Inventory step-up expense (3)	911	—
Share-based compensation (4)	61,166	56,421
Acquisition/divestiture-related costs (5)	49,108	(6)
Impairment of long-lived assets (6)	12,371	—
Restructuring and realignment costs (7)	6,093	—
Upfront, progress and milestone payments related to license and collaboration agreements (8)	3,000	—
Drug substance harmonization costs (9)	—	290
Fees related to refinancing activities (10)	—	54
Total of pre-tax non-GAAP adjustments	**204,242**	**128,068**
Income tax effect of pre-tax non-GAAP adjustments (12)	(73,504)	(31,262)
Total non-GAAP adjustments	**130,738**	**96,806**
Non-GAAP Net income	**$ 7,387**	**$ 83,215**
Non-GAAP Earnings Per Share:		
Weighted average ordinary shares – Basic	**223,920,768**	**190,072,112**
Non-GAAP Earnings Per Share – Basic		
GAAP loss per share – Basic	**$ (0.55)**	**$ (0.07)**
Non-GAAP adjustments	0.58	0.51
Non-GAAP earnings per share – Basic	**$ 0.03**	**$ 0.44**
Non-GAAP Net income	**$ 7,387**	**$ 83,215**
Effect of assumed conversion of Exchangeable Senior Notes, net of tax	—	1,875
Numerator - non-GAAP Net income	**$ 7,387**	**$ 85,090**
Weighted average ordinary shares – Diluted		
Weighted average ordinary shares – Basic	223,920,768	190,072,112
Ordinary share equivalents	10,190,012	22,984,847
Denominator - weighted average ordinary shares – Diluted	**234,110,780**	**213,056,959**
Non-GAAP Earnings Per Share – Diluted		
GAAP loss per share – Diluted	**$ (0.55)**	**$ (0.07)**
Non-GAAP adjustments	0.58	0.51
Diluted earnings per share effect of ordinary share equivalents	—	(0.04)
Non-GAAP earnings per share – Diluted	**$ 0.03**	**$ 0.40**

(1) Represents depreciation expense related to our property, equipment, software and leasehold improvements.

(2) Intangible amortization expenses are associated with our intellectual property rights, developed technology and customer relationships related to TEPEZZA, KRYSTEXXA, RAVICTI, PROCYSBI, ACTIMMUNE, BUPHENYL, UPLIZNA, PENNSAID 2% and RAYOS.

(3) During the three months ended March 31, 2021, we recognized in cost of goods sold $0.9 million for inventory step-up expense related to UPLIZNA inventory revalued in connection with the Viela acquisition. Refer to Note 5 of the notes to the condensed consolidated financial statements, for further details.

(4) Represents share-based compensation expense associated with our stock option, restricted stock unit and performance stock unit grants to our employees and non-employee directors, and our employee share purchase plan.

(5) Represents transaction and integration costs, including, advisory, legal, consulting and certain employee-related costs, incurred in connection with our acquisitions and divestitures. Costs recovered from subleases of acquired facilities and reimbursed expenses incurred under transition arrangements for divestitures are also reflected in this line item.

(6) During the three months ended March 31, 2021, we recorded a right-of-use asset impairment charge of $12.4 million as a result of vacating the leased Lake Forest office.

(7) Represents the recording of a liability for maintenance charges as a result of vacating the leased Lake Forest office.

(8) During the three months ended March 31, 2021, we recognized a $3.0 million progress payment in relation to the collaboration agreement with HemoShear.

(9) During the year ended December 31, 2016, we entered into a definitive agreement to acquire certain rights to interferon gamma-1b, marketed as IMUKIN in an estimated thirty countries primarily in Europe and the Middle East, or the IMUKIN purchase agreement. We already owned the rights to interferon gamma-1b marketed as ACTIMMUNE in the United States, Canada and Japan. In connection with the IMUKIN purchase agreement, we also committed to pay our contract manufacturer certain amounts related to the harmonization of the manufacturing processes for ACTIMMUNE and IMUKIN drug substance, or the harmonization program. At the time we entered into the IMUKIN purchase agreement and the harmonization program commitment was made, we had anticipated achieving certain benefits should the Phase 3 clinical trial evaluating ACTIMMUNE for the treatment of Friedreich's ataxia, be successful. If the study had been successful and if U.S. marketing approval had subsequently been obtained, we had forecasted significant increases in demand for the medicine and the harmonization program would have resulted in significant benefits for us. Following our discontinuation of the Friedreich's ataxia program, we determined that certain assets, including an upfront payment related to the IMUKIN purchase agreement, were impaired, and the costs under the harmonization program would no longer have benefit to us and should be expensed as incurred.

(10) Represents arrangement and other fees relating to our refinancing activities.

(11) Represents amortization of debt discount and deferred financing costs associated with our debt.

(12) Income tax adjustments on pre-tax non-GAAP adjustments represent the estimated income tax impact of each pre-tax non-GAAP adjustment based on the statutory income tax rate of the applicable jurisdictions for each non-GAAP adjustment.

LIQUIDITY, FINANCIAL POSITION AND CAPITAL RESOURCES

We have incurred losses on a GAAP basis in most fiscal years since our inception in June 2005 and, as of March 31, 2021, we had an accumulated deficit of $339.2 million. We expect that our sales and marketing expenses will continue to increase as a result of the commercialization of our medicines and global expansion initiatives, but we believe these cost increases will be more than offset by higher net sales and gross profits in future periods. Additionally, we expect that our research and development costs will increase as we acquire or develop more development-stage medicine candidates and advance our candidates through the clinical development and regulatory approval processes. In particular, we expect to incur substantial costs in connection with advancing Viela's pipeline of medicine candidates and development programs in on-going and planned clinical trials.

On December 17, 2020, we announced that we expected a short-term disruption in TEPEZZA supply as a result of recent U.S. government-mandated COVID-19 vaccine production orders pursuant to the DPA, that dramatically restricted capacity available for the production of TEPEZZA at our drug product contract manufacturer, Catalent. This short-term supply disruption has negatively impacted our net sales of TEPEZZA. In March 2021, the FDA approved a prior approval supplement to the TEPEZZA BLA (which was previously approved in January 2020), giving us authorization to manufacture more TEPEZZA drug product resulting in an increased number of vials with each manufacturing slot. We commenced resupply of TEPEZZA to the market in April 2021. Refer to the *Impact of COVID-19* section above for further information. Due to the timing of new patients and the restarting of therapy for existing patients following the supply disruption, we expect variability in quarterly net sales of TEPEZZA for the remainder of 2021.

Further, following the highly successful launch of TEPEZZA, which significantly exceeded expectations, we are in the process of expanding our production capacity to meet anticipated future demand for TEPEZZA. As of March 31, 2021, we had total purchase commitments, including the minimum annual order quantities and binding firm orders, with AGC Biologics A/S (formerly known as CMC Biologics A/S) for TEPEZZA drug substance of €76.3 million ($89.5 million converted at a Euro-to-Dollar exchange rate as of March 31, 2021 of 1.1732), to be delivered through December 2023. In addition, we had binding purchase commitments with Catalent for TEPEZZA drug product of $6.4 million, to be delivered through March 2022.

We also expect to incur additional costs and to enter into additional purchase commitments in connection with our efforts to expand TEPEZZA production capacity in order to meet this anticipated increase in demand.

In February 2020, we purchased a three-building campus in Deerfield, Illinois, for total consideration and directly attributable transaction costs of $118.5 million. The Deerfield campus totals 70 acres and consists of approximately 650,000 square feet of office space. Our Lake Forest office employees moved to the Deerfield campus in February 2021 and we are marketing the Lake Forest office space for sublease. We made significant capital expenditures during the first quarter of 2021 in order to prepare the Deerfield campus for occupancy. In February 2021, we vacated the Lake Forest leased office building which represented a triggering event for impairment consideration of the right-of-use asset relating to this building. During the three months ended March 31, 2021, we recorded an impairment charge of $12.4 million as a result of vacating the Lake Forest office. This charge was reported within impairment of long-lived assets in the condensed consolidated statement of comprehensive loss. In addition, we recorded a liability of $6.1 million for maintenance charges as a result of vacating the leased Lake Forest office.

During the first quarter of 2021, under our license agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or together referred to as Roche, we made a milestone payment of CHF50.0 million ($56.1 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.1228) in relation to the attainment of net sales milestones. The liability for this milestone payment was recorded during the year ended December 31, 2020. In April 2021, under the acquisition agreement for River Vision Development Corp., or River Vision, we made a milestone payment of $67.0 million. The liability for this milestone payment was recorded during the year ended December 31, 2020. There are no further TEPEZZA net sales milestone obligations remaining to Roche and the former River Vision stockholders.

During the year ended December 31, 2020, we committed to invest as a strategic limited partner in four venture capital funds: Forbion Growth Opportunities Fund I C.V., Forbion Capital Fund V C.V., Aisling Capital V, L.P. and RiverVest Venture Fund V, L.P. As of March 31, 2021, the total carrying amount of our investments in these funds is $17.5 million, which is included in other assets in the consolidated balance sheet, and our total future commitments to these funds are $51.7 million.

We have financed our operations to date through equity financings, debt financings and the issuance of convertible notes, along with cash flows from operations during the last several years. As of March 31, 2021, we had $811.6 million in cash and cash equivalents and total debt with a book value of $2,578.5 million and face value of $2,618.0 million. We believe our existing cash and cash equivalents and our expected cash flows from our operations will be sufficient to fund our business needs for at least the next 12 months from the issuance of the financial statements in this Quarterly Report on Form 10-Q. We do not have any financial covenants or non-financial covenants that we expect to be affected by the economic disruptions and negative effects of the COVID-19 pandemic on the financial environment.

We have a significant amount of debt outstanding on a consolidated basis. For a description of our debt agreements, see Note 13, *Debt Agreements*, of the notes to condensed consolidated financial statements, included in Item 1 of this Quarterly Report on Form 10-Q. This substantial level of debt could have important consequences to our business, including, but not limited to: making it more difficult for us to satisfy our obligations; requiring a substantial portion of our cash flows from operations to be dedicated to the payment of principal and interest on our indebtedness, therefore reducing our ability to use our cash flows to fund acquisitions, capital expenditures, and future business opportunities; limiting our ability to obtain additional financing, including borrowing additional funds; increasing our vulnerability to, and reducing our flexibility to respond to, general adverse economic and industry conditions; limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; and placing us at a disadvantage as compared to our competitors, to the extent that they are not as highly leveraged. We may not be able to generate sufficient cash to service all of our indebtedness and may be forced to take other actions to satisfy our obligations under our indebtedness.

In addition, the indenture governing our 5.5% Senior Notes due 2027 and our Credit Agreement impose various covenants that limit our ability and/or our restricted subsidiaries' ability to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales or merger transactions, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries; and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to us.

During the three months ended March 31, 2021, we issued an aggregate of 3.3 million of our ordinary shares in connection with stock option exercises and the vesting of restricted stock units and performance stock units. We received a total of $19.8 million in proceeds in connection with such stock option exercises. During the three months ended March 31, 2021, we made payments of $128.3 million for employee withholding taxes relating to vesting of share-based awards.

Sources and Uses of Cash

The following table provides a summary of our cash position and cash flows for the three months ended March 31, 2021 and 2020 (in thousands):

	For the Three Months Ended March 31,	
	2021	2020
Cash, cash equivalents and restricted cash	$ 815,448	$ 758,262
Cash (used in) provided by:		
Operating activities	(3,728)	(62,593)
Investing activities	(2,729,499)	(218,204)
Financing activities	1,469,194	(39,614)

Operating Cash Flows

During the three months ended March 31, 2021, net cash used in operating activities of $3.7 million was primarily attributable to payments made related to patient assistance costs for our inflammation segment medicines and government rebates for our orphan segment medicines, payments related to selling, general and administrative expenses, including transaction costs related to the Viela acquisition and payments related to research and development expenses, partially offset by cash collections from gross sales, including TEPEZZA sales prior to the supply disruption.

During the three months ended March 31, 2020, net cash used in operating activities of $62.6 million was primarily attributable to payments made during the first quarter of 2020 related to patient assistance costs for our inflammation segment medicines, government rebates for our orphan segment medicines and an increase in gross sales and the timing of receipts of accounts receivable for our orphan segment medicines.

Investing Cash Flows

During the three months ended March 31, 2021, net cash used in investing activities of $2,729.5 million was primarily attributable to payments for acquisitions, net of $2,707.4 million which was primarily attributable to $2.6 billion paid in relation to the Viela acquisition, net of acquired cash. In addition, we made a milestone payment of CHF50.0 million ($56.1 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.1228) under our license agreement with Roche, during the first quarter of 2021.

During the three months ended March 31, 2020, net cash used in investing activities of $218.2 million was primarily attributable to $112.5 million paid during the first quarter of 2020 in relation to the purchase of a three-building campus in Deerfield, Illinois and contingent consideration and milestone payments for an acquisition set forth below. Under the acquisition agreement for River Vision, we made a milestone payment of $100.0 million related to FDA approval of TEPEZZA, during the first quarter of 2020. Under our license agreement Roche, we made a milestone payment of CHF5.0 million ($5.2 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.0382), during the first quarter of 2020.

Financing Cash Flows

During the three months ended March 31, 2021, net cash provided by financing activities of $1,469.2 million was primarily attributable to an additional $1.6 billion aggregate principal amount of term loans borrowed pursuant to an amendment to our Credit Agreement, the proceeds of which, in addition to a portion of our existing cash on hand, was used to pay the consideration for the Viela acquisition, partially offset by $128.3 million payment of employee withholding taxes relating to share-based awards.

During the three months ended March 31, 2020, net cash used in financing activities of $39.6 million was primarily attributable to payment of employee withholding taxes relating to share-based awards of $46.7 million, partially offset by the proceeds from the issuance of ordinary shares in connection with stock option exercises of $7.1 million.

Financial Condition as of March 31, 2021 compared to December 31, 2020

Accounts receivable, net. Accounts receivable, net, decreased $216.5 million, from $659.7 million as of December 31, 2020 to $443.2 million as of March 31, 2021. The decrease was primarily due to significant cash inflows from the collection in the first quarter of 2021 of receivables from 2020 TEPEZZA sales. In addition, there were no TEPEZZA-related receivables recorded in the first quarter of 2021 due to the TEPEZZA supply disruption.

Inventories, net. Inventories, net, increased $163.0 million, from $75.3 million as of December 31, 2020 to $238.3 million as of March 31, 2021. The increase was primarily due to stepped-up UPLIZNA inventory of $148.4 million, which consisted of $119.0 million of stepped-up work in process, $19.3 million of stepped-up finished goods and $10.1 million stepped-up raw materials.

Prepaid expenses and other current assets. Prepaid expenses and other current assets increased $82.5 million, from $251.9 million as of December 31, 2020 to $334.4 million as of March 31, 2021. The increase was primarily due to an increase in advance payments for TEPEZZA inventory of $30.1 million and a $23.4 million increase in prepaid income taxes and income taxes receivable primarily due to a benefit for income taxes recognized during the three months ended March 31, 2021.

Developed technology, net. Developed technology, net, increased $1,427.3 million, from $1,782.9 million as of December 31, 2020 to $3,210.2 million as of March 31, 2021. During the three months ended March 31, 2021, in connection with the acquisition of Viela, we capitalized $1,493.0 million of developed technology related to UPLIZNA. This was partially offset by amortization of developed technology of $66.4 million during the three months ended March 31, 2021.

In-process research and development. On March 15, 2021, we completed the acquisition of Viela and acquired $910.0 million of in-process research and development, or IPR&D. On March 24, 2021, we announced that our strategic partner, Mitsubishi Tanabe Pharma Corporation, had received manufacturing and marketing approval of UPLIZNA in Japan. As a result, we transferred $30.0 million of IPR&D to developed technology. As of March 31, 2021, the remaining IPR&D relating to the Viela acquisition was $880.0 million.

Goodwill. Goodwill increased $662.7 million, from $413.7 million as of December 31, 2020 to $1,076.4 million as of March 31, 2021 due to the Viela acquisition. Refer to Note 4 of the notes to condensed consolidated financial statements, for further details of this acquisition.

Accrued expenses. Accrued expenses decreased $95.9 million, from $485.5 million as of December 31, 2020 to $389.6 million as of March 31, 2021. During the first quarter of 2021, under our license agreement with Roche, we made a milestone payment of CHF50.0 million ($56.1 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.1228). Additionally, accrued royalties decreased by $44.2 million due to a decrease in royalties payable on net sales of TEPEZZA due to the TEPEZZA supply disruption.

Accrued trade discounts and rebates. Accrued trade discounts and rebates decreased $27.2 million, from $352.4 million as of December 31, 2020 to $325.2 million as of March 31, 2021. This was primarily due to a decrease in accrued co-pay and other patient assistance costs primarily due to lower utilization of our patient assistance programs and a decrease in accrued wholesaler fees as a result of the TEPEZZA supply disruption.

Long-term debt, net. Long-term debt, net increased $1,559.1 million from $1,003.4 million as of December 31, 2020 to $2,562.5 million as of March 31, 2021. The increase was primarily related an additional $1.6 billion aggregate principal amount of term loans we borrowed pursuant to an amendment to our Credit Agreement, the proceeds of which, in addition to a portion of our existing cash on hand, was used to pay the consideration for the Viela acquisition. See Note 13, *Debt Agreements*, of the notes to condensed consolidated financial statements, included in Item 1 of this Quarterly Report on Form 10-Q.

Deferred tax liabilities, net. Deferred tax liabilities, net, increased $457.9 million from $66.5 million as of December 31, 2020 to $524.4 million as of March 31, 2021 primarily due to the Viela acquisition. Refer to Note 4 of the notes to condensed consolidated financial statements, for further details of this acquisition.

Contractual Obligations

During the three months ended March 31, 2021, there were no material changes outside of the ordinary course of business to our contractual obligations as previously disclosed in Part II, Item 7 of our Annual Report on Form 10-K for the fiscal year ended December 31, 2020, except for our entry into the following commitments described below.

On March 15, 2021, we completed the acquisition of Viela, in which we acquired all of the issued and outstanding shares of Viela's common stock for $53.00 per share in cash. The total consideration for the acquisition was approximately $3.0 billion, including cash acquired of $342.3 million. Refer to Note 4 of the notes to condensed consolidated financial statements for further details of this acquisition.

CRITICAL ACCOUNTING POLICIES

The preparation of financial statements in accordance with U.S. GAAP principles requires the use of estimates and assumptions that affect the reported amounts of assets and liabilities and the reported amounts of revenue and expenses. Certain of these policies are considered critical as these most significantly impact a company's financial condition and results of operations and require the most difficult, subjective or complex judgments, often as a result of the need to make estimates about the effect of matters that are inherently uncertain. Actual results may vary from these estimates.

During the three months ended March 31, 2021, there have been no significant changes in our application of our critical accounting policies. A summary of our critical accounting policies is included in Item 7 to our Annual Report on Form 10-K for the year ended December 31, 2020.

OFF-BALANCE SHEET ARRANGEMENTS

Since our inception, we have not engaged in any off-balance sheet arrangements, including the use of structured finance, special purpose entities or variable interest entities, other than the indemnification agreements discussed in Note 15, *Commitments and Contingencies*, of the notes to condensed consolidated financial statements, included in Item 1 of this Quarterly Report on Form 10-Q.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

We are exposed to various market risks, which include potential losses arising from adverse changes in market rates and prices, such as interest rates and foreign exchange fluctuations. We do not enter into derivatives or other financial instruments for trading or speculative purposes.

Interest Rate Risk. We are subject to interest rate fluctuation exposure through our borrowings under our Credit Agreement and our investment in money market accounts which bear a variable interest rate. Our approximately $418.0 million aggregate principal amount of senior secured term loans borrowed under our Credit Agreement in December 2019, or the December 2019 Term Loans, and loans under our incremental revolving credit facility, or Revolving Credit Facility, bear interest, at our option, at a rate equal to the London Inter-Bank Offered Rate, or LIBOR, plus 2.25% per annum (subject to a 0.00% LIBOR floor), or the adjusted base rate plus 1.25% per annum with a step-down to LIBOR plus 2.00% per annum or the adjusted base rate plus 1.00% per annum at the time our leverage ratio is less than or equal to 2.00 to 1.00. The adjusted base rate is defined as the greatest of (a) LIBOR (using one-month interest period) plus 1.00%, (b) the prime rate, (c) the federal funds rate plus 0.50%, and (d) 1.00%. Our December 2019 Term Loans are based on LIBOR. The one-month LIBOR rate as of April 16, 2021, which was the most recent date the interest rate on the December 2019 Term Loans was fixed, was 0.13%, and as a result, the interest rate on our December 2019 Term Loans is currently 2.13% per annum. As of March 31, 2021, the Revolving Credit Facility was undrawn. Our $1.6 billion aggregate principal amount of senior secured term loans borrowed under our Credit Agreement in March 2021, or the Incremental Loans, bear interest, at our option, at a rate equal to LIBOR, plus 2.00% per annum (subject to a 0.50% LIBOR floor), or the adjusted base rate plus 1.00% per annum with a step-down to LIBOR plus 1.75% per annum or the adjusted base rate plus 0.75% per annum at the time our leverage ratio is less than or equal to 2.00 to 1.00. Our Incremental Loans are based on LIBOR. The one-month LIBOR rate as of April 16, 2021, which was the most recent date the interest rate on the Incremental Loans was fixed, was 0.13%, and as a result, the interest rate on our Incremental Loans is currently 2.50% per annum. Because the United Kingdom Financial Conduct Authority, which regulates LIBOR, intends to phase out the use of LIBOR by the end of 2021, future borrowings under our Credit Agreement could be subject to reference rates other than LIBOR.

An increase in the LIBOR of 100 basis points above the current LIBOR rate would increase our interest expense related to the Credit Agreement by $14.2 million per year.

The goals of our investment policy are to preserve capital, fulfill liquidity needs and maintain fiduciary control of cash. To achieve our goal of maximizing income without assuming significant market risk, we maintain our excess cash and cash equivalents in money market funds. Because of the short-term maturities of our cash equivalents, we do not believe that a decrease in interest rates would have any material negative impact on the fair value of our cash equivalents.

Foreign Currency Risk. Our purchase costs of TEPEZZA drug substance and ACTIMMUNE inventory are principally denominated in Euros and are subject to foreign currency risk. In addition, we are obligated to pay certain milestones and a royalty on sales of TEPEZZA to Roche in Swiss Francs, which obligations are subject to foreign currency risk. We have contracts relating to RAVICTI, QUINSAIR and PROCYSBI for sales in Canada which sales are subject to foreign currency risk. We also incur certain operating expenses in currencies other than the U.S. dollar in relation to our Irish operations and foreign subsidiaries. Therefore, we are subject to volatility in cash flows due to fluctuations in foreign currency exchange rates, particularly changes in the Euro, the Swiss Franc and the Canadian dollar.

Inflation Risk. We do not believe that inflation has had a material impact on our business or results of operations during the periods for which the condensed consolidated financial statements are presented in this report.

Credit Risk. Historically, our accounts receivable balances have been highly concentrated with a select number of customers, consisting primarily of large wholesale pharmaceutical distributors who, in turn, sell the medicines to pharmacies, hospitals and other customers. As of March 31, 2021 and December 31, 2020, our top four customers accounted for approximately 86% and 93%, respectively, of our total outstanding accounts receivable balances.

ITEM 4. CONTROLS AND PROCEDURES

Evaluation of Disclosure Controls and Procedures. As required by paragraph (b) of Rules 13a-15 and 15d-15 promulgated under the Exchange Act, our management, including our Chief Executive Officer and Chief Financial Officer, conducted an evaluation as of the end of the period covered by this report of the effectiveness of our disclosure controls and procedures as defined in Exchange Act Rules 13a-15(e) and 15d-15(e). Based on that evaluation, our Chief Executive Officer and Chief Financial Officer concluded that our disclosure controls and procedures were effective as of March 31, 2021, the end of the period covered by this report.

Changes in Internal Control Over Financial Reporting. As discussed above, we completed the Viela acquisition on March 15, 2021. The results of operations of the acquired Viela business are included in our results of operations beginning on March 15, 2021. We are currently in the process of evaluating and integrating Viela's historical internal controls over financial reporting with ours.

During the quarter ended March 31, 2021, other than continuing changes to our internal control processes resulting from the Viela acquisition, there have been no material changes to our internal control over financial reporting, as defined in Rules 13a-15(f) and 15d-15(f), that have materially affected, or are reasonably likely to materially affect, our internal control over financial reporting.

PART II. OTHER INFORMATION

ITEM 1. LEGAL PROCEEDINGS

For a description of our legal proceedings, see Note 16, *Legal Proceedings*, of the Notes to Unaudited Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q.

ITEM 1A: RISK FACTORS

Risk Factors Summary

We face many risks and uncertainties, as more fully described in this section under the heading "Risk Factors." Some of these risks and uncertainties are summarized below. The summary below does not contain all of the information that may be important to you, and you should read this summary together with the more detailed discussion of these risks and uncertainties contained in "Risk Factors."

- The COVID-19 global pandemic has and may continue to adversely impact our business, including the commercialization of our medicines, our supply chain, our clinical trials, our liquidity and access to capital markets and our business development activities.
- Our ability to generate revenues from our medicines is subject to attaining significant market acceptance among physicians, patients and healthcare payers.
- Our future prospects are highly dependent on our ability to successfully develop and execute commercialization strategies for each of our medicines. Failure to do so would adversely impact our financial condition and prospects.
- In order to increase adoption and sales of our medicines, we will need to continue developing our commercial organization as well as recruit and retain qualified sales representatives.
- Coverage and reimbursement may not be available, or reimbursement may be available at only limited levels, for our medicines, which could make it difficult for us to sell our medicines profitably or to successfully execute planned medicine price increases.
- Our medicines are subject to extensive regulation, and we may not obtain additional regulatory approvals for our medicines.
- We may be subject to penalties and litigation and large incremental expenses if we fail to comply with regulatory requirements or experience problems with our medicines.
- We rely on third parties to manufacture commercial supplies of all of our medicines, and we currently intend to rely on third parties to manufacture commercial supplies of any other approved medicines. The commercialization of any of our medicines could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of medicine or fail to do so at acceptable quality levels or prices or fail to maintain or achieve satisfactory regulatory compliance.
- We face significant competition from other biotechnology and pharmaceutical companies, including those marketing generic medicines and our operating results will suffer if we fail to compete effectively.
- Clinical development of drugs and biologics involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.
- If we fail to develop or acquire other medicine candidates or medicines, our business and prospects would be limited.
- We are subject to ongoing obligations and continued regulatory review by the FDA and equivalent foreign regulatory agencies, which may result in significant additional expense and significant penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our medicines.
- We are subject to federal, state and foreign healthcare laws and regulations and implementation or changes to such healthcare laws and regulations could adversely affect our business and results of operations.
- If we are unable to obtain or protect intellectual property rights related to our medicines and medicine candidates, we may not be able to compete effectively in our markets.

Risk Factors

You should consider carefully the risks described below, together with all of the other information included in this report, and in our other filings with the Securities and Exchange Commission, or SEC, before deciding whether to invest in or continue to hold our ordinary shares. The risks described below are all material risks currently known, expected or reasonably foreseeable by us. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our ordinary shares to decline, resulting in a loss of all or part of your investment.

The risk factors set forth below with an asterisk (*) next to the title are new risk factors or risk factors containing changes, including any material changes, from the risk factors previously disclosed in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2020, as filed with the SEC.

Risks Related to Our Business and Industry

*The COVID-19 global pandemic has and may continue to adversely impact our business, including the commercialization of our medicines, our supply chain, our clinical trials, our liquidity and access to capital markets and our business development activities.**

On March 11, 2020, the World Health Organization made the assessment that a novel strain of coronavirus, which causes the COVID-19 disease, was a pandemic. The President of the United States declared the COVID-19 pandemic a national emergency and many states and municipalities in the United States took aggressive actions to reduce the spread of the disease, including limiting non-essential gatherings of people, ceasing all non-essential travel, ordering certain businesses and government agencies to cease non-essential operations at physical locations and issuing "shelter-in-place" orders which direct individuals to shelter at their places of residence (subject to limited exceptions). Similarly, the Irish government has limited gatherings of people and encouraged employees to work from their homes, and may implement more aggressive policies in the future. In addition, in mid-March 2020 we implemented work-from-home policies for all employees and moved to a "virtual" model with respect to our physician, patient and partner support activities. As certain U.S. states started to reduce restrictions, we saw physician offices beginning to reopen, which reopening has varied on a state-by-state basis. As a result, our sales representatives in some areas have transitioned to being back out in the field and are working on ways to re-engage patients and physicians in person. However, as COVID-19 cases have increased in certain areas, certain U.S. states have started to reimplement restrictions and we have seen some physician offices re-establish limits on in-person visits. Restrictions in response to COVID-19 may continue to fluctuate in U.S. states and other geographies and we cannot guarantee that additional U.S. states that have previously reduced restrictions will not reimplement them or that other states will reduce restrictions in the near-term. The effects of government actions and our policies and those of third parties to reduce the spread of COVID-19 may negatively impact productivity and our ability to market and sell our medicines, cause disruptions to our supply chain and ongoing and future clinical trials and impair our ability to execute our business development strategy. These and other disruptions in our operations and the global economy could negatively impact our business, operating results and financial condition.

The commercialization of our medicines has been and will continue to be adversely impacted by COVID-19 and actions taken to slow its spread. For example, patients have postponed visits to healthcare provider facilities, certain healthcare providers have temporarily closed their offices or are restricting patient visits, healthcare provider employees may become generally unavailable and there could be disruptions in the operations of payers, distributors, logistics providers and other third parties that are necessary for our medicines to be prescribed, reimbursed and administered to patients. In March 2020, we transitioned our sales force to a virtual model such that they no longer had in-person interactions with healthcare professionals and while we have been working on ways to re-engage patients and physicians as certain U.S. states have started to reduce restrictions, the virtual model is still being used. While we have attempted to maintain the effectiveness of our sales and marketing efforts in the virtual model, it may not be as effective as in-person interactions in terms of conveying key information about our medicines or aiding physicians and their staff in prescribing and helping their patients obtain appropriate reimbursement for our medicines. Many physicians, in particular in primary care practices that prescribe our inflammation segment medicines, have reduced their operations in light of COVID-19, including delaying patient visits and writing new prescriptions, and this has negatively impacted sales in our inflammation segment. Similarly, many patients have deferred non-essential visits to healthcare providers, which has had a negative impact on prescriptions being written and filled. For example, due to reduced willingness of patients to visit physician offices and infusion centers, sales of KRYSTEXXA have been negatively impacted, and we expect this impact to continue in future quarters until healthcare activities and patient visits return to normal levels. In addition, while we experienced a much higher number of new patients in 2020 for TEPEZZA than our initial estimates, the impact from COVID-19 slowed the generation of patient enrollment forms for TEPEZZA, which drive new patient starts, and this impact may continue following the recent end of the TEPEZZA supply disruption. It is also possible that a prolonged period of "shelter-in-place" orders and social distancing behaviors and the associated reduction of physician office visits could force various healthcare practices to permanently close or to consolidate with larger practices or healthcare groups, which could cause us to lose previously-established physician relationships. We cannot predict how long the COVID-19 pandemic will continue to negatively impact sales of our medicines and we expect that even after government-mandated restrictions are lifted, our sales force activities, healthcare provider operations and patients' willingness to visit healthcare facilities will continue to be limited. We also cannot predict how effective our virtual patient, physician and partner support initiatives will be with respect to marketing and supporting the administration and reimbursement of our medicines, or when we will be able to resume other in-person sales and marketing activities.

Quarantines, shelter-in-place and similar government orders, or the perception that such orders, shutdowns or other restrictions on the conduct of business operations could occur, related to COVID-19 or other infectious diseases could impact personnel at third-party manufacturing facilities upon which we rely, or the availability or cost of materials, which could disrupt the supply chain for our medicines. In particular, some of our suppliers of certain materials used in the production of our medicines are located in regions that have been subject to COVID-19-related actions and policies that limit the conduct of normal business operations. To the extent our suppliers and service providers are unable to comply with their obligations under our agreements with them or they are otherwise unable to deliver or are delayed in delivering goods and services to us due to COVID-19, our ability to continue meeting commercial demand for our medicines in the United States or advancing development of our medicine candidates may become impaired. For example, On December 17, 2020, we announced that we expected a short-term disruption in TEPEZZA supply as a result of recent U.S. government-mandated COVID-19 vaccine production pursuant to the Defense Production Act of 1950, or DPA, that have dramatically restricted capacity available for the production of TEPEZZA at our drug product contract manufacturer, Catalent Indiana, LLC, or Catalent. In March 2021, the FDA approved a prior approval supplement to the TEPEZZA Biologics Licensing Application, or BLA (which was previously approved in January 2020), giving us authorization to manufacture more TEPEZZA drug product resulting in an increased number of vials with each manufacturing slot. We commenced resupply of TEPEZZA to the market in April 2021. However, our ability to continue TEPEZZA supply is dependent on future committed manufacturing slots for TEPEZZA not being cancelled and being run successfully, which could be impacted by additional government-mandated COVID-19 vaccine production orders and other risks associated with our reliance on our third party manufacturers discussed below. If we were to experience another disruption of TEPEZZA supply, it would have a material adverse effect on or operating results and ability to achieve our financial projections in 2021. Refer to the *Impact of COVID-19* section in Item 2 of this Quarterly Report on Form 10-Q for further information. At this time, we consider our inventories on hand of all of our other medicines to be sufficient to meet our commercial requirements.

Our clinical trials may be affected by COVID-19. As described in the *Impact of COVID-19* section in Item 2 of this Quarterly Report on Form 10-Q, two of our clinical trials for TEPEZZA have been delayed due to the impact of the TEPEZZA supply disruption at Catalent. In addition, clinical site initiation and patient enrollment may be delayed due to prioritization of hospital and healthcare resources toward COVID-19. Current or potential patients in our ongoing or planned clinical trials may also choose to not enroll, not participate in follow-up clinical visits or drop out of the trial as a precaution against contracting COVID-19. Further, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Some clinical sites in the United States have slowed or stopped further enrollment of new patients in clinical trials, denied access to site monitors or otherwise curtailed certain operations. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted. These events could delay our clinical trials, increase the cost of completing our clinical trials and negatively impact the integrity, reliability or robustness of the data from our clinical trials.

The spread of COVID-19 and actions taken to reduce its spread may also materially affect us economically. As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly or more dilutive. While the potential economic impact brought by, and the duration of, COVID-19 may be difficult to assess or predict, there could be a significant disruption of global financial markets, reducing our ability to access capital, which could in the future negatively affect our liquidity and financial position or our business development activities.

COVID-19 continues to rapidly evolve. The extent to which COVID-19 may impact the commercialization of our medicines, our supply chain, our clinical trials, our access to capital and our business development activities, will depend on future developments, which are highly uncertain and cannot be predicted with confidence, such as the ultimate geographic spread of the pandemic, the duration of the pandemic and the efforts by governments and business to contain it, business closures or business disruptions and the impact on the economy and capital markets.

*Our ability to generate revenues from our medicines is subject to attaining significant market acceptance among physicians, patients and healthcare payers.**

Our current medicines, and other medicines or medicine candidates that we may develop or acquire, may not attain market acceptance among physicians, patients, healthcare payers or the medical community. Some of our medicines, in particular TEPEZZA and UPLIZNA, have not been on the market for an extended period of time, which subjects us to numerous risks as we attempt to increase our market share. We believe that the degree of market acceptance and our ability to generate revenues from our medicines will depend on a number of factors, including:

- timing of market introduction of our medicines as well as competitive medicines;
- efficacy and safety of our medicines;
- continued projected growth of the markets in which our medicines compete;
- the extent to which physicians diagnose and treat the conditions that our medicines are approved to treat;
- prevalence and severity of any side effects;

- if and when we are able to obtain regulatory approvals for additional indications for our medicines;
- acceptance by patients, physicians and applicable specialists;
- availability of, and ability to maintain, coverage and adequate reimbursement and pricing from government and other third-party payers;
- potential or perceived advantages or disadvantages of our medicines over alternative treatments, including cost of treatment and relative convenience and ease of administration;
- strength of sales, marketing and distribution support;
- the price of our medicines, both in absolute terms and relative to alternative treatments;
- impact of past and limitation of future medicine price increases;
- our ability to maintain a continuous supply of our medicines for commercial sale;
- the effect of current and future healthcare laws;
- the extent and duration of the COVID-19 pandemic, including the extent to which physicians and patients delay visits or writing or filling prescriptions for our medicines, the extent to which operations of healthcare facilities, including infusion centers, are reduced and the length of time and the extent to which our sales force must continue operating in a virtual model;
- the performance of third-party distribution partners, over which we have limited control; and
- medicine labeling or medicine insert requirements of the U.S. Food and Drug Administration, or FDA, or other regulatory authorities

With respect to TEPEZZA, sales will depend on market acceptance and adoption by physicians and healthcare payers, as well as the ability and willingness of physicians who do not have in-house infusion capability to refer patients to infusion sites of care. With respect to KRYSTEXXA, our ability to grow sales will be affected by the success of our sales, marketing and clinical strategies, which are intended to expand the patient population and usage of KRYSTEXXA. This includes our marketing efforts in nephrology and our studies designed to improve the response rate to KRYSTEXXA, to evaluate a shorter infusion time, and to evaluate the use of KRYSTEXXA in kidney transplant patients. With respect to RAVICTI, which is approved to treat a very limited patient population, our ability to grow sales will depend in large part on our ability to transition urea cycle disorder, or UCD, patients from BUPHENYL or generic equivalents, which are comparatively much less expensive, to RAVICTI and to educate patients and physicians on the benefits of continuing RAVICTI therapy once initiated. With respect to PROCYSBI, which is also approved to treat a very limited patient population, our ability to grow sales will depend in large part on our ability to transition patients from the first-generation immediate-release cysteamine therapy to PROCYSBI, to identify additional patients with nephropathic cystinosis and to educate patients and physicians on the benefits of continuing therapy once initiated. With respect to ACTIMMUNE, while it is the only FDA-approved treatment for chronic granulomatous disease, or CGD, and severe, malignant osteopetrosis, or SMO, they are very rare conditions and, as a result, our ability to grow ACTIMMUNE sales will depend on our ability to identify additional patients with such conditions and educate patients and physicians on the benefits of continuing treatment once initiated. With respect to UPLIZNA, sales will depend on market acceptance and adoption by physicians and healthcare payers, as well as the ability and willingness of physicians who do not have in-house infusion capability to refer patients to infusion sites of care. With respect to each of PENNSAID 2% w/w, or PENNSAID 2%, RAYOS and DUEXIS, their higher cost compared to the generic or branded forms of their active ingredients alone may limit adoption by physicians, patients and healthcare payers. With respect to DUEXIS, if physicians remain unaware of, or do not otherwise believe in, the benefits of combining gastrointestinal protective agents with NSAIDs, our market opportunity will be limited. If our current medicines or any other medicine that we may seek approval for, or acquire, fail to attain market acceptance, we may not be able to generate significant revenue to sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects (including, possibly, the value of our ordinary shares).

*Our future prospects are highly dependent on our ability to successfully develop and execute commercialization strategies for each of our medicines. Failure to do so would adversely impact our financial condition and prospects.**

A substantial majority of our resources are focused on the commercialization of our current medicines. Our ability to generate significant medicine revenues and to achieve commercial success in the near-term will initially depend almost entirely on our ability to successfully commercialize these medicines in the United States. With respect to our rare disease medicines, TEPEZZA, KRYSTEXXA, RAVICTI, PROCYSBI, ACTIMMUNE and UPLIZNA, our commercialization strategy includes efforts to increase awareness of the rare conditions that each medicine is designed to treat, enhancing efforts to identify target patients and in certain cases pursue opportunities for label expansion and more effective use through clinical trials. Our comprehensive post-launch commercial strategy for TEPEZZA aims to enable more thyroid eye disease, or TED, patients to benefit from TEPEZZA. We are doing this by: (i) facilitating continued TEPEZZA uptake in the treatment of acute and chronic TED through continued promotion of TEPEZZA to treating physicians; (ii) continuing to develop the TED market by increasing physician awareness of the disease severity, the urgency to diagnose and treat it, as well as the benefits of treatment with TEPEZZA; (iii) driving accelerated disease identification and time to treatment through our digital and broadcast marketing campaigns; (iv) enhancing the patient journey with our high-touch, patient-centric model as well as support for the patient and site-of-care referral processes; and (v) expanding more timely access to TEPEZZA for TED patients. Our strategy with respect to KRYSTEXXA includes existing rheumatology account growth, new rheumatology account growth and accelerating nephrology growth, as well as development efforts to enhance response rates through combination treatment with methotrexate and to shorten the infusion time. With respect to RAVICTI and PROCYSBI, our strategy includes accelerating the transition of patients from first-generation therapies, increasing the diagnosis of the associated rare conditions through patient and physician outreach; and increasing compliance rates. Our strategy with respect to ACTIMMUNE, includes increasing awareness and diagnosis of chronic granulomatous disease and increasing compliance rates. With respect to our strategy for UPLIZNA, which leverages the successful strategies we have employed with TEPEZZA and KRYSTEXXA, our aim is to (i) generate greater demand for the medicine by investing in the commercial and clinical support infrastructure; (ii) drive physician awareness of the benefits of UPLIZNA for the treatment of neuromyelitis optica spectrum disorder, or NMOSD, and what differentiates UPLIZNA from other medicines by generating additional trial data analyses and clinical evidence; and (iii) optimize timely access for patients to UPLIZNA with best-in-class patient services, infusion site-of-care referral processes and reimbursement support services. A key component of the strategy is to complete a comprehensive assessment of the current overall commercial and clinical support infrastructure for UPLIZNA to ensure optimal support for the medicine.

We are focusing a significant portion of our commercial activities and resources on TEPEZZA, and we believe our ability to grow our long-term revenues, and a significant portion of the value of our company, relates to our ability to successfully commercialize TEPEZZA in the United States. As a newly launched medicine for a disease that had no previously-approved treatments, successful commercialization of TEPEZZA is subject to many risks. There are numerous examples of unsuccessful product launches and failures to meet high expectations of market potential, including by pharmaceutical companies with more experience and resources than us. While we have established our commercial team and U.S. sales force, we will need to further train and develop the team in order to successfully commercialize TEPEZZA. There are many factors that could cause commercialization of TEPEZZA to be unsuccessful, including a number of factors that are outside our control. Because no medicine has previously been approved by the FDA for the treatment of TED, it is especially difficult to estimate TEPEZZA's market potential or the time it will take to increase patient and physician awareness of TED and change current treatment paradigms. For example, shortly after the launch of TEPEZZA, we transitioned our sales force to a virtual model in light of the COVID-19 pandemic, which, combined with physicians generally reducing their own availability, has made it more challenging to execute on our strategy to educate physicians about TEPEZZA and the treatment of TED. In addition, some physicians that are potential prescribers of TEPEZZA do not have the necessary infusion capabilities to administer the medicine and may not otherwise be able or willing to refer their patients to third-party infusion centers, which may discourage them from treating their patients with TEPEZZA. The commercial success of TEPEZZA depends on the extent to which patients and physicians accept and adopt TEPEZZA as a treatment for TED. For example, if the patient population suffering from TED is smaller than we estimate, if it proves difficult to identify TED patients or educate physicians as to the availability and potential benefits of TEPEZZA, or if physicians are unwilling to prescribe or patients are unwilling to take TEPEZZA, the commercial potential of TEPEZZA will be limited. In addition, the prior disruption in TEPEZZA supply resulted in existing patients stopping therapy and an inability of new patients to initiate therapy. We began resupplying TEPEZZA to the market in April 2021, and we cannot be certain how many prior TEPEZZA patients will re-initiate therapy or whether or when growth in TEPEZZA adoption will return to levels seen prior to the supply disruption. We also have limited information regarding how physicians, patients and payers will respond to the pricing of TEPEZZA. Physicians may not prescribe TEPEZZA and patients may be unwilling to use TEPEZZA if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Thus, significant uncertainty remains regarding the commercial potential of TEPEZZA. If the continued commercialization of TEPEZZA becomes unsuccessful or perceived as disappointing, the price of our ordinary shares could decline significantly and long-term success of the medicine and our company could be harmed.

With respect to our inflammation segment medicines, PENNSAID 2% and DUEXIS, our strategy has included entering into rebate agreements with pharmacy benefit managers, or PBMs, for certain of our inflammation segment medicines where we believe the rebates and costs justify expanded formulary access for patients and ensuring patient assistance to these drugs when prescribed through our HorizonCares program. However, we cannot guarantee that we will be able to secure additional rebate agreements on commercially reasonable terms, that expected volume growth will sufficiently offset the rebates and fees paid to PBMs or that our existing agreements with PBMs will have the intended impact on formulary access. In addition, as the terms of our existing agreements with PBMs expire, we may not be able to renew the agreements on commercially favorable terms, or at all. For each of our inflammation segment medicines, we expect that our commercial success will depend on our sales and marketing efforts in the United States, reimbursement decisions by commercial payers, the expense we incur through our patient assistance program for fully bought down contracts and the rebates we pay to PBMs, as well as the impact of numerous efforts at federal, state and local levels to further reduce reimbursement and net pricing of inflammation segment medicines.

Our strategy for RAYOS in the United States is to focus on the rheumatology indications approved for RAYOS, including our collaboration with the Alliance for Lupus Research, to study the effect of RAYOS on the fatigue experienced by systemic lupus erythematosus, or SLE, patients.

If any of our commercial strategies are unsuccessful or we fail to successfully modify our strategies over time due to changing market conditions, our ability to increase market share for our medicines, grow revenues and to sustain profitability will be harmed.

We are dependent on wholesale distributors for distribution of our products in the United States and, accordingly, our results of operations could be adversely affected if they encounter financial difficulties.

In 2020, four wholesale distributors accounted for substantially all of our sales in the United States. If one of our significant wholesale distributors encounters financial or other difficulties, such distributor may decrease the amount of business that it does with us, and we may be unable to collect all the amounts that the distributor owes on a timely basis or at all, which could negatively impact our business and results of operations.

*In order to increase adoption and sales of our medicines, we will need to continue developing our commercial organization as well as recruit and retain qualified sales representatives.**

Part of our strategy is to continue to build a biotech company to successfully execute the commercialization of our medicines in the U.S. market, and in selected markets outside the United States where we have commercial rights. We may not be able to successfully commercialize our medicines in the United States or in any other territories where we have commercial rights. In order to commercialize any approved medicines, we must continue to build our sales, marketing, distribution, managerial and other non-technical capabilities. As of March 31, 2021, we had approximately 495 sales representatives in the field, consisting of approximately 265 orphan segment sales representatives and 230 inflammation segment sales representatives. We currently have limited resources compared to some of our competitors, and the continued development of our own commercial organization to market our medicines and any additional medicines we may acquire will be expensive and time-consuming. We also cannot be certain that we will be able to continue to successfully develop this capability.

As we continue to add medicines through development efforts and acquisition transactions and execute on our international expansion initiatives, the members of our sales force may have limited experience promoting certain of our medicines. To the extent we employ an acquired entity's sales forces to promote acquired medicines, we may not be successful in continuing to retain these employees and we otherwise will have limited experience marketing these medicines under our commercial organization. In addition, none of the members of our sales force have promoted TEPEZZA or any other medicine for the treatment of TED prior to the launch of TEPEZZA and prior to completing the acquisition of Viela Bio, Inc., or Viela, in March 2021, we had no experience as an organization commercializing UPLIZNA. We are required to expend significant time and resources to train our sales force to be credible and able to educate physicians on the benefits of prescribing and pharmacists dispensing our medicines. In addition, we must train our sales force to ensure that a consistent and appropriate message about our medicines is being delivered to our potential customers. Our sales representatives may also experience challenges promoting multiple medicines when we call on physicians and their office staff. We have experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire, requiring us to train new sales representatives. If we are unable to recruit and retain qualified personnel outside of the United States, we may not be able to execute our global expansion strategy successfully. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate physicians about the benefits of our medicines and their proper administration and label indication, as well as our patient assistance programs, our efforts to successfully commercialize our medicines could be put in jeopardy, which could have a material adverse effect on our financial condition, share price and operations. For example, we have had to train our sales force to operate in a virtual environment due to the COVID-19 pandemic and are continuing to learn and implement new strategies and techniques to promote our medicines without the benefit of in-person interactions with healthcare providers and their staff. We may not be successful in finding effective ways to promote our medicines remotely or our competitors may be more successful than we are at adapting to virtual marketing.

As a result of the evolving role of various constituents in the prescription decision making process, we focus on hiring sales representatives for our inflammation segment medicines with successful business to business experience. For example, we have faced challenges due to pharmacists switching a patient's intended prescription from DUEXIS to a generic or over-the-counter brand of their active ingredients, despite such substitution being off-label in the case of DUEXIS. We have faced similar challenges for PENNSAID 2% and RAYOS with respect to generic brands. While we believe the profile of our representatives is suited for this environment, we cannot be certain that our representatives will be able to successfully protect our market for PENNSAID 2%, DUEXIS and RAYOS or that we will be able to continue attracting and retaining sales representatives with our desired profile and skills. We will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire, train and retain commercial personnel. To the extent we rely on additional third parties to commercialize any approved medicines, we may receive less revenue than if we commercialized these medicines ourselves. In addition, we may have little or no control over the sales efforts of any third parties involved in our commercialization efforts. In the event we are unable to successfully develop and maintain our own commercial organization or collaborate with a third-party sales and marketing organization, we may not be able to commercialize our medicines and medicine candidates and execute on our business plan.

Coverage and reimbursement may not be available, or reimbursement may be available at only limited levels, for our medicines, which could make it difficult for us to sell our medicines profitably or to successfully execute planned medicine price increases.

Market acceptance and sales of our medicines will depend in large part on global coverage and reimbursement policies and may be affected by future healthcare reform measures, both in the United States and other key international markets. Successful commercialization of our medicines will depend in part on the availability of governmental and third-party payer reimbursement for the cost of our medicines. Government health administration authorities, private health insurers and other organizations generally provide reimbursement for healthcare. In particular, in the United States, private health insurers and other third-party payers often provide reimbursement for medicines and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the United States, the European Union, or EU, and other significant or potentially significant markets for our medicines and medicine candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medicines and services, particularly for new and innovative medicines and therapies, which has resulted in lower average selling prices. Further, the increased scrutiny of prescription drug pricing practices and emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU and other significant or potentially significant markets will put additional pressure on medicine pricing, reimbursement and usage, which may adversely affect our medicine sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, pharmaceutical reimbursement policies and pricing in general. These pressures may create negative reactions to any medicine price increases, or limit the amount by which we may be able to increase our medicine prices, which may adversely affect our medicine sales and results of operations.

We expect to experience pricing pressures in connection with the sale of our medicines due to the trend toward managed healthcare, the increasing influence of health maintenance organizations and additional legislative proposals relating to outcomes and quality. For example, the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act, or collectively the ACA, increased the mandated Medicaid rebate from 15.1% to 23.1%, expanded the rebate to Medicaid managed care utilization and increased the types of entities eligible for the federal 340B drug discount program. As concerns continue to grow over the need for tighter oversight, there remains the possibility that the Health Resources and Services Administration or another agency under the U.S. Department of Health and Human Services, or HHS, will propose a similar regulation or that Congress will explore changes to the 340B program through legislation. For example, a bill was introduced in 2018 that would require hospitals to report their low-income utilization of the program. Further, the CMS issued a final rule in 2018 that implemented civil monetary penalties for manufacturers who exceeded the ceiling price methodology for a covered outpatient drug when selling to a 340B covered entity. Pursuant to the final rule, after January 1, 2019, manufacturers must calculate 340B program ceiling prices on a quarterly basis. Moreover, manufacturers could be subject to a $5,000 penalty for each instance where they knowingly and intentionally overcharge a covered entity under the 340B program. With respect to KRYSTEXXA, the "additional rebate" methodology of the 340B pricing rules, as applied to the historical pricing of KRYSTEXXA both before and after we acquired the medicine, have resulted in a 340B ceiling price of one penny. A material portion of KRYSTEXXA prescriptions (normally in the range of 15 percent to 20 percent) are written by healthcare providers that are eligible for 340B drug pricing and therefore the reduction in 340B pricing to a penny has negatively impacted our net sales of KRYSTEXXA. The CMS had also finalized a proposal in calendar years 2018, 2019 and 2020 that would revise the Medicare hospital outpatient prospective payment system by creating a new, significantly reduced reimbursement methodology for drugs purchased under the 340B program for Medicare patients at hospital and other settings. These reductions were upheld by the U.S. Court of Appeals for the D.C. Circuit in July 2020, and it is unclear whether this matter will be subject to further litigation. Further, the CMS final rule for calendar year 2021 continues these reductions for drugs acquired through the 340B program.

Patients are unlikely to use our medicines unless coverage is provided and reimbursement is adequate to cover a significant portion of the cost of our medicines. Third-party payers may limit coverage to specific medicines on an approved list, also known as a formulary, which might not include all of the FDA-approved medicines for a particular indication. Moreover, a third-party payer's decision to provide coverage for a medicine does not imply that an adequate reimbursement rate will be approved. Additionally, one third-party payer's decision to cover a particular medicine does not ensure that other payers will also provide coverage for the medicine, or will provide coverage at an adequate reimbursement rate. Even though we have contracts with some PBMs in the United States, that does not guarantee that they will perform in accordance with the contracts, nor does that preclude them from taking adverse actions against us, which could materially adversely affect our operating results. In addition, the existence of such PBM contracts does not guarantee coverage by such PBM's contracted health plans or adequate reimbursement to their respective providers for our medicines. For example, some PBMs have placed some of our medicines on their exclusion lists from time to time, which has resulted in a loss of coverage for patients whose healthcare plans have adopted these PBM lists. Additional healthcare plan formularies may also exclude our medicines from coverage due to the actions of certain PBMs, future price increases we may implement, our use of the HorizonCares program or other free medicine programs whereby we assist qualified patients with certain out-of-pocket expenditures for our medicine, including donations to patient assistance programs offered by charitable foundations, or any other co-pay programs, or other reasons. If our strategies to mitigate formulary exclusions are not effective, these events may reduce the likelihood that physicians prescribe our medicines and increase the likelihood that prescriptions for our medicines are not filled.

In light of such policies and the uncertainty surrounding proposed regulations and changes in the coverage and reimbursement policies of governments and third-party payers, we cannot be sure that coverage and reimbursement will be available for any of our medicines in any additional markets or for any other medicine candidates that we may develop. Also, we cannot be sure that reimbursement amounts will not reduce the demand for, or the price of, our medicines. If coverage and reimbursement are not available or are available only at limited levels, we may not be able to successfully commercialize our medicines.

There may be additional pressure by payers, healthcare providers, state governments, federal regulators and Congress, to use generic drugs that contain the active ingredients found in our medicines or any other medicine candidates that we may develop or acquire. If we fail to successfully secure and maintain coverage and adequate reimbursement for our medicines or are significantly delayed in doing so, we will have difficulty achieving market acceptance of our medicines and expected revenue and profitability which would have a material adverse effect on our business, results of operations, financial condition and prospects.

We may also experience pressure from payers as well as state and federal government authorities concerning certain promotional approaches that we may implement such as our HorizonCares program or any other co-pay programs. Certain state and federal enforcement authorities and members of Congress have initiated inquiries about co-pay assistance programs. Some state legislatures have implemented or have been considering implementing laws to restrict or ban co-pay coupons for branded drugs. For example, legislation was signed into law in California that would limit the use of co-pay coupons in cases where a lower cost generic drug is available and if individual ingredients in combination therapies are available over the counter at a lower cost. It is possible that similar legislation could be proposed and enacted in additional states. Additionally, numerous organizations, including pharmaceutical manufacturers, have been subject to ongoing litigation, enforcement actions and settlements related to their patient assistance programs and support. If we are unsuccessful with our HorizonCares program or any other co-pay programs, or we alternatively are unable to secure expanded formulary access through additional arrangements with PBMs or other payers, we would be at a competitive disadvantage in terms of pricing versus preferred branded and generic competitors. We may also experience financial pressure in the future which would make it difficult to support investment levels in areas such as managed care contract rebates, HorizonCares and other access tools.

*Our medicines are subject to extensive regulation, and we may not obtain additional regulatory approvals for our medicines.**

The clinical development, manufacturing, labeling, packaging, storage, recordkeeping, advertising, promotion, export, marketing and distribution and other possible activities relating to our medicines and our medicine candidates are, and will be, subject to extensive regulation by the FDA and other regulatory agencies. Failure to comply with FDA and other applicable regulatory requirements may, either before or after medicine approval, subject us to administrative or judicially imposed sanctions.

To market any drugs or biologics outside of the United States, we and current or future collaborators must comply with numerous and varying regulatory and compliance related requirements of other countries. For example, we are pursuing a global expansion strategy, which includes bringing TEPEZZA to patients with TED outside of the United States, including Japan where we are engaging with the Pharmaceutical and Medical Devices Agency and the Japanese medical community. Furthermore, we are initiating an investment in our European infrastructure to support the potential approval in the first quarter of 2022 of UPLIZNA for NMOSD, which has been granted orphan designation by the European Commission, or EC. In addition, on March 24, 2021, we announced that our strategic partner, Mitsubishi Tanabe Pharma Corporation, or MTPC, had received manufacturing and marketing approval of UPLIZNA for NMOSD in Japan. Approval procedures vary among countries and can involve additional medicine testing and additional administrative review periods, including obtaining reimbursement and pricing approval in select markets. The time required to obtain approval in other countries might differ from that required to obtain FDA approval. The regulatory approval process in other countries may include all of the risks associated with FDA approval as well as additional, presently unanticipated, risks. Regulatory approval in one country does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one country may negatively impact the regulatory process in others.

Applications for regulatory approval, including a marketing authorization application, or MAA, for marketing new drugs in the European Economic Area (which consists of the Member States of the EU, Iceland, Liechtenstein and Norway), or EEA, must be supported by extensive clinical and pre-clinical data, as well as extensive information regarding chemistry, manufacturing and controls, or CMC, to demonstrate the safety and effectiveness of the applicable medicine candidate. The number and types of pre-clinical studies and clinical trials that will be required for regulatory approval varies depending on the medicine candidate, the disease or the condition that the medicine candidate is designed to target and the regulations applicable to any particular medicine candidate. Despite the time and expense associated with pre-clinical and clinical studies, failure can occur at any stage, and we could encounter problems that cause us to repeat or perform additional pre-clinical studies, CMC studies or clinical trials. Regulatory authorities could delay, limit or deny approval of a medicine candidate for many reasons, including because they:

- may not deem a medicine candidate to be adequately safe and effective;
- may not find the data from pre-clinical studies, CMC studies and clinical trials to be sufficient to support a claim of safety and efficacy;
- may interpret data from pre-clinical studies, CMC studies and clinical trials significantly differently than we do;
- may not approve the manufacturing processes or facilities associated with our medicine candidates;
- may conclude that we have not sufficiently demonstrated long-term stability of the formulation for which we are seeking marketing approval;
- may change approval policies (including with respect to our medicine candidates' class of drugs) or adopt new regulations; or
- may not accept a submission due to, among other reasons, the content or formatting of the submission.

Even if we believe that data collected from our pre-clinical studies, CMC studies and clinical trials of our medicine candidates are promising and that our information and procedures regarding CMC are sufficient, our data may not be sufficient to support marketing approval by regulatory authorities, or regulatory interpretation of these data and procedures may be unfavorable. Even if approved, medicine candidates may not be approved for all indications requested and such approval may be subject to limitations on the indicated uses for which the medicine may be marketed, restricted distribution methods or other limitations. Our business and reputation may be harmed by any failure or significant delay in obtaining regulatory approval for the sale of any of our medicine candidates. We cannot predict when or whether regulatory approval will be obtained for any medicine candidate we develop.

The ultimate approval and commercial marketing of any of our medicines in additional indications or geographies is subject to substantial uncertainty. Failure to gain additional regulatory approvals would limit the potential revenues and value of our medicines and could cause our share price to decline.

Since a significant proportion of the regulatory framework in the United Kingdom, or UK, applicable to our business and our products is derived from EU directives and regulations, Brexit has materially impacted the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our products in the UK. The regulatory changes that are a result of Brexit may also materially impact upon the development, manufacture, importation, approval and commercialization of our products in the EEA, should any development or manufacture of these products take place in the UK.

Great Britain is no longer covered by the centralized procedures for obtaining EEA-wide marketing authorizations from the EC (Northern Ireland is still covered by the centralized procedure). Our medicine candidates require a separate marketing authorization for Great Britain, and it is unclear as to whether the relevant authorities in the EU and the UK are adequately prepared for the additional administrative burden caused by Brexit. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could prevent us from or delay us commercializing our medicine candidates in the UK and/or the EEA and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK and/or EEA for our medicine candidates, which could significantly and materially harm our business.

Brexit may influence the attractiveness of the UK as a place to conduct clinical trials. The EU's regulatory environment for clinical trials is being harmonized as part of the Clinical Trial Regulation but it is currently unclear as to what extent the UK will seek to align its regulations with the EU. Failure of the UK to closely align its regulations with the EU may have an effect on the cost of conducting clinical trials in the UK as opposed to other countries and/or make it harder to seek a marketing authorization for our medicine candidates in the EEA on the basis of clinical trials conducted in the UK.

In the short term there is a risk of disrupted import and export processes due to a lack of administrative processing capacity by the respective UK and EU customs agencies that may delay time-sensitive shipments and may negatively impact our product supply chain.

We may be subject to penalties and litigation and large incremental expenses if we fail to comply with regulatory requirements or experience problems with our medicines.

Even after we achieve regulatory approvals, we are subject to ongoing obligations and continued regulatory review with respect to many operational aspects including our manufacturing processes, labeling, packaging, distribution, storage, adverse event monitoring and reporting, dispensation, advertising, promotion and recordkeeping. These requirements include submissions of safety and other post-marketing information and reports, ongoing maintenance of medicine registration and continued compliance with current good manufacturing practices, or cGMPs, good clinical practices, or GCPs, good pharmacovigilance practice, good distribution practices and good laboratory practices, or GLPs. If we, our medicines or medicine candidates, or the third-party manufacturing facilities for our medicines or medicine candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

- impose injunctions or restrictions on the marketing, manufacturing or distribution of a medicine, suspend or withdraw medicine approvals, revoke necessary licenses or suspend medicine reimbursement;
- issue warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- suspend any ongoing clinical trials or delay or prevent the initiation of clinical trials;
- delay or refuse to approve pending applications or supplements to approved applications we have filed;
- refuse to permit drugs or precursor or intermediary chemicals to be imported or exported to or from the United States;
- suspend or impose restrictions or additional requirements on operations, including costly new manufacturing quality or pharmacovigilance requirements;
- seize or detain medicines or require us to initiate a medicine recall; and/or
- commence criminal investigations and prosecutions.

Moreover, existing regulatory approvals and any future regulatory approvals that we obtain will be subject to limitations on the approved indicated uses and patient populations for which our medicines may be marketed, the conditions of approval, requirements for potentially costly, post-market testing and requirements for surveillance to monitor the safety and efficacy of the medicines. Physicians nevertheless may prescribe our medicines to their patients in a manner that is inconsistent with the approved label or that is off-label. Positive clinical trial results in any of our medicine development programs increase the risk that approved pharmaceutical forms of the same active pharmaceutical ingredients, or APIs, may be used off-label in those indications. If we are found to have improperly promoted off-label uses of approved medicines, we may be subject to significant sanctions, civil and criminal fines and injunctions prohibiting us from engaging in specified promotional conduct.

In addition, engaging in improper promotion of our medicines for off-label uses in the United States can subject us to false claims litigation under federal and state statutes. These false claims statutes in the United States include the federal False Claims Act, which allows any individual to bring a lawsuit against a pharmaceutical company on behalf of the federal government alleging submission of false or fraudulent claims or causing to present such false or fraudulent claims for payment by a federal program such as Medicare or Medicaid. Growth in false claims litigation has increased the risk that a pharmaceutical company will have to defend a false claim action, pay civil money penalties, settlement fines or restitution, agree to comply with burdensome reporting and compliance obligations and be excluded from Medicare, Medicaid and other federal and state healthcare programs.

The regulations, policies or guidance of regulatory agencies may change and new or additional statutes or government regulations may be enacted that could prevent or delay regulatory approval of our medicine candidates or further restrict or regulate post-approval activities. For example, in January 2014, the FDA released draft guidance on how drug companies can fulfill their regulatory requirements for post-marketing submission of interactive promotional media, and though the guidance provided insight into how the FDA views a company's responsibility for certain types of social media promotion, there remains a substantial amount of uncertainty regarding internet and social media promotion of regulated medical products. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are unable to achieve and maintain regulatory compliance, we will not be permitted to market our drugs, which would materially adversely affect our business, results of operations and financial condition.

*We have rights to medicines in certain jurisdictions but have little or no control over third parties that have rights to commercialize those medicines in other jurisdictions, which could adversely affect our commercialization of these medicines.**

Following our sale of the rights to RAVICTI (i) outside of North America and Japan to Medical Need Europe AB, part of the Immedica Group, or Immedica, in December 2018 and (ii) in Japan to Immedica, Immedica has marketing and distribution rights to RAVICTI in those regions. Following our sale of the rights to PROCYSBI in the Europe, Middle East and Africa, or EMEA, regions to Chiesi Farmaceutici S.p.A., or Chiesi, in June 2017, or the Chiesi divestiture, Chiesi has marketing and distribution rights to PROCYSBI in the EMEA regions. MTPC has rights to the development and commercialization of UPLIZNA for NMOSD as well as other potential future indications in Japan and certain other countries in Asia. Hansoh Pharmaceutical Group Company Limited, or Hansoh, has rights to the development and commercialization of UPLIZNA for NMOSD as well as other potential future indications in China, Hong Kong and Macau. Miravo Healthcare (formerly known as Nuvo Pharmaceuticals Inc.), or Miravo, has retained its rights to PENNSAID 2% in territories outside of the United States. In March 2017, Miravo announced that it had entered into an exclusive license agreement with Sayre Therapeutics PVT Ltd. to distribute, market and sell PENNSAID 2% in India, Sri Lanka, Bangladesh and Nepal, and in December 2017 Miravo announced that it had entered into a license and distribution agreement with Gebro Pharma AG for the exclusive right to register, distribute, market and sell PENNSAID 2% in Switzerland and Liechtenstein. We have little or no control over Immedica's activities with respect to RAVICTI outside of North America, over Chiesi's activities with respect to PROCYSBI in the EMEA, over MTPC's or Hansoh's activities with respect to UPLIZNA in the certain countries in Asia, or over Miravo's or its existing and future commercial partners' activities with respect to PENNSAID 2% outside of the United States even though those activities could impact our ability to successfully commercialize these medicines. For example, Immedica or its assignees, Chiesi or its assignees or Miravo or its assignees can make statements or use promotional materials with respect to RAVICTI, PROCYSBI or PENNSAID 2% , respectively, outside of the United States that are inconsistent with our positioning of the medicines in the United States, and could sell RAVICTI, PROCYSBI or PENNSAID 2%, respectively, in foreign countries at prices that are dramatically lower than the prices we charge in the United States. These activities and decisions, while occurring outside of the United States, could harm our commercialization strategy in the United States. In addition, medicine recalls or safety issues with these medicines outside the United States, even if not related to the commercial medicine we sell in the United States, could result in serious damage to the brand in the United States and impair our ability to successfully market them. We also rely on Immedica, Chiesi, MTPC, Hansoh and Miravo, or their assignees to provide us with timely and accurate safety information regarding the use of these medicines outside of the United States, as we have or will have limited access to this information ourselves.

*We rely on third parties to manufacture commercial supplies of all of our medicines, and we currently intend to rely on third parties to manufacture commercial supplies of any other approved medicines. The commercialization of any of our medicines could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of medicine or fail to do so at acceptable quality levels or prices or fail to maintain or achieve satisfactory regulatory compliance.**

The facilities used by our third-party manufacturers to manufacture our medicines and medicine candidates must be approved by the applicable regulatory authorities. We do not control the manufacturing processes of third-party manufacturers and are currently completely dependent on our third-party manufacturing partners.

We rely on AGC Biologics A/S (formerly known as CMC Biologics A/S), or AGC Biologics, as our exclusive manufacturer of the TEPEZZA drug substance and Catalent, for TEPEZZA drug product. On December 17, 2020, we announced that we expected a short-term disruption in TEPEZZA supply as a result of recent U.S. government-mandated COVID-19 vaccine production orders pursuant to the DPA that dramatically restricted capacity available for the production of TEPEZZA at our drug product contract manufacturer, Catalent. To offset the reduced slots allowed by the DPA and Catalent, we accelerated plans to increase the production scale of TEPEZZA drug product. In March 2021, the FDA approved a prior approval supplement to the TEPEZZA BLA (which was previously approved in January 2020), giving us authorization to manufacture more TEPEZZA drug product resulting in an increased number of vials with each manufacturing slot. We commenced resupply of TEPEZZA to the market in April 2021. While we are not currently aware of any manufacturing facilities other than Catalent that are part of the supply chain for our medicines that are being utilized for the manufacture of vaccines for COVID-19, similar circumstances could arise in the future and could result in supply disruption to our other medicines. In addition, we cannot guarantee that our currently contracted TEPEZZA manufacturing slots at Catalent will not be rescheduled or canceled as a result of additional U.S. government-mandated COVID-19 vaccine production orders, or that they will be completed successfully.

Further, following the highly successful launch of TEPEZZA, which significantly exceeded expectations, we began the process of expanding our production capacity in 2020 to meet anticipated future demand for TEPEZZA. If AGC Biologics fails to supply TEPEZZA drug substance or if Catalent fails to supply TEPEZZA drug product for a period beyond our current expectation or either manufacturer is otherwise unable to meet our volume requirements due to unexpected market demand for TEPEZZA, it may lead to further TEPEZZA supply constraints. In addition, while we are making progress with our second drug product manufacturer and we are on track to begin shipping TEPEZZA supply from this manufacturer, assuming FDA approval by the end of 2021, it is possible this timeline could be delayed. We rely on NOF Corporation, or NOF, as our exclusive supplier of the PEGylation agent that is a critical raw material in the manufacture of KRYSTEXXA. If NOF fails to supply such PEGylation agent, it may lead to KRYSTEXXA supply constraints. A key excipient used in PENNSAID 2% as a penetration enhancer is dimethyl sulfoxide, or DMSO. We and Miravo, our exclusive supplier of PENNSAID 2%, rely on a sole proprietary form of DMSO for which we maintain a substantial safety stock. However, should this supply become inadequate, damaged, destroyed or unusable, we and Miravo may not be able to qualify a second source. We rely on an exclusive supply agreement with Boehringer Ingelheim Biopharmaceuticals GmbH, or Boehringer Ingelheim Biopharmaceuticals, for manufacturing and supply of ACTIMMUNE. ACTIMMUNE is manufactured by starting with cells from working cell bank samples which are derived from a master cell bank. We and Boehringer Ingelheim Biopharmaceuticals separately store multiple vials of the master cell bank. In the event of catastrophic loss at our or Boehringer Ingelheim Biopharmaceuticals' storage facility, it is possible that we could lose multiple cell banks and have the manufacturing capacity of ACTIMMUNE severely impacted by the need to substitute or replace the cell banks. In addition, we rely on AstraZeneca UK Limited, or AstraZeneca, for the manufacture of the current clinical and commercial supplies of UPLIZNA, and for the current clinical and nonclinical supplies of our other medicine candidates.

If any of our third-party manufacturers cannot successfully manufacture material that conforms to our specifications and the applicable regulatory authorities' strict regulatory requirements, or pass regulatory inspection, they will not be able to secure or maintain regulatory approval for the manufacturing facilities. In addition, we have no control over the ability of third-party manufacturers to maintain adequate quality control, quality assurance and qualified personnel. If the FDA or any other applicable regulatory authorities do not approve these facilities for the manufacture of our medicines or if they withdraw any such approval in the future, or if our suppliers or third-party manufacturers decide they no longer want to supply our primary active ingredients or manufacture our medicines, we may need to find alternative manufacturing facilities, which would significantly impact our ability to develop, obtain regulatory approval for or market our medicines. To the extent any third-party manufacturers that we engage with respect to our medicines are different from those currently being used for commercial supply in the United States, the FDA will need to approve the facilities of those third-party manufacturers used in the manufacture of our medicines prior to our sale of any medicine using these facilities.

Although we have entered into supply agreements for the manufacture and packaging of our medicines, our manufacturers may not perform as agreed or may terminate their agreements with us. We currently rely on single source suppliers for certain of our medicines. If our manufacturers terminate their agreements with us, we may have to qualify new back-up manufacturers. We rely on safety stock to mitigate the risk of our current suppliers electing to cease producing bulk drug product or ceasing to do so at acceptable prices and quality. However, we can provide no assurance that such safety stocks would be sufficient to avoid supply shortfalls in the event we have to identify and qualify new contract manufacturers.

The manufacture of medicines requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of medicines often encounter difficulties in production, particularly in scaling up and validating initial production. These problems include difficulties with production costs and yields, quality control, including stability of the medicine, quality assurance testing, shortages of qualified personnel, as well as compliance with strictly enforced federal, state and foreign regulations. Furthermore, if microbial, viral or other contaminations are discovered in the medicines or in the manufacturing facilities in which our medicines are made, such manufacturing facilities may need to be closed for an extended period of time to investigate and remedy the contamination. We cannot assure that issues relating to the manufacture of any of our medicines will not occur in the future. Additionally, our manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If our manufacturers were to encounter any of these difficulties, or otherwise fail to comply with their contractual obligations, our ability to commercialize our medicines or provide any medicine candidates to patients in clinical trials would be jeopardized.

Any delay or interruption in our ability to meet commercial demand for our medicines will result in the loss of potential revenues and could adversely affect our ability to gain market acceptance for these medicines. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of clinical trials, increase the costs associated with maintaining clinical trial programs and, depending upon the period of delay, require us to commence new clinical trials at additional expense or terminate clinical trials completely.

Failures or difficulties faced at any level of our supply chain, including any further potential disruption caused by the COVID-19 pandemic, could materially adversely affect our business and delay or impede the development and commercialization of any of our medicines or medicine candidates and could have a material adverse effect on our business, results of operations, financial condition and prospects.

*We face significant competition from other biotechnology and pharmaceutical companies, including those marketing generic medicines and our operating results will suffer if we fail to compete effectively.**

The biotechnology and pharmaceutical industries are intensely competitive. We have competitors both in the United States and international markets, including major multinational pharmaceutical companies, biotechnology companies and universities and other research institutions. Many of our competitors have substantially greater financial, technical and other resources, such as larger research and development, or R&D, staff, experienced marketing and manufacturing organizations and well-established sales forces. Additional consolidations in the biotechnology and pharmaceutical industries may result in even more resources being concentrated in our competitors and we will have to find new ways to compete and may have to potentially merge with or acquire other businesses to stay competitive. Competition may increase further as a result of advances in the commercial applicability of technologies and greater availability of capital for investment in these industries. Our competitors may succeed in developing, acquiring or in-licensing on an exclusive basis, medicines that are more effective and/or less costly than our medicines.

Although TEPEZZA does not face direct competition, other therapies, such as corticosteroids, have been used on an off-label basis to alleviate some of the symptoms of TED. While these therapies have not proved effective in treating the underlying disease, and carry with them significant side effects, their off-label use could reduce or delay treatment in the addressable patient population for TEPEZZA. Immunovant Inc., or Immunovant, is conducting Phase 2 clinical trials of a fully human anti-FcRn monoclonal antibody candidate for the treatment of active TED, also referred to as Graves' ophthalmopathy. On February 2, 2021, Immunovant announced a voluntary pause in the clinical dosing of the candidate due to elevated total cholesterol and low-density lipoprotein levels in patients treated with the candidate. Immunovant has indicated it intends to continue developing the candidate but did not provide an estimate of when the dosing might resume. Viridian Therapeutics, Inc. is pursuing development of an anti-IGF-1R monoclonal antibody for TED and has announced plans to initiate a Phase 2 trial in the second half of 2021. While KRYSTEXXA faces limited direct competition, a number of competitors have medicines in clinical trials, including Selecta Biosciences Inc., or Selecta, which has initiated a Phase 3 trial of a candidate for the treatment of chronic refractory gout. In September 2020, Selecta announced topline clinical data that did not meet the primary endpoint or demonstrate statistical superiority for their Phase 2 trial that compared their candidate, which includes an immunomodulator, to KRYSTEXXA alone. In July 2020, Selecta and Swedish Orphan Biovitrum AB, or Sobi, entered into a strategic licensing agreement under which Sobi will assume responsibility for certain development, regulatory, and commercial activities for this candidate. RAVICTI could face competition from a few medicine candidates that are in early-stage development, including a gene-therapy candidate by Ultragenyx Pharmaceutical Inc., a generic taste-masked formulation option of BUPHENYL by ACER Therapeutics Inc., an enzyme replacement for a specific UCD subtype (ARG) by Aeglea Bio Therapeutics Inc. and a mRNA-based therapeutic for a specific UCD subtype (OTC) by Arcturus Therapeutics Holdings Inc. PROCYSBI faces competition from Cystagon® (immediate-release cysteamine bitartrate capsules) for the treatment of cystinosis, Cystadrops® (cysteamine ophthalmic solution) for the treatment of corneal cystine crystal deposits and Cystaran™ (cysteamine ophthalmic solution) for treatment of corneal crystal accumulation in patients with cystinosis. Additionally, we are also aware that AVROBIO, Inc. has an early-stage gene therapy candidate in development for the treatment of cystinosis. UPLIZNA faces competition with eculizumab from Alexion Pharmaceuticals, Inc., or Alexion, marketed as Soliris®, and satralizumab, marketed as Ensprying™ from Chugai Pharmaceuticals Co., Ltd., or Chugai, a subsidiary of Roche, each for the treatment of patients with NMOSD. Both products have achieved successful pivotal studies in NMOSD and in June 2019, Alexion received FDA approval of Soliris for the treatment of adults with NMOSD and in August 2020 Chugai received approval for Ensprying for the treatment of adults with NMOSD. Alexion are also undergoing a Phase 3 trial with Ultomiris® (ravulizumab) in NMOSD and, if approved for this indication, UPLIZNA could face additional competition. UPLIZNA also faces competition from rituximab, an off-label treatment that has been used for years to treat NMOSD given the lack of an approved medicine for this disease prior to 2019. PENNSAID 2% faces competition from generic versions of diclofenac sodium topical solutions that are priced significantly less than the price we charge for PENNSAID 2%. The generic version of Voltaren Gel is the market leader in the topical NSAID category. Legislation enacted in most states in the United States allows, or in some instances mandates, that a pharmacist dispense an available generic equivalent when filling a prescription for a branded medicine, in the absence of specific instructions from the prescribing physician. DUEXIS faces competition from other NSAIDs, including Celebrex®, marketed by Pfizer Inc., and celecoxib, a generic form of the medicine marketed by other pharmaceutical companies. DUEXIS also faces significant competition from the separate use of NSAIDs for pain relief and GI protective medications to reduce the risk of NSAID-induced upper GI ulcers. Both NSAIDs and GI protective medications are available in generic form and may be less expensive to use separately than DUEXIS, despite such substitution being off-label in the case of DUEXIS. Because pharmacists often have economic and other incentives to prescribe lower-cost generics, if physicians prescribe PENNSAID 2% or DUEXIS, those prescriptions may not result in sales. If physicians do not complete prescriptions through our HorizonCares program or otherwise provide prescribing instructions prohibiting generic diclofenac sodium topical solutions as a substitute for PENNSAID 2%, the substitution of generic ibuprofen and famotidine separately as a substitution for DUEXIS, sales of PENNSAID 2% and DUEXIS may suffer despite any success we may have in promoting PENNSAID 2% or DUEXIS to physicians. In addition, other medicine candidates that contain ibuprofen and famotidine in combination or naproxen and esomeprazole in combination, while not currently known or FDA approved, may be developed and compete with DUEXIS in the future.

We have also entered into settlement and license agreements that may allow certain of our competitors to sell generic versions of certain of our medicines in the United States, subject to the terms of such agreements. We granted (i) a non-exclusive license (that is only royalty-bearing in some circumstances) to manufacture and commercialize a generic version of DUEXIS in the United States after January 1, 2023, (ii) non-exclusive licenses to manufacture and commercialize generic versions of PENNSAID 2% in the United States after October 17, 2027, (iii) a non-exclusive license to manufacture and commercialize a generic version of RAYOS tablets in the United States after December 23, 2022, and (iv) non-exclusive licenses to manufacture and commercialize generic versions of RAVICTI in the United States after July 1, 2025, or earlier under certain circumstances.

On February 27, 2020, following a judgment in federal court invalidating certain patents covering VIMOVO, Dr. Reddy's launched a generic version of VIMOVO in the United States. While patent litigation against Dr. Reddy's for infringement continues on additional patents in the New Jersey District Court, we now face generic competition for VIMOVO, which has negatively impacted net sales of VIMOVO. As a result, we have repositioned our promotional efforts previously directed to VIMOVO to the other inflammation segment medicines and expect that our VIMOVO net sales will continue to decrease in future periods.

Patent litigation is currently pending in the Federal Circuit Court of Appeals and the United States District Court of New Jersey against Alkem Laboratories, Inc., or Alkem, and Teva Pharmaceuticals USA, Inc., or Teva USA, respectively, who each intend to market a generic version of DUEXIS prior to the expiration of certain of our patents listed in the FDA's Orange Book, or Orange Book. These cases arise from Paragraph IV Patent Certification notice letters from Alkem and Teva USA advising they had filed an ANDA with the FDA seeking approval to market a generic version of DUEXIS before the expiration of the patents-in-suit.

On June 27, 2020, we received notice from Lupin Limited, or Lupin, that it had filed an ANDA with the FDA seeking approval of a generic version of PROCYSBI. The ANDA contained a Paragraph IV Patent Certification alleging that the patents covering PROCYSBI are invalid and/or will not be infringed by Lupin's manufacture, use or sale of a generic version of PROCYSBI. Patent litigation is currently pending in the United States District Court of New Jersey against Lupin seeking to prevent Lupin from selling its generic version of PROCYSBI before the expiration of the patents-in-suit.

If we are unsuccessful in any of the DUEXIS cases or PROCYSBI case, we will likely face generic competition with respect to DUEXIS and/or PROCYSBI and sales of DUEXIS and/or PROCYSBI will be substantially harmed.

ACTIMMUNE is the only medicine currently approved by the FDA specifically for the treatment of CGD and SMO. While there are additional or alternative approaches used to treat patients with CGD and SMO, there are currently no medicines on the market that compete directly with ACTIMMUNE. A widely accepted protocol to treat CGD in the United States is the use of concomitant "triple prophylactic therapy" comprising ACTIMMUNE, an oral antibiotic agent and an oral antifungal agent. However, the FDA-approved labeling for ACTIMMUNE does not discuss this "triple prophylactic therapy," and physicians may choose to prescribe one or both of the other modalities in the absence of ACTIMMUNE. Because of the immediate and life-threatening nature of SMO, the preferred treatment option for SMO is often to have the patient undergo a bone marrow transplant which, if successful, will likely obviate the need for further use of ACTIMMUNE in that patient. Likewise, the use of bone marrow transplants in the treatment of patients with CGD is becoming more prevalent, which could have a material adverse effect on sales of ACTIMMUNE and its profitability. We are aware of a number of research programs investigating the potential of gene therapy as a possible cure for CGD. Additionally, other companies may be pursuing the development of medicines and treatments that target the same diseases and conditions which ACTIMMUNE is currently approved to treat. As a result, it is possible that our competitors may develop new medicines that manage CGD or SMO more effectively, cost less or possibly even cure CGD or SMO. In addition, U.S. healthcare legislation passed in March 2010 authorized the FDA to approve biological products, known as biosimilars, that are similar to or interchangeable with previously approved biological products, like ACTIMMUNE, based upon potentially abbreviated data packages. Biosimilars are likely to be sold at substantially lower prices than branded medicines because the biosimilar manufacturer would not have to recoup the R&D and marketing costs associated with the branded medicine. Though we are not currently aware of any biosimilar under development, the development and commercialization of any competing medicines or the discovery of any new alternative treatment for CGD or SMO could have a material adverse effect on sales of ACTIMMUNE and its profitability. We have licenses to U.S. patents covering ACTIMMUNE. If not otherwise invalidated, those patents expire in 2022.

BUPHENYL's composition of matter patent protection and orphan drug exclusivity have expired. Because BUPHENYL has no regulatory exclusivity or listed patents, there is nothing to prevent a competitor from submitting an ANDA for a generic version of BUPHENYL and receiving FDA approval. Generic versions of BUPHENYL to date have been priced at a discount relative to RAVICTI, and physicians, patients, or payers may decide that this less expensive alternative is preferable to RAVICTI. If this occurs, sales of RAVICTI could be materially reduced, but we would nevertheless be required to make royalty payments to Bausch Health Companies Inc. (formerly Ucyclyd Pharma, Inc.), or Bausch, and another external party, at the same royalty rates. While Bausch and its affiliates are generally contractually prohibited from developing or commercializing new medicines, anywhere in the world, for the treatment of UCD or hepatic encephalopathy, or HE, which are chemically similar to RAVICTI, they may still develop and commercialize medicines that compete with RAVICTI. For example, medicines approved for indications other than UCD and HE may still compete with RAVICTI if physicians prescribe such medicines off-label for UCD or HE. We are also aware that Recordati S.p.A (formerly known as Orphan Europe SARL), or Recordati, is conducting clinical trials of carglumic acid to assess the efficacy for acute hyperammonemia in some of the UCD enzyme deficiencies for which RAVICTI is approved for chronic treatment. Carglumic acid is approved for maintenance therapy for chronic hyperammonemia and to treat hyperammonemic crises in N-acetylglutamate synthase deficiency, a rare UCD subtype, and is sold under the name Carbaglu. If the results of this trial are successful and Recordati is able to complete development and obtain approval of Carbaglu to treat additional UCD enzyme deficiencies, RAVICTI may face additional competition from this compound.

The availability and price of our competitors' medicines could limit the demand, and the price we are able to charge, for our medicines. We will not successfully execute on our business objectives if the market acceptance of our medicines is inhibited by price competition, if physicians are reluctant to switch from existing medicines to our medicines, or if physicians switch to other new medicines or choose to reserve our medicines for use in limited patient populations.

In addition, established pharmaceutical companies may invest heavily to accelerate discovery and development of novel compounds or to acquire novel compounds that could make our medicines obsolete. Our ability to compete successfully with these companies and other potential competitors will depend largely on our ability to leverage our experience in clinical, regulatory and commercial development to:

- develop and acquire medicines that are superior to other medicines in the market;
- attract qualified clinical, regulatory, and sales and marketing personnel;
- obtain patent and/or other proprietary protection for our medicines and technologies;
- obtain required regulatory approvals; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicine candidates.

Our medicine candidates for which we intend to seek approval may face generic or biosimilar competition sooner than anticipated. *******

Even if we are successful in achieving regulatory approval to commercialize a medicine candidate ahead of our competitors, certain of our medicine candidates may face competition from biosimilar products. In the United States, certain of our medicine candidates are regulated by the FDA as biological products and we intend to seek approval for these medicine candidates pursuant to the BLA pathway. The Biologics Price Competition and Innovation Act of 2009, or BPCIA, created an abbreviated pathway for FDA approval of biosimilar and interchangeable biological products based on a previously licensed reference product. Under the BPCIA, an application for a biosimilar biological product cannot be approved by the FDA until 12 years after the original reference biological product was approved under a BLA. The law is complex and is still being interpreted and implemented by the FDA. As a result, its ultimate impact, implementation, and meaning are subject to uncertainty. While it is uncertain when such processes intended to implement BPCIA may be fully adopted by the FDA, any such processes could have a material adverse effect on the future commercial prospects for certain of our medicine candidates.

We believe that any of our medicine candidates approved as a biological product under a BLA should qualify for the 12-year period of exclusivity available to reference biological products. However, there is a risk that this exclusivity could be shortened due to congressional action or otherwise, or that the FDA will not consider our medicine candidates to be reference biological products pursuant to its interpretation of the exclusivity provisions of the BPCIA for competing products, potentially creating the opportunity for generic follow-on biosimilar competition sooner than anticipated. Moreover, the extent to which a biosimilar product, once approved, will be substituted for any one of our reference medicines in a way that is similar to traditional generic substitution for non-biological products is not yet clear, and will depend on a number of marketplace and regulatory factors that are still developing including whether a future competitor seeks an interchangeability designation for a biosimilar of one of our medicines. Under the BPCIA as well as state pharmacy laws, only interchangeable biosimilar products are considered substitutable for the reference biological product without the intervention of the health care provider who prescribed the original biological product. However, as with all prescribing decisions made in the context of a patient-provider relationship and a patient's specific medical needs, healthcare providers are not restricted from prescribing biosimilar products in an off-label manner. In addition, a competitor could decide to forego the abbreviated approval pathway available for biosimilar products and to submit a full BLA for product licensure after completing its own preclinical studies and clinical trials. In such a situation, any exclusivity to which we may be eligible under the BPCIA would not prevent the competitor from marketing its biological product as soon as it is approved.

In Europe, the EC has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In addition, companies may be developing biosimilar products in other countries that could compete with our medicines, if approved.

If competitors are able to obtain marketing approval for biosimilars referencing our medicine candidates, if approved, our future medicines may become subject to competition from such biosimilars, whether or not they are designated as interchangeable, with the attendant competitive pressure and potential adverse consequences. Such competitive products may be able to immediately compete with us in each indication for which our medicine candidates may have received approval.

*If we are unable to maintain or realize the benefits of orphan drug exclusivity, we may face increased competition with respect to certain of our medicines.**

Under the Orphan Drug Act of 1983, the FDA may designate a medicine as an orphan drug if it is a drug intended to treat a rare disease or condition affecting fewer than 200,000 people in the United States. A company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years from the date of its approval. PROCYSBI received ten years of market exclusivity, through 2023, as an orphan drug in Europe. PROCYSBI received seven years of market exclusivity, through 2022, for patients two years of age to less than six years of age, and seven years of market exclusivity, through 2024, for patients one year of age to less than two years of age, as an orphan drug in the United States. TEPEZZA has been granted orphan drug exclusivity for treatment of active (dynamic) phase Graves' ophthalmopathy, which we expect will provide orphan drug marketing exclusivity in the United States until January 2027. In addition, UPLIZNA was granted orphan drug designation for UPLIZNA for the treatment of patients with NMOSD in February 2016. However, despite orphan drug exclusivity, the FDA can still approve another drug containing the same active ingredient and used for the same orphan indication if it determines that a subsequent drug is safer, more effective or makes a major contribution to patient care, and orphan exclusivity can be lost if the orphan drug manufacturer is unable to ensure that a sufficient quantity of the orphan drug is available to meet the needs of patients with the rare disease or condition. Orphan drug exclusivity may also be lost if the FDA later determines that the initial request for designation was materially defective. In addition, orphan drug exclusivity does not prevent the FDA from approving competing drugs for the same or similar indication containing a different active ingredient. If orphan drug exclusivity is lost and we were unable to successfully enforce any remaining patents covering the applicable medicine, we could be subject to generic competition and revenues from the medicine could decrease materially. In addition, if a subsequent drug is approved for marketing for the same or a similar indication as our medicines despite orphan drug exclusivity, we may face increased competition and lose market share with respect to these medicines.

*A Breakthrough Therapy Designation by the FDA may not lead to a faster development or regulatory review or approval process, and does not increase the likelihood that our medicine candidates will receive marketing approval.**

The FDA granted Breakthrough Therapy Designation to TEPEZZA for the treatment of thyroid eye disease and UPLIZNA for the treatment of NMOSD, and we may seek such designation in the future for other medicine candidates. A Breakthrough Therapy is defined as a drug that is intended, alone or in combination with one or more other drugs, to treat a serious or life-threatening disease or condition, and preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints, such as substantial treatment effects observed early in clinical development. For drugs that have been designated as Breakthrough Therapies, interaction and communication between the FDA and the sponsor can help to identify the most efficient path for development. Drugs designated as Breakthrough Therapies are also eligible for accelerated approval.

The FDA has discretion to determine whether the criteria for a Breakthrough Therapy has been met and whether to grant a Breakthrough Therapy Designation to an investigational product. Accordingly, even if we believe, after completing early clinical trials, that one of our medicine candidates meets the criteria for designation as a Breakthrough Therapy, the FDA may disagree and instead determine not to make such designation. In any event, the receipt of a Breakthrough Therapy Designation for a medicine candidate may not result in a faster development process, review or approval compared to medicine candidates considered for approval under conventional FDA procedures and does not assure ultimate approval by the FDA. In addition, even after granting Breakthrough Therapy Designation to our medicine candidates, the FDA may later decide that such medicine candidates no longer meet the conditions for qualification and withdraw such designation.

*A Fast Track Designation by the FDA, even if granted for any of our medicine candidates, may not lead to a faster development or regulatory review or approval process and does not increase the likelihood that our medicine candidates will receive marketing approval.**

We do not currently have Fast Track Designation for any of our medicine candidates, but may seek such designation in the future. If a drug is intended for the treatment of a serious or life-threatening condition and the drug demonstrates the potential to address unmet medical needs for this condition, the drug sponsor may apply for FDA Fast Track Designation. The FDA has broad discretion whether to grant this designation. Even if we believe a particular medicine candidate is eligible for this designation, we cannot assure you that the FDA would decide to grant it. Even if we do receive Fast Track Designation, we may not experience a faster development process, review or approval compared to conventional FDA procedures. The FDA may withdraw Fast Track Designation if it believes that the designation is no longer supported by data from our clinical development program. Many drugs that have received Fast Track Designation have failed to obtain regulatory approval.

If we cannot successfully implement our patient assistance programs or increase formulary access and reimbursement for our medicines in the face of increasing pressure to reduce the price of medications, the adoption of our medicines by physicians, patients and payers may decline.

There continues to be immense pressure from healthcare payers, PBMs and others to use less expensive or generic medicines or over-the-counter brands instead of certain branded medicines. For example, some PBMs have placed certain of our medicines on their exclusion lists from time to time, which has resulted in a loss of coverage for patients whose healthcare plans have adopted these PBM lists. Additional healthcare plans, including those that contract with these PBMs but use different formularies, may also choose to exclude our medicines from their formularies or restrict coverage to situations where a generic or over-the-counter medicine has been tried first. Many payers and PBMs also require patients to make co-payments for branded medicines, including many of our medicines, in order to incentivize the use of generic or other lower-priced alternatives instead. Legislation enacted in most states in the United States allows, or in some instances mandates, that a pharmacist dispenses an available generic equivalent when filling a prescription for a branded medicine, in the absence of specific instructions from the prescribing physician. Because our medicines (other than BUPHENYL and VIMOVO) do not currently have FDA-approved generic equivalents in the United States, we do not believe our medicines should be subject to mandatory generic substitution laws. We understand that some pharmacies may attempt to obtain physician authorization to switch prescriptions for DUEXIS to prescriptions for multiple generic medicines with similar APIs to ensure payment for the medicine if the physician’s prescription for the branded medicine is not immediately covered by the payer, despite such substitution being off-label in the case of DUEXIS. If these limitations in coverage and other incentives result in patients refusing to fill prescriptions or being dissatisfied with the out-of-pocket costs of their medications, or if pharmacies otherwise seek and receive physician authorization to switch prescriptions, not only would we lose sales on prescriptions that are ultimately not filled, but physicians may be dissuaded from writing prescriptions for our medicines in the first place in order to avoid potential patient non-compliance or dissatisfaction over medication costs, or to avoid spending the time and effort of responding to pharmacy requests to switch prescriptions.

Part of our commercial strategy to increase adoption and access to our medicines in the face of these incentives to use generic alternatives is to offer physicians the opportunity to have eligible patients fill prescriptions through independent pharmacies participating in our HorizonCares patient assistance program, including shipment of prescriptions to patients. We also have contracted with a third-party prescription clearinghouse that offers physicians a single point of contact for processing prescriptions through these independent pharmacies, reducing physician administrative costs, increasing the fill rates for prescriptions and enabling physicians to monitor refill activity. Through HorizonCares, financial assistance may be available to reduce eligible patients' out-of-pocket costs for prescriptions filled. Because of this assistance, eligible patients' out-of-pocket cost for our medicines when dispensed through HorizonCares may be significantly lower than such costs when our medicines are dispensed outside of the HorizonCares program. However, to the extent physicians do not direct prescriptions currently filled through traditional pharmacies, including those associated with or controlled by PBMs, to pharmacies participating in our HorizonCares program, we may experience a significant decline in PENNSAID 2% and DUEXIS prescriptions. Our ability to increase utilization of our patient assistance programs will depend on physician and patient awareness and comfort with the programs, and we do not control whether physicians will ultimately use our patient assistance programs to prescribe our medicines or whether patients will agree to receive our medicines through our HorizonCares program. In addition, the HorizonCares program is not available to federal health care program (such as Medicare and Medicaid) beneficiaries. We have also contracted with certain PBMs and other payers to secure formulary status and reimbursement for certain of our inflammation segment medicines, which generally require us to pay administrative fees and rebates to the PBMs and other payers for qualifying prescriptions. While we have business relationships with two of the largest PBMs, Express Scripts, Inc., or Express Scripts, and CVS Caremark, as well as rebate agreements with other PBMs, and we believe these agreements will secure formulary status for certain of our medicines, we cannot guarantee that we will be able to agree to terms with other PBMs and other payers, or that such terms will be commercially reasonable to us. Despite our agreements with PBMs, the extent of formulary status and reimbursement will ultimately depend to a large extent upon individual healthcare plan formulary decisions. If healthcare plans that contract with PBMs with which we have agreements do not adopt formulary changes recommended by the PBMs with respect to our medicines, we may not realize the expected access and reimbursement benefits from these agreements. In addition, we generally pay higher rebates for prescriptions covered under plans that adopt a PBM-chosen formulary than for plans that adopt custom formularies. Consequently, the success of our PBM contracting strategy will depend not only on our ability to expand formulary adoption among healthcare plans, but also upon the relative mix of healthcare plans that have PBM-chosen formularies versus custom formularies. If we are unable to realize the expected benefits of our contractual arrangements with the PBMs we may continue to experience reductions in net sales from our inflammation segment medicines and/or reductions in net pricing for our inflammation segment medicines due to increasing patient assistance costs. If we are unable to increase adoption of HorizonCares for filling prescriptions of our medicines and to secure formulary status and reimbursement through arrangements with PBMs and other payers, particularly with healthcare plans that use custom formularies, our ability to achieve net sales growth for our inflammation segment medicines would be impaired.

There has been negative publicity and inquiries from Congress and enforcement authorities regarding the use of specialty pharmacies and drug pricing. Our patient assistance programs are not involved in the prescribing of medicines and are solely to assist in ensuring that when a physician determines one of our medicines offers a potential clinical benefit to their patients and they prescribe one for an eligible patient, financial assistance may be available to reduce the patient's out-of-pocket costs. In addition, all pharmacies that fill prescriptions for our medicines are fully independent, including those that participate in HorizonCares. We do not own or possess any option to purchase an ownership stake in any pharmacy that distributes our medicines, and our relationship with each pharmacy is non-exclusive and arm's length. All of our sales are processed through pharmacies independent of us. Despite this, the negative publicity and interest from Congress and enforcement authorities regarding specialty pharmacies may result in physicians being less willing to participate in our patient assistance programs and thereby limit our ability to increase patient assistance and adoption of our medicines.

We may also encounter difficulty in forming and maintaining relationships with pharmacies that participate in our patient assistance programs. We currently depend on a limited number of pharmacies participating in HorizonCares to fulfill patient prescriptions under the HorizonCares program. If these HorizonCares participating pharmacies are unable to process and fulfill the volume of patient prescriptions directed to them under the HorizonCares program, our ability to maintain or increase prescriptions for our medicines will be impaired. The commercialization of our medicines and our operating results could be affected should any of the HorizonCares participating pharmacies choose not to continue participation in our HorizonCares program or by any adverse events at any of those HorizonCares participating pharmacies. For example, pharmacies that dispense our medicines could lose contracts that they currently maintain with managed care organizations, or MCOs, including PBMs. Pharmacies often enter into agreements with MCOs. They may be required to abide by certain terms and conditions to maintain access to MCO networks, including terms and conditions that could limit their ability to participate in patient assistance programs like ours. Failure to comply with the terms of their agreements with MCOs could result in a variety of penalties, including termination of their agreement, which could negatively impact the ability of those pharmacies to dispense our medicines and collect reimbursement from MCOs for such medicines.

The HorizonCares program may implicate certain federal and state laws related to, among other things, unlawful schemes to defraud, excessive fees for services, healthcare kickbacks, tortious interference with patient contracts and statutory or common law fraud. We have a comprehensive compliance program in place to address adherence with various laws and regulations relating to the selling, marketing and manufacturing of our medicines, as well as certain third-party relationships, including pharmacies. Specifically, with respect to pharmacies, the compliance program utilizes a variety of methods and tools to monitor and audit pharmacies, including those that participate in the HorizonCares program, to confirm their activities, adjudication and practices are consistent with our compliance policies and guidance. Despite our compliance efforts, to the extent the HorizonCares program is found to be inconsistent with applicable laws or the pharmacies that participate in our patient assistance programs do not comply with applicable laws, we may be required to restructure or discontinue such programs, terminate our relationship with certain pharmacies, or be subject to other significant penalties. In November 2015, we received a subpoena from the U.S. Attorney's Office for the Southern District of New York requesting documents and information related to our patient assistance programs and other aspects of our marketing and commercialization activities. We are unable to predict how long this investigation will continue or its outcome, but we have incurred and anticipate that we may continue to incur significant costs in connection with the investigation, regardless of the outcome. We may also become subject to similar investigations by other governmental agencies or Congress. The investigation by the U.S. Attorney's Office and any additional investigations of our patient assistance programs and sales and marketing activities may result in significant damages, fines, penalties, exclusion, additional reporting requirements and/or oversight or other administrative sanctions against us.

If the cost of maintaining our patient assistance programs increases relative to our sales revenues, we could be forced to reduce the amount of patient financial assistance that we offer or otherwise scale back or eliminate such programs, which could in turn have a negative impact on physicians' willingness to prescribe and patients' willingness to fill prescriptions of our medicines. While we believe that our arrangements with PBMs will result in broader inclusion of certain of our inflammation segment medicines on healthcare plan formularies, and therefore increase payer reimbursement and lower our cost of providing patient assistance programs, these arrangements generally require us to pay administrative and rebate payments to the PBMs and/or other payers and their effectiveness will ultimately depend to a large extent upon individual healthcare plan formulary decisions that are beyond the control of the PBMs. If our arrangements with PBMs and other payers do not result in increased prescriptions and reductions in our costs to provide our patient assistance programs that are sufficient to offset the administrative fees and rebate payments to the PBMs and/or other payers, our financial results may continue to be harmed.

If we are unable to successfully implement our commercial plans and facilitate adoption by patients and physicians of any approved medicines through our sales, marketing and commercialization efforts, then we will not be able to generate sustainable revenues from medicine sales which will have a material adverse effect on our business and prospects.

*Our business operations may subject us to numerous commercial disputes, claims and/or lawsuits and such litigation may be costly and time-consuming and could materially and adversely impact our financial position and results of operations.**

Operating in the pharmaceutical industry, particularly the commercialization of medicines, involves numerous commercial relationships, complex contractual arrangements, uncertain intellectual property rights, potential product liability and other aspects that create heightened risks of disputes, claims and lawsuits. In particular, we may face claims related to the safety of our medicines, intellectual property matters, employment matters, tax matters, commercial disputes, competition, sales and marketing practices, environmental matters, personal injury, insurance coverage and acquisition or divestiture-related matters. Any commercial dispute, claim or lawsuit may divert management's attention away from our business, we may incur significant expenses in addressing or defending any commercial dispute, claim or lawsuit, and we may be required to pay damage awards or settlements or become subject to equitable remedies that could adversely affect our operations and financial results.

We are currently in litigation with multiple generic drug manufacturers regarding intellectual property infringement. For example, we are currently involved in Hatch Waxman litigation with generic drug manufacturers related to DUEXIS, VIMOVO and PROCYSBI.

Similarly, from time to time we are involved in disputes with distributors, PBMs and licensing partners regarding our rights and performance of obligations under contractual arrangements. For example, we were previously in litigation with Express Scripts related to alleged breach of contract claims.

Litigation related to these disputes may be costly and time-consuming and could materially and adversely impact our financial position and results of operations if resolved against us.

*A variety of risks associated with operating our business internationally could adversely affect our business.**

In addition to our U.S. operations, we have operations in Ireland, Bermuda, the Grand Duchy of Luxembourg, or Luxembourg, Switzerland, Germany and in Canada. Furthermore, we are pursuing a global expansion strategy, which includes bringing TEPEZZA to patients with TED outside of the United States, including Japan where we are engaging with the Pharmaceutical and Medical Devices Agency and the Japanese medical community. Furthermore, we are initiating an investment in our European infrastructure to support the potential approval in the first quarter of 2022 of UPLIZNA for NMOSD, which has been granted orphan designation by the EC. We face risks associated with our international operations, including possible unfavorable political, tax and labor conditions, which could harm our business. We are subject to numerous risks associated with international business activities, including:

- compliance with Irish laws and the maintenance of our Irish tax residency with respect to our overall corporate structure and administrative operations, including the need to generally hold meetings of our board of directors and make decisions in Ireland, which may make certain corporate actions more cumbersome, costly and time-consuming;
- difficulties in staffing and managing foreign operations;
- foreign government taxes, regulations and permit requirements;
- U.S. and foreign government tariffs, trade restrictions, price and exchange controls and other regulatory requirements;
- anti-corruption laws, including the Foreign Corrupt Practices Act, or the FCPA;
- economic weakness, including inflation, natural disasters, war, events of terrorism or political instability in particular foreign countries;
- fluctuations in currency exchange rates, which could result in increased operating expenses and reduced revenues, and other obligations related to doing business in another country;
- compliance with tax, employment, immigration and labor laws, regulations and restrictions for employees living or traveling abroad;
- workforce uncertainty in countries where labor unrest is more common than in the United States;
- production shortages resulting from any events affecting raw material supply or manufacturing capabilities abroad;
- changes in diplomatic and trade relationships; and
- challenges in enforcing our contractual and intellectual property rights, especially in those foreign countries that do not respect and protect intellectual property rights to the same extent as the United States.

Our business activities outside of the United States are subject to the FCPA and similar anti-bribery or anti-corruption laws, regulations or rules of other countries in which we operate. The FCPA and similar anti-corruption laws generally prohibit offering, promising, giving, or authorizing others to give anything of value, either directly or indirectly, to non-U.S. government officials in order to improperly influence any act or decision, secure any other improper advantage, or obtain or retain business. The FCPA also requires public companies to make and keep books and records that accurately and fairly reflect the transactions of the company and to devise and maintain an adequate system of internal accounting controls. As described above, our business is heavily regulated and therefore involves significant interaction with public officials, including officials of non-U.S. governments. Additionally, in many other countries, the health care providers who prescribe pharmaceuticals are employed by their government, and the purchasers of pharmaceuticals are government entities; therefore, any dealings with these prescribers and purchasers may be subject to regulation under the FCPA. Recently the SEC and the U.S. Department of Justice, or DOJ, have increased their FCPA enforcement activities with respect to pharmaceutical companies. In addition, under the Dodd–Frank Wall Street Reform and Consumer Protection Act, private individuals who report to the SEC original information that leads to successful enforcement actions may be eligible for a monetary award. We are engaged in ongoing efforts that are designed to ensure our compliance with these laws, including due diligence, training, policies, procedures and internal controls. However, there is no certainty that all employees and third-party business partners (including our distributors, wholesalers, agents, contractors, and other partners) will comply with anti-bribery laws. In particular, we do not control the actions of manufacturers and other third-party agents, although we may be liable for their actions. Violation of these laws may result in civil or criminal sanctions, which could include monetary fines, criminal penalties, and disgorgement of past profits, which could have a material adverse impact on our business and financial condition.

We are subject to tax audits around the world, and such jurisdictions may assess additional income tax against us. Although we believe our tax positions are reasonable, the final determination of tax audits could be materially different from our recorded income tax provisions and accruals. The ultimate results of an audit could have a material adverse effect on our operating results or cash flows in the period or periods for which that determination is made and could result in increases to our overall tax expense in subsequent periods.

These and other risks associated with our international operations may materially adversely affect our business, financial condition and results of operations.

*If we fail to develop or acquire other medicine candidates or medicines, our business and prospects would be limited.**

A key element of our strategy is to develop or acquire and commercialize a portfolio of other medicines or medicine candidates in addition to our current medicines, through business or medicine acquisitions such as our acquisition of Viela. Because we do not engage in proprietary drug discovery, the success of this strategy depends in large part upon the combination of our regulatory, development and commercial capabilities and expertise and our ability to identify, select and acquire approved or clinically enabled medicine candidates for therapeutic indications that complement or augment our current medicines, or that otherwise fit into our development or strategic plans on terms that are acceptable to us. Identifying, selecting and acquiring promising medicines or medicine candidates requires substantial technical, financial and human resources expertise. Efforts to do so may not result in the actual acquisition or license of a particular medicine or medicine candidate, potentially resulting in a diversion of our management's time and the expenditure of our resources with no resulting benefit. If we are unable to identify, select and acquire suitable medicines or medicine candidates from third parties or acquire businesses at valuations and on other terms acceptable to us, or if we are unable to raise capital required to acquire businesses or new medicines, our business and prospects will be limited.

Moreover, any medicine candidate we acquire may require additional, time-consuming development or regulatory efforts prior to commercial sale or prior to expansion into other indications, including pre-clinical studies if applicable, and extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All medicine candidates are prone to the risk of failure that is inherent in pharmaceutical medicine development, including the possibility that the medicine candidate will not be shown to be sufficiently safe and/or effective for approval by regulatory authorities. In addition, we cannot assure that any such medicines that are approved will be manufactured or produced economically, successfully commercialized or widely accepted in the marketplace or be more effective or desired than other commercially available alternatives.

In addition, if we fail to successfully commercialize and further develop our medicines, there is a greater likelihood that we will fail to successfully develop a pipeline of other medicine candidates to follow our existing medicines or be able to acquire other medicines to expand our existing portfolio, and our business and prospects would be harmed.

*We have experienced growth and expanded the size of our organization substantially in connection with our acquisition transactions, and we may experience difficulties in managing this growth as well as potential additional growth in connection with future medicine, development program or company acquisitions.**

As of December 31, 2013, we employed approximately 300 full-time employees as a consolidated entity. As of March 31, 2021, we employed approximately 1,640 full-time employees, including approximately 495 sales representatives, representing a substantial change to the size of our organization. We have also experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire in connection with the commercialization of our medicines, requiring us to hire and train new sales representatives. Our management, personnel, systems and facilities currently in place may not be adequate to support anticipated growth, and we may not be able to retain or recruit qualified personnel in the future due to competition for personnel among pharmaceutical businesses.

As our commercialization plans and strategies continue to develop, including as a result of our acquisition of Viela, we will need to continue to recruit and train sales and marketing personnel. Our ability to manage any future growth effectively may require us to, among other things:

- continue to manage and expand the sales and marketing efforts for our existing medicines;
- enhance our operational, financial and management controls, reporting systems and procedures;
- expand our international resources;
- successfully identify, recruit, hire, train, maintain, motivate and integrate additional employees;
- establish and increase our access to commercial supplies of our medicines and medicine candidates;
- expand our facilities and equipment; and
- manage our internal development efforts effectively while complying with our contractual obligations to licensors, licensees, contractors, collaborators, distributors and other third parties.

Our acquisitions have resulted in many changes, and our acquisition of Viela may result in additional changes, including significant changes in the corporate business and legal entity structure, the integration of other companies and their personnel with us, and changes in systems. We may encounter unexpected difficulties or incur unexpected costs, including:

- difficulties in achieving growth prospects from combining third-party businesses with our business;
- difficulties in the integration of operations and systems;
- difficulties in the assimilation of employees and corporate cultures;
- challenges in preparing financial statements and reporting timely results at both a statutory level for multiple entities and jurisdictions and at a consolidated level for public reporting;
- challenges in keeping existing physician prescribers and patients and increasing adoption of acquired medicines;
- difficulties in achieving anticipated cost savings, synergies, business opportunities and growth prospects from the combination;
- potential unknown liabilities, adverse consequences and unforeseen increased expenses associated with the transaction; and
- challenges in attracting and retaining key personnel.

If any of these factors impair our ability to continue to integrate our operations with those of any companies or businesses we acquire, including Viela, we may not be able to realize the business opportunities, growth prospects and anticipated tax synergies from combining the businesses. In addition, we may be required to spend additional time or money on integration that otherwise would be spent on the development and expansion of our business. For example, we will need to spend additional time and money on the integration of Viela's R&D and sales and marketing functions with our own functions.

We may not be successful in growing our commercial operations outside the United States, and could encounter other challenges in growing our commercial presence, including due to risks associated with political and economic instability, operating under different legal requirements and tax complexities. If we are unable to manage our commercial growth outside of the United States, our opportunities to expand sales in other countries will be limited or we may experience greater costs with respect to our ex-U.S. commercial operations.

We have also broadened our acquisition strategy to include development-stage assets or programs, which entails additional risk to us. For example, if we are unable to identify programs that ultimately result in approved medicines, we may spend material amounts of our capital and other resources evaluating, acquiring and developing medicines that ultimately do not provide a return on our investment. We have less experience evaluating development-stage assets and may be at a disadvantage compared to other entities pursuing similar opportunities. Regardless, development-stage programs generally have a high rate of failure and we cannot guarantee that any such programs will ultimately be successful. While we have significantly enhanced our R&D function in recent years, we may need to enhance our clinical development and regulatory functions to properly evaluate and develop earlier-stage opportunities, which may include recruiting personnel that are knowledgeable in therapeutic areas we have not yet pursued. If we are unable to acquire promising development-stage assets or eventually obtain marketing approval for them, we may not be able to create a meaningful pipeline of new medicines and eventually realize a return on our investments. For example, a core strategic rationale for the Viela acquisition is Viela's pipeline of medicine candidates and R&D capabilities, but if we experience clinical failures with respect to Viela's medicine candidates and research programs or such candidates and programs do not otherwise result in marketed medicines, we will not realize the expected benefits from the substantial investment we intend to make in the acquisition and subsequent development of the Viela pipeline. As our R&D plans and strategies continue to develop, including as a result of our acquisition of Viela, we will need to continue to recruit and train R&D personnel.

Our management may also have to divert a disproportionate amount of its attention away from day-to-day activities and toward managing these growth and integration activities. Our future financial performance and our ability to execute on our business plan will depend, in part, on our ability to effectively manage any future growth and our failure to effectively manage growth could have a material adverse effect on our business, results of operations, financial condition and prospects.

*Our prior medicine and company acquisitions and any other strategic transactions that we may pursue in the future could have a variety of negative consequences, and we may not realize the benefits of such transactions or attempts to engage in such transactions.**

We have completed multiple medicine and company acquisitions, including most recently Viela, and our strategy is to engage in additional strategic transactions with third parties, such as acquisitions of companies or divisions of companies and asset purchases of medicines, medicine candidates or technologies that we believe will complement or augment our existing business. We may also consider a variety of other business arrangements, including spin-offs, strategic partnerships, joint ventures, restructurings, divestitures, business combinations and other investments. Any such transaction may require us to incur non-recurring and other charges, increase our near and long-term expenditures, pose significant integration challenges, create additional tax, legal, accounting and operational complexities in our business, require additional expertise, result in dilution to our existing shareholders and disrupt our management and business, which could harm our operations and financial results.

We are subject to contractual obligations under an amended and restated license agreement with the Regents of the University of California, San Diego, or UCSD, as amended, with respect to PROCYSBI. To the extent that we fail to perform our obligations under the agreement, UCSD may, with respect to applicable indications, terminate the license or otherwise cause the license to become non-exclusive. If this license was terminated, we would have no further right to use or exploit the related intellectual property, which would limit our ability to develop PROCYSBI in other indications, and could impact our ability to continue commercializing PROCYSBI in its approved indications.

We face significant competition in seeking appropriate strategic transaction opportunities and the negotiation process for any strategic transaction can be time-consuming and complex. In addition, we may not be successful in our efforts to engage in certain strategic transactions because our financial resources may be insufficient and/or third parties may not view our commercial and development capabilities as being adequate. We may not be able to expand our business or realize our strategic goals if we do not have sufficient funding or cannot borrow or raise additional capital. There is no assurance that following any of our recent acquisition transactions or any other strategic transaction, including the acquisition of Viela, we will achieve the anticipated revenues, net income or other benefits that we believe justify such transactions. In addition, any failures or delays in entering into strategic transactions anticipated by analysts or the investment community could seriously harm our consolidated business, financial condition, results of operations or cash flow.

We may not be able to successfully maintain our current advantageous tax status and resulting tax rates, which could adversely affect our business and financial condition, results of operations and growth prospects.

Our parent company is incorporated in Ireland and has subsidiaries maintained in multiple jurisdictions, including Ireland, the United States, Switzerland, Luxembourg, Germany, Canada and Bermuda. We are able to achieve a favorable tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, including Ireland and Bermuda, together with the use of intercompany service and transfer pricing agreements, each on an arm's length basis. Our effective tax rate may be different than experienced in the past due to numerous factors including, changes to the tax laws of jurisdictions that we operate in, the enactment of new tax treaties or changes to existing tax treaties, changes in the mix of our profitability from jurisdiction to jurisdiction, the implementation of the EU Anti-Tax Avoidance Directive (see further discussion below), the implementation of the Bermuda Economic Substance Act 2018 (effective December 31, 2018) and our inability to secure or sustain acceptable agreements with tax authorities (if applicable). Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations. Taxing authorities, such as the U.S. Internal Revenue Service, or IRS, actively audit and otherwise challenge these types of arrangements, and have done so in the pharmaceutical industry. We expect that these challenges will continue as a result of the recent increase in scrutiny and political attention on corporate tax structures. The IRS and/or the Irish tax authorities may challenge our structure and transfer pricing arrangements through an audit or lawsuit. Responding to or defending such a challenge could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We cannot predict whether taxing authorities will conduct an audit or file a lawsuit challenging this structure, the cost involved in responding to any such audit or lawsuit, or the outcome. If we are unsuccessful in defending such a challenge, we may be required to pay taxes for prior periods, as well as interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our medicines or seek to raise additional funds, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

The IRS may not agree with our conclusion that our parent company should be treated as a foreign corporation for U.S. federal income tax purposes following the combination of the businesses of Horizon Pharma, Inc., or HPI, our predecessor, and Vidara Therapeutics International Public Limited Company, or Vidara.

Although our parent company is incorporated in Ireland, the IRS may assert that it should be treated as a U.S. corporation (and, therefore, a U.S. tax resident) for U.S. federal income tax purposes pursuant to Section 7874 of the Internal Revenue Code of 1986, as amended, or the Code. A corporation is generally considered a tax resident in the jurisdiction of its organization or incorporation for U.S. federal income tax purposes. Because our parent company is an Irish incorporated entity, it would generally be classified as a foreign corporation (and, therefore, a non-U.S. tax resident) under these general rules. Section 7874 of the Code provides an exception pursuant to which a foreign incorporated entity may, in certain circumstances, be treated as a U.S. corporation for U.S. federal income tax purposes.

In July 2018, the IRS issued regulations under Section 7874. We do not believe that our classification as a foreign corporation for U.S. federal income tax purposes is affected by Section 7874 or the regulations thereunder, though the IRS may disagree.

Recent and future changes to U.S. and non-U.S. tax laws could materially adversely affect our company.

Under current law, we expect our parent company to be treated as a foreign corporation for U.S. federal income tax purposes. However, changes to the rules in Section 7874 of the Code or regulations promulgated thereunder or other guidance issued by the U.S. Department of the Treasury, or the U.S. Treasury, or the IRS could adversely affect our parent company's status as a foreign corporation for U.S. federal income tax purposes or the taxation of transactions between members of our group, and any such changes could have prospective or retroactive application. If our parent company is treated as a domestic corporation, more of our income will be taxed by the United States which may substantially increase our effective tax rate.

In addition, the Organization for Economic Co-operation and Development, or the OECD, released its Base Erosion and Profit Shifting project final report on October 5, 2015. This report provides the basis for international standards for corporate taxation that are designed to prevent, among other things, the artificial shifting of income to tax havens and low-tax jurisdictions, the erosion of the tax base through interest deductions on intercompany debt and the artificial avoidance of permanent establishments (i.e., tax nexus with a jurisdiction). Legislation to adopt these standards has been enacted or is currently under consideration in a number of jurisdictions. On June 7, 2017, several countries, including many countries that we operate and have subsidiaries in, participated in the signing ceremony adopting the OECD's Multilateral Convention to Implement Tax Treaty Related Measures to Prevent Base Erosion and Profit Shifting, commonly referred to as the MLI. The MLI came into effect on July 1, 2018. In January 2019, Ireland deposited the instrument of ratification of Ireland's MLI choices with the OECD. Ireland's MLI came into force on May 1, 2019, however the provisions in respect of withholding taxes and other taxes levied by Ireland did not come into effect for us until January 1, 2020 (with application also depending on whether the MLI has been ratified in other jurisdictions whose tax treaties with Ireland are affected). The MLI may modify affected tax treaties making it more difficult for us to obtain advantageous tax-treaty benefits. The number of affected tax treaties could eventually be in the thousands. As a result, our income may be taxed in jurisdictions where it is not currently taxed and at higher rates of tax than it is currently taxed, which may increase our effective tax rate.

The Irish Finance Act 2019, or Finance Act 2019, which was signed into law on December 22, 2019, introduced changes to Ireland's transfer pricing rules, which came into force with effect from January 1, 2020. The changes introduce the 2017 version of the OECD Transfer Pricing Guidelines, or 2017 OECD Guidelines, as the reference guidelines for Ireland's domestic transfer pricing regime. The 2017 OECD Guidelines were already applicable under Ireland's international tax treaties and therefore the introduction of these guidelines should only affect transactions with non-tax treaty countries. In addition to updating Irish tax law for the 2017 OECD Guidelines, these changes also extend the transfer pricing rules to certain non-trading transactions and to certain capital transactions. We have restructured certain intercompany arrangements, such that we do not expect there to be a material impact on our effective tax rate as a result of the introduction of these provisions.

On July 12, 2016, the Anti-Tax Avoidance Directive, or ATAD, was formally adopted by the Economic and Financial Affairs Council of the EU. The stated objective of the ATAD is to provide for the effective and swift coordinated implementation of anti-base erosion and profit shifting measures at EU level. Like all directives, the ATAD is binding as to the results it aims to achieve though EU Member States are free to choose the form and method of achieving those results. In addition, the ATAD contains a number of optional provisions that present an element of choice as to how it will be implemented into law. On December 25, 2018, the Finance Act 2018 was signed into Irish law, which introduced certain elements of the ATAD, such as the Controlled Foreign Company, or CFC, regime, into Irish law. The CFC regime became effective as of January 1, 2019. The ATAD also set out a high-level framework for the introduction of Anti-hybrid provisions. Finance Act 2019 introduced Anti-hybrid legislation in Ireland with effect from January 1, 2020. It is anticipated that Finance Act 2021 will introduce further ATAD measures, such as the interest limitation rules and anti-hybrid rules to neutralize reverse-hybrid mismatches into Irish law with effect from January 1, 2022. Although it is difficult at this stage to determine with precision the impact that these remaining provisions will have, their implementation could materially increase our effective tax rate.

On December 22, 2017, U.S. federal income tax legislation was signed into law (H.R. 1, "An Act to provide for reconciliation pursuant to titles II and V of the concurrent resolution on the budget for fiscal year 2018", informally titled the Tax Cuts and Jobs Act, or the Tax Act) that significantly revised the Code in the United States. The Tax Act, among other things, contained significant changes to corporate taxation, including reduction of the corporate tax rate from a top marginal rate of 35% to a flat rate of 21%, limitation of the tax deduction for interest expense to 30% of adjusted earnings (except for certain small businesses), implementation of a "base erosion anti-abuse tax" which requires U.S. corporations to make an alternative determination of taxable income without regard to tax deductions for certain payments to affiliates, taxation of certain non-U.S. corporations' earnings considered to be "global intangible low taxed income", or GILTI, repeal of the alternative minimum tax, or AMT, for corporations and changes to a taxpayer's ability to either utilize or refund the AMT credits previously generated, changes to the limitation on deductions for certain executive compensation particularly with respect to the removal of the previously allowed performance based compensation exception, changes in the attribution rules relating to shareholders of certain "controlled foreign corporations", limitation of the deduction for net operating losses to 80% of current year taxable income and elimination of net operating loss carrybacks, one-time taxation of offshore earnings at reduced rates regardless of whether they are repatriated, elimination of U.S. tax on foreign earnings (subject to certain important exceptions), immediate deductions for certain new investments instead of deductions for depreciation expense over time, and modifying or repealing many business deductions and credits. For example, U.S. federal income tax law resulting in additional taxes owed by U.S. shareholders under the GILTI rules, together with the Tax Act's change to the attribution rules related to "controlled foreign corporations" may discourage U.S. investors from owning or acquiring 10% or greater of our outstanding ordinary shares, which other shareholders may have viewed as beneficial or may otherwise negatively impact the trading price of our ordinary shares.

On March 27, 2020, H.R.748, the Coronavirus Aid, Relief, and Economic Security Act, or the CARES Act, was enacted in the United States, which provides temporary relief from certain aspects of the Tax Act that had imposed limitations on the utilization of certain losses, interest expense deductions, and the timing of refunds of alternative minimum tax credits.

We are unable to predict what tax laws may be proposed or enacted in the future or what effect such changes would have on our business. To the extent new tax laws are enacted, or new guidance released, this could have an adverse effect on our future effective tax rate. It could also lead to an increase in the complexity and cost of tax compliance. We urge our shareholders to consult with their legal and tax advisors with respect to the potential tax consequences of investing in or holding our ordinary shares.

If a United States person is treated as owning at least 10% of our ordinary shares, such holder may be subject to adverse U.S. federal income tax consequences.

If a United States person is treated as owning (directly, indirectly, or constructively) at least 10% of the value or voting power of our ordinary shares, such person may be treated as a "United States shareholder" with respect to each "controlled foreign corporation" in our group (if any). Because our group includes one or more U.S. subsidiaries, certain of our non-U.S. subsidiaries could be treated as controlled foreign corporations (regardless of whether or not we are treated as a controlled foreign corporation). A United States shareholder of a controlled foreign corporation may be required to report annually and include in its U.S. taxable income its pro rata share of "Subpart F income," "global intangible low-taxed income," and investments in U.S. property by controlled foreign corporations, regardless of whether we make any distributions. An individual that is a United States shareholder with respect to a controlled foreign corporation generally would not be allowed certain tax deductions or foreign tax credits that would be allowed to a U.S. corporation that is a United States shareholder with respect to a controlled foreign corporation. Failure to comply with these reporting and tax paying obligations may subject a United States shareholder to significant monetary penalties and may prevent the statute of limitations from starting with respect to such shareholder's U.S. federal income tax return for the year for which reporting was due. We cannot provide any assurances that we will assist investors in determining whether any of our non-U.S. subsidiaries is treated as a controlled foreign corporation or whether any investor is treated as a United States shareholder with respect to any such controlled foreign corporation or furnish to any United States shareholders information that may be necessary to comply with the aforementioned reporting and tax paying obligations. A United States investor should consult its advisors regarding the potential application of these rules to an investment in our ordinary shares.

If we are not successful in attracting and retaining highly qualified personnel, we may not be able to successfully implement our business strategy.

Our ability to compete in the highly competitive biotechnology and pharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, scientific and medical personnel. We are highly dependent on our management, sales and marketing and scientific and medical personnel, including our executive officers. In order to retain valuable employees at our company, in addition to salary and annual cash incentives, we provide a mix of performance stock units, or PSUs, that vest subject to attainment of specified corporate performance goals and continued services, stock options and restricted stock units, or RSUs, that vest over time subject to continued services. The value to employees of PSUs, stock options and RSUs will be significantly affected by movements in our share price that are beyond our control, and may at any time be insufficient to counteract more lucrative offers from other companies.

Despite our efforts to retain valuable employees, members of our management, sales and marketing, regulatory affairs, clinical development, medical affairs and development teams may terminate their employment with us on short notice. Although we have written employment arrangements with all of our employees, these employment arrangements generally provide for at-will employment, which means that our employees can leave our employment at any time, with or without notice. The loss of the services of any of our executive officers or other key employees and our inability to find suitable replacements could potentially harm our business, financial condition and prospects. We do not maintain "key man" insurance policies on the lives of these individuals or the lives of any of our other employees. Our success also depends on our ability to continue to attract, retain and motivate highly skilled junior, mid-level, and senior managers as well as junior, mid-level, and senior sales and marketing and scientific and medical personnel.

Many of the other biotechnology and pharmaceutical companies with whom we compete for qualified personnel have greater financial and other resources, different risk profiles and longer histories in the industry than we do. They also may provide more diverse opportunities and better chances for career advancement. Some of these characteristics may be more appealing to high quality candidates than that which we have to offer. If we are unable to continue to attract and retain high quality personnel, the rate and success at which we can develop and commercialize medicines and medicine candidates will be limited.

We are subject to ongoing obligations and continued regulatory review by the FDA and equivalent foreign regulatory agencies, which may result in significant additional expense and significant penalties if we fail to comply with regulatory requirements or experience unanticipated problems with our medicines.

Any regulatory approvals that we obtain for our medicine candidates may also be subject to limitations on the approved indicated uses for which the medicine may be marketed or to the conditions of approval, or contain requirements for potentially costly post-marketing testing, including Phase 4 clinical trials and surveillance to monitor the safety and efficacy of the medicine candidate. In addition, with respect to our current FDA-approved medicines (and with respect to our medicine candidates, if approved), the manufacturing processes, labeling, packaging, distribution, adverse event reporting, storage, advertising, promotion and recordkeeping for the medicine are subject to extensive and ongoing regulatory requirements. These requirements include submissions of safety and other post-marketing information and reports, registration, as well as continued compliance with cGMPs, GCPs, International Council for Harmonisation, or ICH, guidelines and GLPs, which are regulations and guidelines enforced by the FDA for all of our medicines in clinical development, for any clinical trials that we conduct post-approval.

In addition, the FDA closely regulates the marketing and promotion of drugs and biologics. The FDA does not regulate the behaviour of physicians in their choice of treatments. The FDA does, however, restrict manufacturers' promotional communications. A significant number of pharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities in connection with the promotion of medicines for off-label uses and other sales practices. These investigations have alleged violations of various U.S. federal and state laws and regulations, including claims asserting antitrust violations, violations of the Food, Drug and Cosmetic Act, false claims laws, the Prescription Drug Marketing Act, anti-kickback laws, and other alleged violations in connection with the promotion of medicines for unapproved uses, pricing and Medicare and/or Medicaid reimbursement.

Later discovery of previously unknown problems with a medicine, including adverse events of unanticipated severity or frequency, or with our third-party manufacturers or manufacturing processes, or failure to comply with regulatory requirements, may result in, among other things:

- restrictions on the marketing or manufacturing of the medicine, withdrawal of the medicine from the market, or voluntary or mandatory medicine recalls;
- refusal by the FDA to approve pending applications or supplements to approved applications filed by us or our strategic partners, or suspension or revocation of medicine license approvals;
- medicine seizure or detention, or refusal to permit the import or export of medicines; and
- injunctions, the imposition of civil or criminal penalties, or exclusion, debarment or suspension from government healthcare programs.

If we are not able to maintain regulatory compliance, we may lose any marketing approval that we may have obtained and we may not sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects.

*We are subject to federal, state and foreign healthcare laws and regulations and implementation or changes to such healthcare laws and regulations could adversely affect our business and results of operations.**

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals that change the healthcare system in ways that could impact profitability. In the United States and abroad there is significant interest in implementing regulations and legislation with the stated goals of containing healthcare costs, improving quality, and/or expanding access. The pharmaceutical industry has been a focus of these efforts and has been significantly affected by major legislative initiatives, particularly in the United States.

The healthcare system is highly regulated in the United States and, as a biotech company that participates in government-regulated healthcare programs, we are subject to complex laws and regulations. Violation of these laws, or any other federal or state regulations, may subject us to significant administrative, civil and/or criminal penalties, damages, disgorgement, fines, exclusion, imprisonment, additional reporting requirements, and/or oversight from federal health care programs that could require the restructuring of our operations. Any of these could have a material adverse effect on our business and financial results. Any action against us for violation of these laws, even if we ultimately are successful in our defense, will cause us to incur significant legal expenses and divert our management's attention away from the operation of our business.

There were efforts by the Trump administration as well as Congressional and judicial actions taken to replace or weaken certain aspects of the Patient Protection and Affordable Care Act, as amended by the Health Care and Education Reconciliation Act (collectively, the ACA). For example, President Trump signed several Executive Orders and other directives designed to eliminate, delay or otherwise modify the implementation of certain provisions of the ACA. Concurrently, Congress considered legislation that would repeal and/or replace all or part of the ACA. While Congress has not passed comprehensive repeal legislation, it has enacted laws that modify certain provisions of the ACA. In particular, the Tax Act included a provision which decreased, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA to $0. Commonly referred to as the "individual mandate," this provision imposed a fine on certain individuals who fail to maintain qualifying health coverage for all or part of the year. In addition, the 2020 federal spending package permanently eliminated, effective January 1, 2020, the ACA-mandated "Cadillac" tax on high-cost employer-sponsored health coverage and medical device tax and, effective January 1, 2021, also eliminated the health insurer tax. Finally, Congress increased the manufacturer coverage gap discount that is owed by pharmaceutical manufacturers of branded drugs and biosimilars who participate in Medicare Part D from 50% to 70%.

Challenges to the ACA are also taking place in courts, including the U.S. Supreme Court, with some lower court's ruling some or all of the ACA unconstitutional. For example, on December 14, 2018, a Texas U.S. District Court Judge ruled that the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress as part of the Tax Act. Additionally, on December 18, 2019, the U.S. Court of Appeals for the 5th Circuit upheld the District Court ruling that the individual mandate was unconstitutional and remanded the case back to the District Court to determine whether the remaining provisions of the ACA are invalid as well. The U.S. Supreme Court is currently reviewing this case, although it is unclear when a decision will be made. Although the U.S. Supreme Court has not yet ruled on the constitutionality of the ACA, on January 28, 2021, President Biden issued an executive order to initiate a special enrollment period from February 15, 2021 through May 15, 2021 for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructs certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA. There is a wide range of potential outcomes to this litigation and it is unclear how the Supreme Court ruling, other such litigation and the healthcare reform measures of the Biden administration will impact the ACA's many different provisions affecting the health system, the pharmaceutical sector and our business.

In addition, drug pricing by pharmaceutical companies in the United States has come under increased scrutiny. Specifically, there have been several recent state and U.S. congressional inquiries into pricing practices by pharmaceutical companies.

At the federal level, the Trump Administration used several means to propose or implement drug pricing reform, including through federal budget proposals and issuing executive orders and proposals in an effort to reduce the cost of drugs under Medicare and reform government program reimbursement methodologies, while calling on Congress to pass legislation that addresses drug prices and competition.

Additionally, in 2020, the Administration advanced its agenda on drug pricing through a series of executive orders. For example, on July 24, 2020, President Trump announced several executive orders related to prescription drug pricing that attempt to implement several of the Trump Administration proposals, including a policy that would tie both Medicare Part B and Part D drug prices to international drug prices, or the "most favored nation price," the details of which were released on September 13, 2020; one that directs HHS to finalize the Canadian drug importation proposed rule previously issued by HHS and makes other changes allowing for personal importation of drugs from Canada; one that directs HHS to finalize the rulemaking process on modifying the anti-kickback law safe harbors for plans, pharmacies, and PBMs, commonly known as the "rebate rule"; and one that reduces the cost of insulin and injectable epinephrine to patients acquired through the 340B program. Further, on August 6, 2020, the Trump administration issued another executive order that instructs the federal government to develop a list of "essential" medicines and then buy them and other medical supplies from U.S. manufacturers instead of from companies around the world, including China. The order is meant to reduce regulatory barriers to domestic pharmaceutical manufacturing and catalyze manufacturing technologies needed to keep drug prices low and the production of drug products in the United States. The FDA issued the list of "essential" medicines pursuant to this order on October 30, 2020.

In November 2020, CMS issued an interim final rule, or IFR, implementing the Most Favored Nation, or MFN, Model basing Medicare Part B reimbursement rates for the top fifty drugs covered by Part B based to the lowest price drug manufacturers receive in Organization for Economic Cooperation and Development, or OECD, countries with a similar gross domestic product per capita. The MFN Model mandates participation for providers prescribing drugs included on the list and will apply in all U.S. states and territories for a seven-year period that was scheduled to begin on January 1, 2021 and end December 31, 2027. However, several lawsuits were filed challenging the rule. On December 28, 2020, the United States District Court in Northern California issued a nationwide preliminary injunction against implementation of the interim final rule. One court granted a preliminary injunction enjoining CMS from moving forward with the rule until CMS completed regular notice and comment rulemaking, delaying implementation. It is unclear if the Biden Administration will support, modify, or reverse the MFN model or implement other alternative measures. President Biden's presidential election campaign had indicated that Biden would direct Medicare to negotiate drug prices using international prices as a reference. The FDA released a final rule implementing a portion of the importation executive order providing guidance for states to build and submit importation plans. Several states have acted to implement importation plans or have introduced legislation to do so. FDA also finalized guidance for manufacturers to obtain an additional National Drug Code for an FDA-approved drug as part of a process to provide a manufacturer a means to import its drugs that were originally intended to be marketed in and authorized for sale in a foreign country. In addition, HHS and FDA are in the process of accepting industry proposals to facilitate personal importation of prescription drugs. On November 20, 2020, HHS also finalized the "rebate rule" regulation by removing safe harbor protection for price reductions from pharmaceutical manufacturers to plan sponsors under Part D, either directly or through PBMs, unless the price reduction is required by law. The implementation of the rule has been delayed by the Biden administration from January 1, 2022 to January 1, 2023 in response to ongoing litigation. The rule also creates a new safe harbor for price reductions reflected at the point-of-sale, as well as a safe harbor for certain fixed fee arrangements between PBMs, the implementation of which have also been delayed until January 1, 2023.

Congress continued to seek new legislative and/or administrative measures to control drug costs. For example, in June 2020, the U.S. House of Representatives passed a bill, H.R. 1425, "Patient Protection and Affordable Care Enhancement Act", which would strengthen and expand parts of the ACA and incentivize Medicaid expansion, but also proposes to implement a "Fair Price Negotiation Program" to utilize international price referencing metrics for certain drugs that are considered high-cost or are reimbursable by both Medicare Part D and Part B, while giving commercial payers, including employer and individual market plans, access to the reference price. The majority of our medicines are purchased by private payers, and much of the focus of pending legislation is on government program reimbursement.

Additionally, certain proposals have been contemplated that would implement a cap on annual price increases for certain drugs covered under Medicare at the rate of inflation or require the respective manufacturers to pay a rebate. There has also been advocacy for increasing the Medicaid drug rebates cap, currently at 100% of a drug's average manufacturer price or removing such cap in its entirety.

In addition to the federal government, many states have taken action in an effort to address rising health care costs. Generally, states have been more focused on introducing and enacting legislation that brings more transparency to drug pricing by requiring drug companies subject to these laws to notify insurers and government regulators of price increases and provide an explanation of the reasons for the increases, reducing the out-of-pocket cost of prescription drugs, and reviewing the relationship between pricing and manufacturer patient programs. However, in the 2020 budget, the California legislature directed the California Health and Human Services Agency to develop a process to use international reference pricing for Medicaid drugs. Certain states, including California, have enacted drug transparency laws requiring drug manufacturers to provide advance notice and explanation for price increases above a certain threshold. In addition, a growing number of states have implemented, or are contemplating implementing, drug affordability boards to establish "allowable rates" for certain high-cost drugs identified by such boards.

In addition to the aforementioned price reform measures, there are other potential reform measures relating to the pharmaceutical industry. For example, there have been efforts to amend the Orphan Drug Act, including a bill passed in the House of Representatives in November 2020, the Orphan Drug Exclusivity Act, that would have limited manufacturers' ability to receive orphan drug exclusivity under the "cost recovery" pathway under the Orphan Drug Act. While the Senate did not take further action on this bill in 2020, the bill's co-sponsors were re-elected, and it remains unclear whether it will be re-introduced. Further, on December 31, 2020, CMS issued a final rule that broadened the definition of "line extension" under the ACA. This portion of the rule will be effective on January 1, 2022. It is unclear whether this final rule will be challenged similar to other final rules that were issued shortly prior to the change in presidential administration.

In countries in the EU, legislators, policymakers, and healthcare insurance funds continue to propose and implement cost-containing measures to keep healthcare costs down, due in part to the attention being paid to healthcare cost containment in the EU. Certain of these changes could impose limitations on the prices we will be able to charge for our medicines and any approved medicine candidates or the amounts of reimbursement available for these products from governmental agencies or third-party payers, may increase the tax obligations on pharmaceutical companies such as ours, or may facilitate the introduction of generic competition with respect to our products.

The implementation of cost containment measures or other healthcare reforms may prevent us from being able to generate revenue, attain profitability, or commercialize our current medicines and/or those for which we may receive regulatory approval in the future.

We are subject, directly or indirectly, to federal and state healthcare fraud and abuse, transparency laws and false claims laws. Prosecutions under such laws have increased in recent years and we may become subject to such litigation. If we are unable to comply, or have not fully complied, with such laws, we could face substantial penalties.

In the United States, we are subject directly, or indirectly through our customers and other third parties, to various state and federal fraud and abuse and transparency laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, civil monetary penalty statutes prohibiting, among other things, beneficiary inducements, and similar state and local laws, federal and state privacy and security laws, such as the Health Insurance Portability and Accountability Act of 1996, sunshine laws, government price reporting laws, and other fraud laws. Some states, such as Massachusetts, make certain reported information public. In addition, there are state and local laws that require pharmaceutical representatives to be licensed and comply with codes of conduct, transparency reporting, and other obligations. Collectively, these laws may affect, among other things, our current and proposed research, sales, marketing and educational programs, as well as other possible relationships with customers, pharmacies, physicians, payers, and patients. We are subject to similar laws in the EU/EEA, including the EU General Data Protection Regulation (2016/679), or GDPR, under which fines of up to €20.0 million or up to 4% of the annual global turnover of the infringer, whichever is greater, could be imposed for significant non-compliance.

Compliance with these laws, including the development of a comprehensive compliance program, is difficult, costly and time consuming. Because of the breadth of these laws and the narrowness of available statutory and regulatory exemptions, it is possible that some of our business activities could be subject to challenge under one or more of such laws. Moreover, state governmental agencies may propose or enact laws and regulations that extend or contradict federal requirements. These risks may be increased where there are evolving interpretations of applicable regulatory requirements, such as those applicable to manufacturer co-pay programs. Pharmaceutical manufacturer co-pay programs, including pharmaceutical manufacturer donations to patient assistance programs offered by charitable foundations, are the subject of ongoing litigation, enforcement actions and settlements (involving other manufacturers and to which we are not a party) and evolving interpretations of applicable regulatory requirements and certain state laws, and any change in the regulatory or enforcement environment regarding such programs could impact our ability to offer such programs. Other recent legislation and regulatory policies contain provisions that disincentivizes the use of co-pay coupons by requiring their value to be included in average sales price or best price calculations, potentially lowering reimbursement for drugs with a high use of copay coupons in Medicare Part B and Medicaid. If we are unsuccessful with our co-pay programs, we would be at a competitive disadvantage in terms of pricing versus preferred branded and generic competitors, or be subject to significant penalties. We are engaged in various business arrangements with current and potential customers, and we can give no assurance that such arrangements would not be subject to scrutiny under such laws, despite our efforts to properly structure such arrangements. Even if we structure our programs with the intent of compliance with such laws, there can be no certainty that we would not need to defend our business activities against enforcement or litigation. Further, we cannot give any assurances that prior business activities or arrangements of other companies that we acquire will not be scrutinized or subject to enforcement or litigation. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have an impact on our business, including the imposition of significant civil, criminal and administrative sanctions, damages, disgorgement, monetary fines, possible exclusion from participation in Medicare, Medicaid and other federal healthcare programs, imprisonment, integrity oversight and reporting obligations, contractual damages, reputational harm, diminished profits and future earnings, and curtailment or restructuring of our operations, any of which could adversely affect our ability to operate our business and our results of operations.

There has also been a trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposed reporting requirements on drug manufacturers for payments made by them to physicians and teaching hospitals, as well as ownership and investment interests held by physicians, defined to include dentists, podiatrists, optometrists and licensed chiropractors, and their immediate family members. Beginning in 2022, applicable manufacturers also will be required to report such information regarding payments and transfers of value provided during the previous year to include physician assistants, nurse practitioners, clinical nurse specialists, anesthesiologist assistants, certified registered nurse anesthetists and certified nurse midwives. Failure to submit required information may result in significant civil monetary penalties.

On March 5, 2019, we received a civil investigative demand, or CID, from the DOJ pursuant to the Federal False Claims Act regarding assertions that certain of our payments to PBMs were potentially in violation of the Anti-Kickback Statute. The CID requests certain documents and information related to our payments to PBMs, pricing and our patient assistance program regarding DUEXIS, VIMOVO and PENNSAID 2%. We are cooperating with the investigation. While we believe that our payments and programs are compliant with the Anti-Kickback Statute, no assurance can be given as to the timing or outcome of the DOJ’s investigation, or that it will not result in a material adverse effect on our business.

We are unable to predict whether we could be subject to other actions under any of these or other healthcare laws, or the impact of such actions. If we are found to be in violation of, or to have encouraged or assisted the violation by third parties of any of the laws described above or other applicable state and federal fraud and abuse laws, we may be subject to penalties, including significant administrative, civil and criminal penalties, damages, fines, withdrawal of regulatory approval, imprisonment, exclusion from government healthcare reimbursement programs, contractual damages, reputational harm, diminished profits and future earnings, injunctions and other associated remedies, or private “qui tam” actions brought by individual whistleblowers in the name of the government, and the curtailment or restructuring of our operations, all of which could have a material adverse effect on our business and results of operations. Any action against us for violation of these laws, even if we successfully defend against it, could cause us to incur significant legal expenses and divert our management’s attention from the operation of our business.

*Our medicines or any other medicine candidate that we develop may cause undesirable side effects or have other properties that could delay or prevent regulatory approval or commercialization, result in medicine re-labeling or withdrawal from the market or have a significant impact on customer demand.**

Undesirable side effects caused by any medicine candidate that we develop could result in the denial of regulatory approval by the FDA or other regulatory authorities for any or all targeted indications, or cause us to evaluate the future of our development programs. In our Phase 3 clinical trial evaluating TEPEZZA for the treatment of active TED, the most commonly reported treatment-emergent adverse events were muscle spasms, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache and dry skin. With respect to KRYSTEXXA, the most commonly reported serious adverse reactions in the pivotal trial were gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis, exacerbation of pre-existing congestive heart failure and vomiting. With respect to RAVICTI, the most common side effects are diarrhea, nausea, decreased appetite, gas, vomiting, high blood levels of ammonia, headache, tiredness and dizziness. The most common side effects observed in pivotal trials for ACTIMMUNE were "flu-like" or constitutional symptoms such as fever, headache, chills, myalgia and fatigue. With respect to UPLIZNA, the most common adverse reactions across both the randomized and open-label treatment in our N-MOmentum trial for UPLIZNA were urinary tract infection, nasopharyngitis, infusion reaction, arthralgia and headache. The most common infections reported by treated patients in the randomized and open-label periods included urinary tract infection, nasopharyngitis, upper respiratory tract infection and influenza. In addition, two deaths were reported in the ongoing open-label period. One death occurred in a patient experiencing a myelitis attack and was considered unrelated to UPLIZNA by the investigator. The second death was due to complications from mechanical ventilator-associated pneumonia in a patient who developed new neurological symptoms and seizures, the cause of which could not be definitively established. The possibility that the death was treatment-related could not be ruled out, and as a result, under the terms of the protocol for the trial, the death was assessed as treatment-related. There can be no assurance a foreign regulatory authority will agree with the classifications of the deaths made by the investigators or that we will not be required to conduct additional clinical trials of UPLIZNA in order to establish an adequate safety database. With respect to PROCYSBI, the most common side effects include vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue, rash and headache. The most common adverse events reported in a Phase 2 clinical trial of PENNSAID 2% were application site reactions, such as dryness, exfoliation, erythema, pruritus, pain, induration, rash and scabbing. In our two Phase 3 clinical trials with DUEXIS, the most commonly reported treatment-emergent adverse events were nausea, dyspepsia, diarrhea, constipation and upper respiratory tract infection. The most commonly reported treatment-emergent adverse events in the Phase 3 clinical trials with RAYOS included flare in rheumatoid arthritis related symptoms, abdominal pain, nasopharyngitis, headache, flushing, upper respiratory tract infection, back pain and weight gain.

The FDA or other regulatory authorities may also require, or we may undertake, additional clinical trials to support the safety profile of our medicines or medicine candidates.

In addition, if we or others identify undesirable side effects caused by our medicines or any other medicine candidate that we may develop that receives marketing approval, or if there is a perception that the medicine is associated with undesirable side effects:

- regulatory authorities may require the addition of labeling statements, such as a "black box" warning or a contraindication;
- regulatory authorities may withdraw their approval of the medicine or place restrictions on the way it is prescribed;
- we may be required to change the way the medicine is administered, conduct additional clinical trials or change the labeling of the medicine or implement a risk evaluation and mitigation strategy; and
- we may be subject to increased exposure to product liability and/or personal injury claims.

If any of these events occurred with respect to our medicines, our ability to generate significant revenues from the sale of these medicines would be significantly harmed.

We rely on third parties to conduct our pre-clinical and clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines or if they experience regulatory compliance issues, we may not be able to obtain regulatory approval for or commercialize our medicine candidates and our business could be substantially harmed.

We have agreements with third-party contract research organizations, or CROs, to conduct our clinical programs, including those required for post-marketing commitments, and we expect to continue to rely on CROs for the completion of on-going and planned clinical trials. We may also have the need to enter into other such agreements in the future if we were to develop other medicine candidates or conduct clinical trials in additional indications for our existing medicines. We also rely heavily on these parties for the execution of our clinical studies and control only certain aspects of their activities. Nevertheless, we are responsible for ensuring that each of our studies is conducted in accordance with the applicable protocol. We, our CROs and our academic research organizations are required to comply with current GCP or ICH regulations. The FDA, and regulatory authorities in other jurisdictions, enforce these GCP or ICH regulations through periodic inspections of trial sponsors, principal investigators and trial sites. If we or our CROs or collaborators fail to comply with applicable GCP or ICH regulations, the data generated in our clinical trials may be deemed unreliable and our submission of marketing applications may be delayed or the FDA, or such other regulatory authorities, may require us to perform additional clinical trials before approving our marketing applications. We cannot assure that, upon inspection, the FDA, or such other regulatory authorities, will determine that any of our clinical trials comply or complied with GCP or ICH regulations. In addition, our clinical trials must be conducted with medicine produced under cGMP regulations, and may require a large number of test subjects. Our failure to comply with these regulations may require us to repeat clinical trials, which would delay the regulatory approval process. Moreover, our business may be implicated if any of our CROs or collaborators violates federal or state fraud and abuse or false claims laws and regulations or privacy and security laws. We must also obtain certain third-party institutional review board, or IRB, and ethics committee approvals in order to conduct our clinical trials. Delays by IRBs and ethics committees in providing such approvals may delay our clinical trials.

If any of our relationships with these third-party CROs or collaborators terminate, we may not be able to enter into similar arrangements on commercially reasonable terms, or at all. If CROs or collaborators do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced or if the quality or accuracy of the clinical data they obtain is compromised due to the failure to adhere to our clinical protocols or regulatory requirements or for other reasons, our clinical trials may be extended, delayed or terminated and we may not be able to obtain regulatory approval for or successfully commercialize our medicines and medicine candidates. As a result, our results of operations and the commercial prospects for our medicines and medicine candidates would be harmed, our costs could increase and our ability to generate revenues could be delayed.

Switching or adding additional CROs or collaborators can involve substantial cost and require extensive management time and focus. In addition, there is a natural transition period when a new CRO or collaborator commences work. As a result, delays may occur, which can materially impact our ability to meet our desired clinical development timelines. Though we carefully manage our relationships with our CROs and collaborators, there can be no assurance that we will not encounter similar challenges or delays in the future or that these delays or challenges will not have a material adverse impact on our business, financial condition or prospects. In particular, the ability of our CROs to conduct certain of their operations, including monitoring of clinical sites, has been limited by the COVID-19 pandemic, and to the extent that our CROs are unable to fulfil their contractual obligations as a result of the COVID-19 pandemic or government orders in response to the pandemic, we may have limited or no recourse under the terms of our contractual agreements with our CROs.

*Clinical development of drugs and biologics involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.**

Clinical testing is expensive and can take many years to complete, and its outcome is uncertain. Failure can occur at any time during the clinical trial process. The results of pre-clinical studies and early clinical trials of potential medicine candidates may not be predictive of the results of later-stage clinical trials. Medicine candidates in later stages of clinical trials may fail to show the desired safety and efficacy traits despite having progressed through pre-clinical studies and initial clinical testing. For example, in December 2016, we announced that the Phase 3 trial, Safety, Tolerability and Efficacy of ACTIMMUNE Dose Escalation in Friedreich's ataxia, evaluating ACTIMMUNE for the treatment of Friedreich's ataxia did not meet its primary endpoint. Additionally, we discontinued our ACTIMMUNE investigator-initiated trials in oncology to focus on our strategic pipeline where we see more promise and long-term intellectual property protection.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same medicine candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. Various pipeline programs among our current pipeline are subject to this risk; for example, in a Phase 1b clinical trial, Viela observed that HZN-4920 decreased disease activity in patients with rheumatoid arthritis. Viela subsequently initiated a Phase 2 clinical trial for HZN-4920 in patients with rheumatoid arthritis, a separate Phase 2b clinical trial for HZN-4920 in Sjögren's syndrome and a separate Phase 2 clinical trial for HZN-4920 in kidney transplant rejection, which clinical trials we have assumed and are conducting. There is no assurance that HZN-4920 will have a similar impact on disease activity in such clinical trials.

We may experience delays in clinical trials or investigator-initiated studies. We do not know whether any additional clinical trials will be initiated in the future, begin on time, need to be redesigned, enroll patients on time or be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays related to:

- obtaining regulatory approval to commence a trial;
- reaching agreement on acceptable terms with prospective CROs and clinical trial sites, the terms of which can be subject to extensive negotiation and may vary significantly among different CROs and trial sites;
- obtaining IRB or ethics committee approval at each site;
- recruiting suitable patients to participate in a trial;
- having patients complete a trial or return for post-treatment follow-up;
- clinical sites dropping out of a trial;
- adding new sites; or
- manufacturing sufficient quantities of medicine candidates for use in clinical trials.

Our clinical trials may also be affected by COVID-19. For example, two of our clinical trials for TEPEZZA have been delayed until later in 2021 due to the impact of the TEPEZZA supply disruption at Catalent. In addition, clinical site initiation and patient enrollment may be delayed due to prioritization of hospital and healthcare resources toward COVID-19. Current or potential patients in our ongoing or planned clinical trials may also choose to not enroll, not participate in follow-up clinical visits or drop out of the trial as a precaution against contracting COVID-19. Further, some patients may not be able or willing to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Some clinical sites in the United States have slowed or stopped further enrollment of new patients in clinical trials, denied access to site monitors or otherwise curtailed certain operations. Similarly, our ability to recruit and retain principal investigators and site staff who, as healthcare providers, may have heightened exposure to COVID-19, may be adversely impacted. The availability of supplies needed for the conduct of clinical trials may be impacted by COVID-19 supply disruptions, including laboratory tubes needed for lab testing. These events could delay our clinical trials, increase the cost of completing our clinical trials and negatively impact the integrity, reliability or robustness of the data from our clinical trials.

Patient enrollment, a significant factor in the timing of clinical trials, is affected by many factors including the size and nature of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the trial, the design of the clinical trial, competing clinical trials and clinicians' and patients' perceptions as to the potential advantages of the medicine candidate being studied in relation to other available therapies, including any new drugs or biologics that may be approved for the indications we are investigating. In addition, if patients drop out of our trials, miss scheduled doses or follow-up visits or otherwise fail to follow trial protocols, or if our trials are otherwise disputed due to COVID-19 or actions taken to slow its spread, the integrity of data from our trials may be compromised or not accepted by the FDA or other regulatory authorities, which would represent a significant setback for the applicable program.

We could encounter delays if prescribing physicians encounter unresolved ethical issues associated with enrolling patients in clinical trials of our medicine candidates in lieu of prescribing existing treatments that have established safety and efficacy profiles. Further, a clinical trial may be suspended or terminated by us, our collaborators, the FDA or other regulatory authorities due to a number of factors, including failure to conduct the clinical trial in accordance with regulatory requirements or our clinical protocols, inspection of the clinical trial operations or trial site by the FDA or other regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a medicine candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or if we terminate, any clinical trial of our medicine candidates, the commercial prospects of our medicine candidates will be harmed, and our ability to generate medicine revenues from any of these medicine candidates will be delayed or reduced. In addition, any delays in completing our clinical trials will increase our costs, slow down our medicine development and approval process and jeopardize our ability to commence medicine sales and generate revenues.

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. Under certain circumstances, we may be required to report some of these relationships to the FDA. The FDA may conclude that a financial relationship between us and a principal investigator has created a conflict of interest or otherwise affected interpretation of the study. The FDA may therefore question the integrity of the data generated at the applicable clinical trial site and the utility of the clinical trial itself may be jeopardized. This could result in a delay in approval, or rejection, of our marketing applications by the FDA and may ultimately lead to the denial of marketing approval of one or more of our medicine candidates.

Any of these occurrences may harm our business, financial condition, results of operations and prospects significantly. In addition, many of the factors that cause, or lead to, a delay in the commencement or completion of clinical trials may also ultimately lead to the denial of regulatory approval of our medicine candidates.

*The sizes of the patient populations suffering from some of the diseases we are targeting are small and based on estimates that may not be accurate.**

Because certain of our clinical trials are focused on indications with small patient populations, our ability to enroll eligible patients may be limited or may result in slower enrollment than we anticipate. In addition, our projections of both the number of people who have some of the diseases we are targeting, as well as the subset of people with these diseases who have the potential to benefit from treatment with our medicines and any of our future medicine candidates, are estimates. These estimates have been derived from a variety of sources, including scientific literature, surveys of clinics, physician interviews, patient foundations and market research, and may prove to be incorrect. Further, new studies may change the estimated incidence or prevalence of these diseases. The number of patients may turn out to be lower than expected. Additionally, the potentially addressable patient population for our medicines and any future medicine candidates may be limited or may not be amenable to treatment with our medicines and any of our medicine candidates, if and when approved. Even if we obtain significant market share for our medicines and any of our medicine candidates (if and when they are approved), small potential target populations for certain indications means we may never achieve profitability without obtaining market approval for additional indications.

Business interruptions could seriously harm our future revenue and financial condition and increase our costs and expenses.

Our operations could be subject to earthquakes, power shortages, telecommunications failures, water shortages, floods, hurricanes, typhoons, fires, extreme weather conditions, medical epidemics or health pandemics, such as the current COVID-19 pandemic, and other natural or man-made disasters or business interruptions. While we carry insurance for certain of these events and have implemented disaster management plans and contingencies, the occurrence of any of these business interruptions could seriously harm our business and financial condition and increase our costs and expenses. We conduct significant management operations at both our global headquarters located in Dublin, Ireland and our U.S. office located in Deerfield, Illinois. If our Dublin or Deerfield offices were affected by a natural or man-made disaster or other business interruption, our ability to manage our domestic and foreign operations could be impaired, which could materially and adversely affect our results of operations and financial condition. We currently rely, and intend to rely in the future, on third-party manufacturers and suppliers to produce our medicines and third-party logistics partners to ship our medicines. Our ability to obtain commercial supplies of our medicines could be disrupted and our results of operations and financial condition could be materially and adversely affected if the operations of these third-party suppliers or logistics partners were affected by a man-made or natural disaster or other business interruption. The ultimate impact of such events on us, our significant suppliers and our general infrastructure is unknown.

*We are dependent on information technology systems, infrastructure and data, which exposes us to data security risks.**

We generate and store sensitive data, including research data, intellectual property, personal data, and proprietary business information owned or controlled by ourselves or our employees, partners and other parties. We manage and maintain our applications and data utilizing a combination of our own on-site systems and third-party information technology systems, including cloud-based data centers. We are dependent upon such systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems and those of our third-party service providers may make them vulnerable to service interruption or destruction, disruption of data integrity, inadvertent actions or inactions that expose our data or systems, malicious intrusion, or random attacks. Likewise, data privacy or security incidents or breaches by employees or others may pose a risk that sensitive data, including our intellectual property, trade secrets or personal information of our employees, patients, customers or other business partners may be exposed to unauthorized persons or to the public. Cyber incidents are increasing in their frequency, sophistication and intensity.

Cyber incidents could include the deployment of harmful malware, ransomware, denial-of-service, supply chain attacks, social engineering and other means to exploit our systems and affect service reliability and threaten data confidentiality, integrity and availability. Changes in how our employees work and access our systems during the COVID-19 pandemic could lead to additional opportunities for bad actors to launch cyberattacks or for employees to cause inadvertent security risks or incidents. Our business partners, particularly our third-party service providers, face similar risks and any security breach of their systems could adversely affect our security posture. A security breach or privacy violation that leads to disclosure or modification of or prevents access to patient information, including personally identifiable information or protected health information, could harm our reputation, compel us to comply with federal and/or state breach notification laws and foreign law equivalents, subject us to mandatory corrective action, require us to verify the correctness of database contents and otherwise subject us to litigation or other liability under laws and regulations that protect personal data, any of which could disrupt our business and/or result in increased costs or loss of revenue. The effects of a security breach or privacy violation could be further amplified during the COVID-19 pandemic. Moreover, the prevalent use of mobile devices that access confidential information increases the risk of data security breaches, which could lead to the loss of confidential information, trade secrets or other intellectual property.

Despite significant efforts to create security barriers to the above described threats, it is impossible for us to entirely mitigate these risks. We may be unable to anticipate or prevent techniques used to obtain unauthorized access or to compromise our systems because they change frequently and are generally not detected until after an incident has occurred. In addition, an accidental or intentional cybersecurity event could result in significant increases in costs, including costs for remediating the effects of such an event, fines imposed by regulators, lost revenues due to decrease in customer trust and network downtime, increases in insurance premiums due to cybersecurity incidents and damages to our reputation because of any such incident. While we have invested, and continue to invest, in the protection of our data and information technology infrastructure, there can be no assurance that our efforts will prevent service interruptions, or identify vulnerabilities or breaches in our systems, that could adversely affect our business and operations and/or result in the loss of critical or sensitive information, which could result in financial, legal, business or reputational harm to us. In addition, we cannot be certain that (a) our liability insurance will be sufficient in type or amount to cover us against claims related to security incidents, cyberattacks and other related breaches; (b) such coverage will cover any indemnification claims against us relating to any incident, will continue to be available to us on economically reasonable terms, or at all; or (c) any insurer will not deny coverage as to any future claim. The successful assertion of one or more large claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could adversely affect our reputation, business, financial condition and results of operations.

*We are subject to extensive worldwide laws and regulations related to data privacy, and our failure to comply with these laws and regulations could harm our business.**

We are subject to laws and regulations governing data privacy and the protection of personal information. These laws and regulations govern our processing of personal data, including the collection, access, use, analysis, modification, storage, transfer, security breach notification, destruction and disposal of personal data. There are foreign and state law versions of these laws and regulations to which we are currently and/or may in the future, be subject. For example, the collection and use of personal health data in the EU is governed by the GDPR. The GDPR, which is wide-ranging in scope, imposes several requirements relating to the consent of the individuals to whom the personal data relates, the information disclosed to the individuals about our privacy practices, the security and confidentiality of the personal data, data breach notification and the use of third-party processors in connection with the processing of personal data. The GDPR also imposes strict rules on the transfer of personal data out of the EU to the United States or other jurisdictions deemed not to have adequate controls, provides an enforcement authority and imposes potentially large monetary penalties for noncompliance. The GDPR requirements apply not only to third-party transactions, but also to transfers of information within our company, including employee information. The GDPR and similar data privacy laws of other jurisdictions place significant responsibilities on us and create potential liability in relation to personal data that we or our third-party service providers process, including in clinical trials conducted in the United States and EU. In addition, we expect that there will continue to be new proposed laws, regulations and industry standards relating to privacy and data protection in the United States, the EU and other jurisdictions, and we cannot determine the impact such future laws, regulations and standards may have on our business.

The UK's vote in favor of exiting the EU, often referred to as Brexit, and ongoing developments in the UK have created uncertainty with regard to data protection regulation in the UK. As of January 1, 2021, and the expiry of transitional arrangements agreed to between the UK and EU, data processing in the UK is governed by a UK version of the GDPR (combining the GDPR and the Data Protection Act 2018), exposing us to two parallel regimes, each of which potentially authorizes similar fines and other potentially divergent enforcement actions for certain violations. Pursuant to the Trade and Cooperation Agreement, or TCA, which went into effect on January 1, 2021, the UK and EU agreed to a specified period during which the UK will be treated like an EU member state in relation to transfers of personal data to the UK for four months from January 1, 2021. This period may be extended by two further months. Unless the EC makes an 'adequacy finding' in respect of the UK before the expiration of such specified period, the UK will become an 'inadequate third country' under the GDPR and transfers of data from the EEA to the UK will require an 'transfer mechanism,' such as the standard contractual clauses. Furthermore, following the expiration of the specified period, there will be increasing scope for divergence in application, interpretation and enforcement of the data protection law as between the UK and EEA. As a result, we may incur liabilities, expenses, costs, and other operational losses under GDPR and applicable EU Member States and the UK privacy laws in connection with any measures we take to comply with them.

Recent legal developments in Europe have created further complexity and uncertainty regarding transfers of personal data from the EU and UK to the United States. On July 16, 2020, the Court of Justice of the European Union, or CJEU, invalidated the EU-US Privacy Shield Framework, or Privacy Shield, under which personal data could be transferred from the EU and UK to United States entities who had self-certified under the Privacy Shield scheme. Nine of our United States entities have self-certified under the Privacy Shield framework and we have entered into the standard contractual clauses within our group for transfers of data from the EU and UK to the United States. The UK's supervisory authority may similarly invalidate use of the Privacy Shield as a vehicle for lawful data transfers from the UK to the United States. As such, our transfers of personal data to the United States may not comply with European data protection law and may increase our exposure to the GDPR's heightened sanctions for violations of its cross-border data transfer restrictions, including fines of up to 4% of annual global revenue and injunctions against transfers. While the CJEU upheld the adequacy of the standard contractual clauses (a standard form of contract approved by the EC as an adequate personal data transfer mechanism, and potential alternative to the Privacy Shield), it made clear that reliance on them alone may not necessarily be sufficient in all circumstances. Use of the standard contractual clauses must now be assessed on a case-by-case basis taking into account the legal regime applicable in the destination country, in particular applicable surveillance laws and rights of individuals and additional measures and/or contractual provisions may need to be put in place. The nature of these additional measures, however, remains uncertain. As supervisory authorities issue further guidance on personal data export mechanisms, including circumstances where the standard contractual clauses cannot be used, and/or start taking enforcement action, we could suffer additional costs, complaints and/or regulatory investigations or fines, and/or if we are otherwise unable to transfer personal data between and among countries and regions in which we operate, it could affect the manner in which we provide our services, the geographical location or segregation of our relevant systems and operations, and could adversely affect our financial results.

Additionally, the California Consumer Privacy Act, or CCPA, went into effect on January 1, 2020. The CCPA has been dubbed the first "GDPR-like" law in the United States since it creates new individual privacy rights for consumers (as that word is broadly defined in the law) and places increased privacy and security obligations on entities handling personal data of consumers or households. The CCPA requires covered companies to provide new disclosures to California consumers (as that word is broadly defined in the CCPA), provide such consumers new ways to opt-out of certain sales of personal information, and allow for a new private right of action for data breaches. It remains unclear how the CCPA will be interpreted, but as currently written, it will likely impact our business activities and exemplifies the vulnerability of our business to not only cyber threats but also the evolving regulatory environment related to personal data and protected health information. Further, California voters approved a new privacy law, the California Privacy Rights Act, or CPRA, in the November 3, 2020 election. Effective starting on January 1, 2023, the CPRA will significantly modify the CCPA, including by expanding consumers' rights with respect to certain sensitive personal information. The CPRA also creates a new state agency that will be vested with authority to implement and enforce the CCPA and the CPRA. New legislation proposed or enacted in various other states will continue to shape the data privacy environment nationally. Certain state laws may be more stringent or broader in scope, or offer greater individual rights, with respect to confidential, sensitive and personal information than federal, international or other state laws, and such laws may differ from each other, which may complicate compliance efforts. As we expand our operations and trials (both preclinical or clinical), the CCPA and CPRA may increase our compliance costs and potential liability. Some observers have noted that the CCPA and CPRA could mark the beginning of a trend toward more stringent privacy legislation in the United States. Other states are beginning to pass similar laws, including Virginia (which passed the Consumer Data Protection Act on March 2, 2021) and pending bills in Washington, New York, and Minnesota.

Compliance with these and any other applicable privacy and data security laws and regulations is a rigorous and time-intensive process, and we may be required to put in place additional mechanisms ensuring compliance with the new data protection rules. Any actual or perceived failure by us to comply with any applicable federal, state or similar foreign laws and regulations relating to data privacy and security could result in damage to our reputation, as well as proceedings or litigation by governmental agencies or other third parties, including class action privacy litigation in certain jurisdictions, which would subject us to significant fines, sanctions, awards, penalties or judgments, all of which could have a material adverse effect on our business, financial condition, results of operations and prospects. Furthermore, the laws are not consistent, and compliance in the event of a widespread data breach is costly.

If product liability lawsuits are brought against us, we may incur substantial liabilities and may be required to limit commercialization of our medicines.

We face an inherent risk of product liability claims as a result of the commercial sales of our medicines and the clinical testing of our medicine candidates. For example, we may be sued if any of our medicines or medicine candidates allegedly causes injury or is found to be otherwise unsuitable during clinical testing, manufacturing, marketing or sale. Any such product liability claims may include allegations of defects in manufacturing, defects in design, a failure to warn of dangers inherent in the medicine, negligence, strict liability or a breach of warranties. Claims could also be asserted under state consumer protection acts. If we cannot successfully defend ourselves against product liability claims, we may incur substantial liabilities or be required to limit commercialization of our medicines and medicine candidates. Even a successful defense would require significant financial and management resources. Regardless of the merits or eventual outcome, liability claims may result in:

- decreased demand for our medicines or medicine candidates that we may develop;
- injury to our reputation;
- withdrawal of clinical trial participants;
- initiation of investigations by regulators;
- costs to defend the related litigation;
- a diversion of management's time and resources;
- substantial monetary awards to trial participants or patients;
- medicine recalls, withdrawals or labeling, marketing or promotional restrictions;
- loss of revenue;
- exhaustion of any available insurance and our capital resources; and
- the inability to commercialize our medicines or medicine candidates.

Our inability to obtain and retain sufficient product liability insurance at an acceptable cost to protect against potential product liability claims could prevent or inhibit the commercialization of medicines we develop. We currently carry product liability insurance covering our clinical studies and commercial medicine sales in the amount of $125.0 million in the aggregate. Although we maintain such insurance, any claim that may be brought against us could result in a court judgment or settlement in an amount that is not covered, in whole or in part, by our insurance or that is in excess of the limits of our insurance coverage. If we determine that it is prudent to increase our product liability coverage due to the on-going commercialization of our current medicines in the United States, and/or the potential commercial launches of any of our medicines in additional markets or for additional indications, we may be unable to obtain such increased coverage on acceptable terms or at all. Our insurance policies also have various exclusions, and we may be subject to a product liability claim for which we have no coverage. We will have to pay any amounts awarded by a court or negotiated in a settlement that exceed our coverage limitations or that are not covered by our insurance, and we may not have, or be able to obtain, sufficient capital to pay such amounts.

Our business involves the use of hazardous materials, and we and our third-party manufacturers must comply with environmental laws and regulations, which can be expensive and restrict how we do business.

Our third-party manufacturers' activities involve the controlled storage, use and disposal of hazardous materials owned by us, including the components of our medicine candidates and other hazardous compounds. We and our manufacturers are subject to federal, state and local as well as foreign laws and regulations governing the use, manufacture, storage, handling and disposal of these hazardous materials. Although we believe that the safety procedures utilized by our third-party manufacturers for handling and disposing of these materials comply with the standards prescribed by these laws and regulations, we cannot eliminate the risk of accidental contamination or injury from these materials. In the event of an accident, state, federal or foreign authorities may curtail the use of these materials and interrupt our business operations. We currently only maintain hazardous materials insurance coverage related to our South San Francisco facility. If we are subject to any liability as a result of our third-party manufacturers' activities involving hazardous materials, our business and financial condition may be adversely affected. In the future we may seek to establish longer-term third-party manufacturing arrangements, pursuant to which we would seek to obtain contractual indemnification protection from such third-party manufacturers potentially limiting this liability exposure.

Risks Related to our Financial Position and Capital Requirements

*We have incurred significant operating losses.**

We have financed our operations primarily through equity and debt financings and have incurred significant operating losses in prior years. We recorded an operating loss of $160.0 million for the three months ended March 31, 2021 and an operating income of $490.0 million and $126.6 million for the years ended December 31, 2020 and 2019, respectively. We recorded a net loss of $123.4 million for the three months ended March 31, 2021 and a net income of $389.8 million and $573.0 million for the years ended December 31, 2020 and 2019, respectively. As of March 31, 2021, we had an accumulated deficit of $339.2 million. Our prior losses have resulted principally from costs incurred in our development activities for our medicines and medicine candidates, commercialization activities related to our medicines and costs associated with our acquisition transactions. Our prior losses, combined with possible future losses, have had and will continue to have an adverse effect on our shareholders' equity and working capital. While we anticipate that we will continue to generate operating profits in the future, whether we can accomplish this will depend on the revenues we generate from the sale of our medicines being sufficient to cover our operating expenses. We also expect our operating expenses to increase substantially as a result of continuing to develop Viela's pipeline of medicine candidates, which will negatively impact our future profitability until such time that these potential medicine candidates are approved and successfully commercialized.

We have limited sources of revenues and significant expenses. We cannot be certain that we will sustain profitability, which would depress the market price of our ordinary shares and could cause our investors to lose all or a part of their investment.

Our ability to sustain profitability depends upon our ability to generate sales of our medicines. The commercialization of our medicines has been primarily in the United States. We may never be able to successfully commercialize our medicines or develop or commercialize other medicines in the United States, which we believe represents our most significant commercial opportunity. Our ability to generate future revenues depends heavily on our success in:

- continued commercialization of our existing medicines and any other medicine candidates for which we obtain approval;
- securing additional foreign regulatory approvals for our medicines in territories where we have commercial rights; and
- developing, acquiring and commercializing a portfolio of other medicines or medicine candidates in addition to our current medicines.

Even if we do generate additional medicine sales, we may not be able to sustain profitability on a quarterly or annual basis. Our failure to become and remain profitable would depress the market price of our ordinary shares and could impair our ability to raise capital, expand our business, diversify our medicine offerings or continue our operations.

*We may need to obtain additional financing to fund additional acquisitions.**

Our operations have consumed substantial amounts of cash since inception. We expect to continue to spend substantial amounts to:

- commercialize our existing medicines in the United States, including the substantial expansion of our sales force in recent years;
- complete the regulatory approval process, and any future required clinical development related thereto, for our medicines and medicine candidates;
- potentially acquire other businesses or additional complementary medicines or medicines that augment our current medicine portfolio, including costs associated with refinancing debt of acquired companies;
- satisfy progress and milestone payments under our existing and future license, collaboration and acquisition agreements; and
- conduct clinical trials with respect to potential additional indications, as well as conduct post-marketing requirements and commitments, with respect to our medicines and medicines we acquire.

While we believe that our existing cash and cash equivalents, along with future cash flows based on our current expectations of continued revenue growth, will be sufficient to fund our operations, we may need to raise additional funds if we choose to expand our commercialization or development efforts more rapidly than presently anticipated, if we develop or acquire additional medicines or acquire companies, or if our revenue does not meet expectations.

We cannot be certain that additional funding will be available on acceptable terms, or at all. As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have at times experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly and more dilutive. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our medicines or medicine candidates or one or more of our other R&D initiatives, or delay, cut back or abandon our plans to grow the business through acquisitions. We also could be required to:

- seek collaborators for one or more of our current or future medicine candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or

- relinquish or license on unfavorable terms our rights to technologies or medicine candidates that we would otherwise seek to develop or commercialize ourselves.

In addition, if we are unable to secure financing to support future acquisitions, our ability to execute on a key aspect of our overall growth strategy would be impaired.

Any of the above events could significantly harm our business, financial condition and prospects.

*We have incurred a substantial amount of debt, which could adversely affect our business, including by restricting our ability to engage in additional transactions or incur additional indebtedness, and prevent us from meeting our debt obligations.**

As of March 31, 2021, we had $2,562.5 million book value, or $2,618.0 million aggregate principal amount of indebtedness, including $2,018.0 million in secured indebtedness.

This substantial level of debt could have important consequences to our business, including, but not limited to:

- reducing the benefits we expect to receive from our prior and any future acquisition transactions;

- making it more difficult for us to satisfy our obligations;

- requiring a substantial portion of our cash flows from operations to be dedicated to the payment of principal and interest on our indebtedness, therefore reducing our ability to use our cash flows to fund acquisitions, capital expenditures, and future business opportunities;

- exposing us to the risk of increased interest rates to the extent of any future borrowings, including borrowings under our credit agreement, at variable rates of interest;

- making it more difficult for us to satisfy our obligations with respect to our indebtedness, including our outstanding notes, our credit agreement, and any failure to comply with the obligations of any of our debt instruments, including restrictive covenants and borrowing conditions, could result in an event of default under the agreements governing such indebtedness;

- increasing our vulnerability to, and reducing our flexibility to respond to, changes in our business or general adverse economic and industry conditions;

- limiting our ability to obtain additional financing for working capital, capital expenditures, debt service requirements, acquisitions, and general corporate or other purposes and increasing the cost of any such financing;

- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; and placing us at a competitive disadvantage as compared to our competitors, to the extent they are not as highly leveraged and who, therefore, may be able to take advantage of opportunities that our leverage may prevent us from exploiting; and

- restricting us from pursuing certain business opportunities.

Our credit agreement and the indenture governing our 5.5% Senior Notes due 2027, or 2027 Senior Notes, impose, and the terms of any future indebtedness may impose, various covenants that limit our ability and/or the ability of our restricted subsidiaries' (as designated under such agreements) to, among other things, pay dividends or distributions, repurchase equity, prepay junior debt and make certain investments, incur additional debt and issue certain preferred stock, incur liens on assets, engage in certain asset sales, consolidate with or merge or sell all or substantially all of our assets, enter into transactions with affiliates, designate subsidiaries as unrestricted subsidiaries, and allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to us.

Our ability to obtain future financing and engage in other transactions may be restricted by these covenants. In addition, any credit ratings will impact the cost and availability of future borrowings and our cost of capital. Our ratings at any time will reflect each rating organization's then opinion of our financial strength, operating performance and ability to meet our debt obligations. There can be no assurance that we will achieve a particular rating or maintain a particular rating in the future. A reduction in our credit ratings may limit our ability to borrow at acceptable interest rates. If our credit ratings were downgraded or put on watch for a potential downgrade, we may not be able to sell additional debt securities or borrow money in the amounts, at the times or interest rates or upon the more favorable terms and conditions that might otherwise be available. Any impairment of our ability to obtain future financing on favorable terms could have an adverse effect on our ability to refinance any of our then-existing debt and may severely restrict our ability to execute on our business strategy, which includes the continued acquisition of additional medicines or businesses.

As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly or more dilutive.

We may not be able to generate sufficient cash to service all of our indebtedness and may be forced to take other actions to satisfy our obligations under our indebtedness, which may not be successful.

Our ability to make scheduled payments under or to refinance our debt obligations depends on our financial condition and operating performance, which is subject to prevailing economic, industry and competitive conditions and to certain financial, business and other factors beyond our control. For example, we expect that the COVID-19 pandemic and actions taken to slow its spread will continue to have a negative impact on net sales of our medicines, which will in turn negatively impact our cash flows. Our ability to generate cash flow to meet our payment obligations under our debt may also depend on the successful implementation of our operating and growth strategies. Any refinancing of our debt could be at higher interest rates and may require us to comply with more onerous covenants, which could further restrict our business operations. We cannot assure that we will maintain a level of cash flows from operating activities sufficient to pay the principal, premium, if any, and interest on our indebtedness.

If our cash flows and capital resources are insufficient to fund our debt service obligations, we may be forced to reduce or delay capital expenditures, sell assets or business operations, seek additional capital or restructure or refinance our indebtedness. We cannot ensure that we would be able to take any of these actions, that these actions would be successful and permit us to meet our scheduled debt service obligations or that these actions would be permitted under the terms of existing or future debt agreements, including the indenture that governs the 2027 Senior Notes and our credit agreement. In addition, any failure to make payments of interest and principal on our outstanding indebtedness on a timely basis would likely result in a reduction of our credit rating, which could harm our ability to incur additional indebtedness.

If we cannot make scheduled payments on our debt, we will be in default and, as a result:

- our debt holders could declare all outstanding principal and interest to be due and payable;
- the administrative agent and/or the lenders under our credit agreement could foreclose against the assets securing the borrowings then outstanding; and
- we could be forced into bankruptcy or liquidation, which could result in you losing your investment.

We generally have broad discretion in the use of our cash and may not use it effectively.

Our management has broad discretion in the application of our cash, and investors will be relying on the judgment of our management regarding the use of our cash. Our management may not apply our cash in ways that ultimately increase the value of any investment in our securities. We expect to use our existing cash to fund commercialization activities for our medicines, to potentially fund additional medicine, medicine candidate or business acquisitions, to potentially fund additional regulatory approvals of certain of our medicines, to potentially fund development, life cycle management or manufacturing activities of our medicines and medicine candidates, to potentially fund share repurchases, and for working capital, milestone payments, capital expenditures and general corporate purposes. We may also invest our cash in short-term, investment-grade, interest-bearing securities. These investments may not yield a favorable return to our shareholders. If we do not invest or apply our cash in ways that enhance shareholder value, we may fail to achieve expected financial results, which could cause the price of our ordinary shares to decline.

*Our ability to use net operating loss carryforwards and certain other tax attributes to offset U.S. income taxes may be limited.**

Under Sections 382 and 383 of the Code, if a corporation undergoes an "ownership change" (generally defined as a greater than 50 percent change (by value) in its equity ownership over a three-year period), the corporation's ability to use pre-change net operating loss carryforwards and other pre-change tax attributes to offset post-change income may be limited. For example, we continue to carry forward our annual limitation resulting from an ownership change date of August 2, 2012. The limitation on pre-change net operating losses incurred prior to the August 2, 2012 change date is approximately $7.7 million for 2021 through 2028. The net operating loss carryforward and tax credit carryforward limitations are cumulative such that any use of the carryforwards below the limitations in one year will result in a corresponding increase in the limitations for the subsequent tax year. Under the Tax Act, as modified by the CARES Act, U.S. federal net operating losses incurred in taxable years beginning after December 31, 2017 may be carried forward indefinitely, but the deductibility of federal net operating losses generated in taxable years beginning after December 31, 2017, to the extent such net operating losses are carried forward into taxable years beginning after December 31, 2020, is limited to 80 percent of the then current year's taxable income. Under the CARES Act, U.S. federal net operating losses arising in a tax year beginning after December 31, 2017, and before January 1, 2021, can be carried back five years. We continue to monitor legislation regarding the states' conformity to the Tax Act and the CARES Act.

Following certain acquisitions of a U.S. corporation by a foreign corporation, Section 7874 of the Code limits the ability of the acquired U.S. corporation and its U.S. affiliates to utilize U.S. tax attributes such as net operating losses to offset U.S. taxable income resulting from certain transactions. Based on the limited guidance available, we expect this limitation is applicable for approximately ten years following our merger transaction with Vidara with respect to certain intercompany transactions. As a result, we or our other U.S. affiliates may not be able to utilize U.S. tax attributes to offset U.S. taxable income or U.S. tax liability respectively, if any, resulting from certain intercompany taxable transactions during such period. Notwithstanding this limitation, we expect that we will be able to fully use our U.S. net operating losses and tax credits prior to their expiration. As a result of this limitation, however, it may take Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc. and as the successor to HPI) longer to use its net operating losses and tax credits. Moreover, contrary to these expectations, it is possible that the limitation under Section 7874 of the Code on the utilization of U.S. tax attributes could prevent us from fully utilizing our U.S. tax attributes prior to their expiration if we do not generate sufficient taxable income or tax obligations.

Any limitation on our ability to use our net operating loss and tax credit carryforwards, including the carryforwards of companies that we acquire, will likely increase the taxes we would otherwise pay in future years if we were not subject to such limitations.

*Unstable market and economic conditions may have serious adverse consequences on our business, financial condition and share price.**

From time to time, including recently as a result of the COVID-19 pandemic and actions taken to slow its spread, global credit and financial markets have experienced extreme volatility and disruptions, including severely diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates, and uncertainty about economic stability. Our general business strategy may be adversely affected by any such economic downturn, volatile business environment and continued unpredictable and unstable market conditions. If the equity and credit markets deteriorate, it may make any necessary debt or equity financing more difficult to complete, more costly, and more dilutive. Failure to secure any necessary financing in a timely manner and on favorable terms could have a material adverse effect on our growth strategy, financial performance and share price and could require us to delay or abandon commercialization or development plans. There is a risk that one or more of our current service providers, manufacturers and other partners may not survive an economic down-turn, which could directly affect our ability to attain our operating goals on schedule and on budget.

At March 31, 2021, we had $811.6 million of cash and cash equivalents consisting of cash and money market funds. While we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents since March 31, 2021, no assurance can be given that deterioration in conditions of the global credit and financial markets would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

The UK's referendum to leave the EU and the UK's exit from the EU on January 31, 2020, or "Brexit," has caused and may continue to cause disruptions to capital and currency markets worldwide. The full impact of Brexit, however, remains uncertain. Pursuant to the formal withdrawal arrangements agreed to between the UK and the EU, the UK was subject to a transition period, or Transition Period, until December 31, 2020, during which EU rules continued to apply. The TCA, which outlines the future trading relationship between the UK and the EU was agreed in December 2020 and has been approved by each EU member state and the UK. The TCA is due to be voted upon by the European Parliament in the near future, but has provisionally applied since January 1, 2021.

There remains uncertainty as to the practical impacts of Brexit and, especially in the early stages of the UK and the EU operating under different legislation, our results of operations and access to capital may be negatively affected by interest rate, exchange rate and other market and economic volatility, as well as political uncertainty. Brexit may also have a detrimental effect on our customers, distributors and suppliers, which would, in turn, adversely affect our revenues and financial condition.

While the TCA provides for the tariff-free trade of medicinal products between the UK and the EU there may be additional non-tariff costs to such trade which did not exist prior to the end of the Transition Period. Further, should the UK diverge from the EU from a regulatory perspective in relation to medicinal products, tariffs could be put into place in the future. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us.

We could therefore, both now and in the future, face additional expenses (when compared to the position prior to the end of the Transition Period) to operate our business, which could harm or delay our business. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK.

*If the London Inter-Bank Offered Rate, or LIBOR, is discontinued, interest payments under our credit agreement may be calculated using another reference rate.**

In July 2017, the Chief Executive of the United Kingdom Financial Conduct Authority, or FCA, which regulates LIBOR, announced that the FCA intends to phase out the use of LIBOR by the end of 2021. In addition, the U.S. Federal Reserve, in conjunction with the Alternative Reference Rates Committee, a steering committee composed of large U.S. financial institutions, is considering replacing U.S. dollar LIBOR with the Secured Overnight Financing Rate, or SOFR, a new index calculated by short-term repurchase agreements, backed by Treasury securities. Although there have been certain issuances utilizing SOFR, it is unknown whether this or any other alternative reference rate will attain market acceptance as a replacement for LIBOR. LIBOR is used as a benchmark rate throughout our credit agreement, and our credit agreement does not address all circumstances in which LIBOR ceases to be published. There remains uncertainty regarding the future utilization of LIBOR and the nature of any replacement rate, and any potential effects of the transition away from LIBOR on us are not known. The transition process may involve, among other things, increased volatility and illiquidity in markets for instruments that currently rely on LIBOR and may result in increased borrowing costs, the effectiveness of related transactions such as hedges, uncertainty under applicable documentation, including the credit agreement, or difficult and costly processes to amend such documentation. As a result, our ability to refinance our credit agreement or other indebtedness or to hedge our exposure to floating rate instruments may be impaired, which would adversely affect the operations of our business.

Changes in accounting rules or policies may affect our financial position and results of operations.

Accounting principles generally accepted in the United States, or GAAP, and related implementation guidelines and interpretations can be highly complex and involve subjective judgments. Changes in these rules or their interpretation, the adoption of new guidance or the application of existing guidance to changes in our business could significantly affect our financial position and results of operations. In addition, our operation as an Irish company with multiple subsidiaries in different jurisdictions adds additional complexity to the application of GAAP and this complexity will be exacerbated further if we complete additional strategic transactions. Changes in the application of existing rules or guidance applicable to us or our wholly-owned subsidiaries could significantly affect our consolidated financial position and results of operations.

Covenants under the indenture governing our 2027 Senior Notes and our credit agreement may restrict our business and operations in many ways, and if we do not effectively manage our covenants, our financial conditions and results of operations could be adversely affected.

The indenture governing the 2027 Senior Notes and the credit agreement impose various covenants that limit our ability and/or our restricted subsidiaries' ability to, among other things:

- pay dividends or distributions, repurchase equity, prepay, redeem or repurchase certain debt and make certain investments;
- incur additional debt and issue certain preferred stock;
- provide guarantees in respect of obligations of other persons;
- incur liens on assets;
- engage in certain asset sales;
- merge, consolidate with or sell all or substantially all of our assets to another person;
- enter into transactions with affiliates;
- sell assets and capital stock of our subsidiaries;
- enter into agreements that restrict distributions from our subsidiaries;
- designate subsidiaries as unrestricted subsidiaries; and
- allow to exist certain restrictions on the ability of restricted subsidiaries to pay dividends or make other payments to us.

These covenants 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 less leveraged competitors; and
- increase our vulnerability to the impact of adverse economic and industry conditions.

If we are unable to successfully manage the limitations and decreased flexibility on our business due to our significant debt obligations, we may not be able to capitalize on strategic opportunities or grow our business to the extent we would be able to without these limitations.

Our failure to comply with any of the covenants could result in a default under the credit agreement or the indenture governing the 2027 Senior Notes, which could permit the administrative agent or the trustee, as applicable, or permit the lenders or the holders of the 2027 Senior Notes to cause the administrative agent or the trustee, as applicable, to declare all or part of any outstanding senior secured term loans or revolving loans, or the 2027 Senior Notes to be immediately due and payable or to exercise any remedies provided to the administrative agent or the trustee, including, in the case of the credit agreement proceeding against the collateral granted to secure our obligations under the credit agreement. An event of default under the credit agreement or the indenture governing the 2027 Senior Notes could also lead to an event of default under the terms of the other agreement. Any such event of default or any exercise of rights and remedies by our creditors could seriously harm our business.

If intangible assets that we have recorded in connection with our acquisition transactions become impaired, we could have to take significant charges against earnings.

In connection with the accounting for our various acquisition transactions, we have recorded significant amounts of intangible assets. Under GAAP, we must assess, at least annually and potentially more frequently, whether the value of goodwill has been impaired. Amortizing intangible assets will be assessed for impairment in the event of an impairment indicator. For example, during the year ended December 31, 2018, we recorded an impairment of $33.6 million to fully write off the book value of developed technology related to PROCYSBI in Canada and Latin America. Such impairment and any reduction or other impairment of the value of goodwill or other intangible assets will result in a charge against earnings, which could materially adversely affect our results of operations and shareholders' equity in future periods.

Risks Related to Our Intellectual Property

*If we are unable to obtain or protect intellectual property rights related to our medicines and medicine candidates, we may not be able to compete effectively in our markets.**

We rely upon a combination of patents, trade secret protection and confidentiality agreements to protect the intellectual property related to our medicines and medicine candidates. The strength of patents in the biotechnology and pharmaceutical field involves complex legal and scientific questions and can be uncertain. The patent applications that we own may fail to result in issued patents with claims that cover our medicines in the United States or in other foreign countries. If this were to occur, early generic competition could be expected against our current medicines and other medicine candidates in development. There is no assurance that all potentially relevant prior art relating to our patents and patent applications has been found, which prior art can invalidate a patent or prevent a patent from issuing based on a pending patent application. In particular, because the APIs in RAYOS, DUEXIS and PENNSAID 2% have been on the market as separate medicines for many years, it is possible that these medicines have previously been used off-label in such a manner that such prior usage would affect the validity of our patents or our ability to obtain patents based on our patent applications. In addition, claims directed to dosing and dose adjustment may be substantially less likely to issue in light of the Supreme Court decision in *Mayo Collaborative Services v. Prometheus Laboratories, Inc*., where the court held that claims directed to methods of determining whether to adjust drug dosing levels based on drug metabolite levels in the red blood cells were not patent eligible because they were directed to a law of nature. This decision may have wide-ranging implications on the validity and scope of pharmaceutical method claims.

Even if patents do successfully issue, third parties may challenge their validity, enforceability or scope, which may result in such patents being narrowed or invalidated.

Patent litigation is currently pending in the Federal Circuit of Appeals and the United States District Court of New Jersey against Alkem and Teva USA, respectively, who each intend to market a generic version of DUEXIS prior to the expiration of certain of our patents listed in the Orange Book. These cases arise from Paragraph IV Patent Certification notice letters from Alkem and Teva USA advising they had filed an ANDA with the FDA seeking approval to market a generic version of DUEXIS before the expiration of the patents-in-suit. For a more detailed description of the DUEXIS litigation, see Note 16, Legal Proceedings, of the notes to unaudited condensed consolidated financial statements, included in Item 1 of this Quarterly Report on Form 10-Q.

Patent litigation is currently pending in the United States District Court of New Jersey against Lupin, who intends to market a generic version of PROCYSBI prior to the expiration of certain of our patents listed in the Orange Book. The case arises from Paragraph IV Patent Certification notice letter from Lupin advising it has filed an ANDA with the FDA seeking approval to market a generic version of PROCYSBI before the expiration of the patents-in-suit. For a more detailed description of the PROCYSBI litigation, see Note 16, Legal Proceedings, of the notes to unaudited condensed consolidated financial statements, included in Item 1 of this Quarterly Report on Form 10-Q.

We intend to vigorously defend our intellectual property rights relating to our medicines, but we cannot predict the outcome of the DUEXIS cases and the PROCYSBI case. Any adverse outcome in these matters or any new generic challenges that may arise could result in one or more generic versions of our medicines being launched before the expiration of the listed patents, which could adversely affect our ability to successfully execute our business strategy to increase sales of our medicines, and would negatively impact our financial condition and results of operations, including causing a significant decrease in our revenues and cash flows.

Furthermore, even if they are unchallenged, our patents and patent applications may not adequately protect our intellectual property or prevent others from designing around our claims. If the patent applications we hold with respect to our medicines fail to issue or if their breadth or strength of protection is threatened, it could dissuade companies from collaborating with us to develop them and threaten our ability to commercialize our medicines. We cannot offer any assurances about which, if any, patents will issue or whether any issued patents will be found not invalid and not unenforceable or will go unthreatened by third parties. Since patent applications in the United States and most other countries are confidential for a period of time after filing, and some remain so until issued, we cannot be certain that we were the first to file any patent application related to our medicines or any other medicine candidates. Furthermore, if third parties have filed such patent applications, an interference proceeding in the United States can be provoked by a third-party or instituted by us to determine which party was the first to invent any of the subject matter covered by the patent claims of our applications.

In addition to the protection afforded by patents, we rely on trade secret protection and confidentiality agreements to protect proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery and development processes that involve proprietary know-how, information or technology that is not covered by patents. Although we expect all of our employees to assign their inventions to us, and all of our employees, consultants, advisors and any third parties who have access to our proprietary know-how, information or technology to enter into confidentiality agreements, we cannot provide any assurances that all such agreements have been duly executed or that our trade secrets and other confidential proprietary information will not be disclosed or that competitors will not otherwise gain access to our trade secrets or independently develop substantially equivalent information and techniques.

Further, the laws of some foreign countries do not protect proprietary rights to the same extent or in the same manner as the laws of the United States. As a result, we may encounter significant problems in protecting and defending our intellectual property both in the United States and abroad. For example, if the issuance, in a given country, of a patent to us, covering an invention, is not followed by the issuance, in other countries, of patents covering the same invention, or if any judicial interpretation of the validity, enforceability, or scope of the claims in, or the written description or enablement in, a patent issued in one country is not similar to the interpretation given to the corresponding patent issued in another country, our ability to protect our intellectual property in those countries may be limited. Changes in either patent laws or in interpretations of patent laws in the United States and other countries may materially diminish the value of our intellectual property or narrow the scope of our patent protection. If we are unable to prevent material disclosure of the non-patented intellectual property related to our technologies to third parties, and there is no guarantee that we will have any such enforceable trade secret protection, we may not be able to establish or maintain a competitive advantage in our market, which could materially adversely affect our business, results of operations and financial condition.

*If we fail to comply with our obligations in the agreements under which we license rights to technology from third parties, we could lose license rights that are important to our business.**

We are party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. For example, we rely on a license from Bausch with respect to technology developed by Bausch in connection with the manufacturing of RAVICTI. The purchase agreement under which Hyperion purchased the rights to RAVICTI contains obligations to pay Bausch regulatory and sales milestone payments relating to RAVICTI, as well as royalties on the net sales of RAVICTI. On May 31, 2013, when Hyperion acquired BUPHENYL under a restated collaboration agreement with Bausch, Hyperion received a license to use some of the manufacturing technology developed by Bausch in connection with the manufacturing of BUPHENYL. The restated collaboration agreement also contains obligations to pay Bausch regulatory and sales milestone payments, as well as royalties on net sales of BUPHENYL. If we fail to make a required payment to Bausch and do not cure the failure within the required time period, Bausch may be able to terminate the license to use its manufacturing technology for RAVICTI and BUPHENYL. If we lose access to the Bausch manufacturing technology, we cannot guarantee that an acceptable alternative method of manufacture could be developed or acquired. Even if alternative technology could be developed or acquired, the loss of the Bausch technology could still result in substantial costs and potential periods where we would not be able to market and sell RAVICTI and/or BUPHENYL. We also license intellectual property necessary for commercialization of RAVICTI from an external party. This party may be entitled to terminate the license if we breach the agreement, including failure to pay required royalties on net sales of RAVICTI, or we do not meet specified diligence obligations in our development and commercialization of RAVICTI, and we do not cure the failure within the required time period. If the license is terminated, it may be difficult or impossible for us to continue to commercialize RAVICTI, which would have a material adverse effect on our business, financial condition and results of operations.

We hold an exclusive, worldwide license from F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or Roche, to patents and know-how for TEPEZZA. We also have exclusive sub-licenses for rights licensed to Roche for TEPEZZA by certain third-party licensors. Roche may have the right to terminate the license upon our breach, if not cured within a specified period of time. Roche may also terminate the license in the event of our bankruptcy or insolvency, or if we challenge the validity of Roche's patents. If the license is terminated for our breach or based on our challenging the validity of Roche's patents, then all rights and licenses granted to us by Roche would also terminate, and we may be required to assign and transfer to Roche certain filings and approvals, trademarks, and data in our possession necessary for the development and commercialization of TEPEZZA, and assign clinical trial agreements to the extent permitted. We may also be required to grant Roche an exclusive license under our patents and know-how for TEPEZZA, and to manufacture and supply TEPEZZA to Roche for a transitional period. We also have a license of patent rights to TEPEZZA under a license agreement with Lundquist Institute (formerly known as Los Angeles Biomedical Research Institute at Harbor-UCLA Medical Center), or Lundquist. Lundquist has the right to terminate the license agreement upon our material breach, if not cured within a specified period of time, or in the event of our bankruptcy or insolvency. If one or more of these licenses is terminated, it may be impossible for us to continue to commercialize TEPEZZA, which would have a material adverse effect on our business, financial condition and results of operations.

We also hold an exclusive license to patents and technology from Duke University, or Duke, and Mountain View Pharmaceuticals, Inc., or MVP, covering KRYSTEXXA. Duke and MVP may terminate the license if we commit fraud or for our willful misconduct or illegal conduct. Duke and MVP may also terminate the license upon our material breach of the agreement, if not cured within a specified period of time, or upon written notice if we have committed two or more material breaches under the agreement. Duke and MVP may also terminate the license in the event of our bankruptcy or insolvency. If the license is terminated, it may be impossible for us to continue to commercialize KRYSTEXXA, which would have a material adverse effect on our business, financial condition and results of operations.

We are subject to contractual obligations under our amended and restated license agreement with UCSD, as amended, with respect to PROCYSBI. If one or more of these licenses was terminated, we would have no further right to use or exploit the related intellectual property, which would limit our ability to develop PROCYSBI in other indications, and could impact our ability to continue commercializing PROCYSBI in its approved indications.

We also license rights to know-how and trademarks for ACTIMMUNE from Genentech Inc., or Genentech. Genentech may terminate the agreement upon our material default, if not cured within a specified period of time. Genentech may also terminate the agreement in the event of our bankruptcy or insolvency. Upon such a termination of the agreement, all intellectual property rights conveyed to us under the agreement, including the rights to the ACTIMMUNE trademark, revert to Genentech. If we fail to comply with our obligations under this agreement, we could lose the ability to market and distribute ACTIMMUNE, which would have a material adverse effect on our business, financial condition and results of operations.

Following our acquisition of Viela on March 15, 2021, we are a party to a number of intellectual property license agreements including (i) our licenses with Duke University and Dana-Farber Cancer Institute related to UPLIZNA, (ii) our license with SBI Biotech Co. Ltd related to HZN-7734, (iii) our license with MedImmune, LLC, or MedImmune, related to HZN-4920, (iv) our sublicense with MedImmune for its license with Lonza Sales AG, or Lonza, related to UPLIZNA and HZN-7734, (v) our sublicense with MedImmune for its license with BioWa, Inc., or BioWa, related to UPLIZNA, and (vi) our sublicense with MedImmune for its license with BioWa and Lonza related to HZN-7734. If we fail to comply with our obligations under these agreements, or we are subject to a bankruptcy, we may be required to make certain payments to the licensor, we may lose the exclusivity of our license, or the licensor may have the right to terminate the license, in which event we would not be able to develop or market products covered by the license.

We hold an exclusive license to Vectura Group plc's, or Vectura, proprietary technology and know-how covering the delayed release of corticosteroids relating to RAYOS. If we fail to comply with our obligations under our agreement with Vectura or our other license agreements, or if we are subject to a bankruptcy, the licensor may have the right to terminate the license, in which event we would not be able to market medicines covered by the license, including RAYOS.

*Some intellectual property has been discovered through government-funded programs and thus may be subject to federal regulations such as "march-in" rights, certain reporting requirements and a preference for U.S.-based companies. Compliance with such regulations may limit our exclusive rights, and limit our ability to contract with non-U.S. manufacturers.**

Some of our intellectual property rights, specifically, intellectual property rights related to UPLIZNA that are in-licensed from Duke University, were generated through the use of U.S. government funding and are therefore subject to certain federal regulations. As a result, the U.S. government may have certain rights to intellectual property embodied in certain of our current or future medicine candidates pursuant to the Bayh-Dole Act of 1980, or the Bayh-Dole Act. These U.S. government rights in certain inventions developed under a government-funded program include a non-exclusive, non-transferable, irrevocable worldwide license to use inventions for any governmental purpose. In addition, the U.S. government has the right, under certain limited circumstances, to require us to grant exclusive, partially exclusive, or non-exclusive licenses to any of these inventions to a third party if it determines that: (i) adequate steps have not been taken to commercialize the invention; (ii) government action is necessary to meet public health or safety needs; or (iii) government action is necessary to meet requirements for public use under federal regulations (also referred to as "march-in rights"). To our knowledge, however, the U.S. government has, to date, not exercised any march-in rights on any patented technology that was generated using U.S. government funds. The U.S. government also has the right to take title to these inventions if we or the applicable grantee fail to disclose the invention to the government and fail to file an application to register the intellectual property within specified time limits. Intellectual property generated under a government funded program is also subject to certain reporting requirements, compliance with which may require us to expend substantial resources. In addition, the U.S. government requires that any products embodying the subject invention or produced through the use of the subject invention be manufactured substantially in the United States. The manufacturing preference requirement can be waived if the owner of the intellectual property can show that reasonable but unsuccessful efforts have been made to grant licenses on similar terms to potential licensees that would be likely to manufacture substantially in the United States or that under the circumstances domestic manufacture is not commercially feasible. This preference for U.S. manufacturers may limit our ability to contract with non-U.S. product manufacturers for products covered by such intellectual property. To the extent any of our current or future intellectual property is generated through the use of U.S. government funding, the provisions of the Bayh-Dole Act may similarly apply.

*The patent protection and patent prosecution for some of our medicine candidates is dependent on third parties.**

While we normally seek and gain the right to fully prosecute the patents relating to our medicine candidates, there may be times when patents relating to our medicine candidates are controlled by our licensors. This is the case with current patents and patent applications licensed from MedImmune related to HZN-4920, and those licensed from Duke University related to inebilizumab. If we, or any of our future licensing partners fail to appropriately file, prosecute and maintain patent protection for patents covering any of our medicine candidates, our ability to develop and commercialize those medicine candidates may be adversely affected and we may not be able to prevent competitors from making, using, and selling competing products. In addition, even where we now have the right to control patent prosecution of patents and patent applications we have licensed from third parties, we may still be adversely affected or prejudiced by actions or inactions of our licensors.

Risks Related to Ownership of Our Ordinary Shares

The market price of our ordinary shares historically has been volatile and is likely to continue to be volatile, and you could lose all or part of any investment in our ordinary shares.

The trading price of our ordinary shares has been volatile and could be subject to wide fluctuations in response to various factors, some of which are beyond our control. In addition to the factors discussed in this "Risk Factors" section and elsewhere in this report, these factors include:

- our failure to successfully execute our commercialization strategy with respect to our approved medicines, particularly our commercialization of our medicines in the United States;
- the impact of the COVID-19 pandemic on our business and industry as well as the global economy;
- actions or announcements by third-party or government payers with respect to coverage and reimbursement of our medicines;
- disputes or other developments relating to intellectual property and other proprietary rights, including patents, litigation matters and our ability to obtain patent protection for our medicines and medicine candidates;
- unanticipated serious safety concerns related to the use of our medicines;
- adverse regulatory decisions;
- changes in laws or regulations applicable to our business, medicines or medicine candidates, including but not limited to clinical trial requirements for approvals or tax laws;
- inability to comply with our debt covenants and to make payments as they become due;
- inability to obtain adequate commercial supply for any approved medicine or inability to do so at acceptable prices;
- developments concerning our commercial partners, including but not limited to those with our sources of manufacturing supply;
- our decision to initiate a clinical trial, not to initiate a clinical trial or to terminate an existing clinical trial;
- adverse results or delays in clinical trials;
- our failure to successfully develop and/or acquire additional medicine candidates or obtain approvals for additional indications for our existing medicine candidates;
- introduction of new medicines or services offered by us or our competitors;
- overall performance of the equity markets, including the pharmaceutical sector, and general political and economic conditions;
- failure to meet or exceed revenue and financial projections that we may provide to the public;
- actual or anticipated variations in quarterly operating results;
- failure to meet or exceed the estimates and projections of the investment community;
- inaccurate or significant adverse media coverage;
- publication of research reports about us or our industry or positive or negative recommendations or withdrawal of research coverage by securities analysts;
- our inability to successfully enter new markets;
- the termination of a collaboration or the inability to establish additional collaborations;
- announcements of significant acquisitions, strategic partnerships, joint ventures or capital commitments by us or our competitors;
- our inability to maintain an adequate rate of growth;
- ineffectiveness of our internal controls or our inability to otherwise comply with financial reporting requirements;
- adverse U.S. and foreign tax exposure;
- additions or departures of key management, commercial or regulatory personnel;
- issuances of debt or equity securities;
- significant lawsuits, including patent or shareholder litigation;
- changes in the market valuations of similar companies to us;
- sales of our ordinary shares by us or our shareholders in the future;
- trading volume of our ordinary shares;
- effects of natural or man-made catastrophic events or other business interruptions; and
- other events or factors, many of which are beyond our control.

In addition, the stock market in general, and The Nasdaq Global Select Market and the stock of biotechnology companies in particular, have experienced extreme price and volume fluctuations that have often been unrelated or disproportionate to the operating performance of these companies. Broad market and industry factors may adversely affect the market price of our ordinary shares, regardless of our actual operating performance.

We have never declared or paid dividends on our share capital and we do not anticipate paying dividends in the foreseeable future.

We have never declared or paid any cash dividends on our ordinary shares. We currently anticipate that we will retain future earnings for the development, operation and expansion of our business and do not anticipate declaring or paying any cash dividends for the foreseeable future, including due to limitations that are currently imposed by our credit agreement and the indenture governing the 2027 Senior Notes. Any return to shareholders will therefore be limited to the increase, if any, of our ordinary share price.

*Future sales and issuances of our ordinary shares, securities convertible into our ordinary shares or rights to purchase ordinary shares or convertible securities could result in additional dilution of the percentage ownership of our shareholders and could cause our share price to decline.**

Additional capital may be needed in the future to continue our planned operations. To the extent we raise additional capital by issuing equity securities or securities convertible into or exchangeable for ordinary shares, our shareholders may experience substantial dilution. We may sell ordinary shares, and we may sell convertible or exchangeable securities or other equity securities in one or more transactions at prices and in a manner we determine from time to time. If we sell such ordinary shares, convertible or exchangeable securities or other equity securities in subsequent transactions, existing shareholders may be materially diluted. New investors in such subsequent transactions could gain rights, preferences and privileges senior to those of holders of ordinary shares. We also maintain equity incentive plans, including our Amended and Restated 2020 Equity Incentive Plan, Amended and Restated 2018 Equity Incentive Plan, 2014 Non-Employee Equity Plan, as amended, and 2020 Employee Share Purchase Plan, and intend to grant additional ordinary share awards under these and future plans, which will result in additional dilution to our existing shareholders.

Irish law differs from the laws in effect in the United States and may afford less protection to holders of our securities.

It may not be possible to enforce court judgments obtained in the United States against us in Ireland based on the civil liability provisions of the U.S. federal or state securities laws. In addition, there is some uncertainty as to whether the courts of Ireland would recognize or enforce judgments of U.S. courts obtained against us or our directors or officers based on the civil liabilities provisions of the U.S. federal or state securities laws or hear actions against us or those persons based on those laws. We have been advised that the United States currently does not have a treaty with Ireland providing for the reciprocal recognition and enforcement of judgments in civil and commercial matters. Therefore, a final judgment for the payment of money rendered by any U.S. federal or state court based on civil liability, whether or not based solely on U.S. federal or state securities laws, would not automatically or necessarily be enforceable in Ireland.

As an Irish company, we are governed by the Irish Companies Act 2014 (as amended), which differs in some material respects from laws generally applicable to U.S. corporations and shareholders, including, among others, differences relating to interested director and officer transactions and shareholder lawsuits. Likewise, the duties of directors and officers of an Irish company generally are owed to the company only. Shareholders of Irish companies generally do not have a personal right of action against directors or officers of the company and may exercise such rights of action on behalf of the company only in limited circumstances. Accordingly, holders of our securities may have more difficulty protecting their interests than would holders of securities of a corporation incorporated in a jurisdiction of the United States.

Provisions of our articles of association, and Irish law could delay or prevent a takeover of us by a third party.

Our articles of association could delay, defer or prevent a third-party from acquiring us, despite the possible benefit to our shareholders, or otherwise adversely affect the price of our ordinary shares. For example, our articles of association:

- impose advance notice requirements for shareholder proposals and nominations of directors to be considered at shareholder meetings;
- stagger the terms of our board of directors into three classes; and
- require the approval of a supermajority of the voting power of the shares of our share capital entitled to vote generally at a meeting of shareholders to amend or repeal our articles of association.

In addition, several mandatory provisions of Irish law could prevent or delay an acquisition of us. For example, Irish law does not permit shareholders of an Irish public limited company to take action by written consent with less than unanimous consent. We are also subject to various provisions of Irish law relating to mandatory bids, voluntary bids, requirements to make a cash offer and minimum price requirements, as well as substantial acquisition rules and rules requiring the disclosure of interests in our ordinary shares in certain circumstances.

These provisions may discourage potential takeover attempts, discourage bids for our ordinary shares at a premium over the market price or adversely affect the market price of, and the voting and other rights of the holders of, our ordinary shares. These provisions could also discourage proxy contests and make it more difficult for you and our other shareholders to elect directors other than the candidates nominated by our board of directors, and could depress the market price of our ordinary shares.

Any attempts to take us over will be subject to Irish Takeover Rules and subject to review by the Irish Takeover Panel.

We are subject to the Irish Takeover Rules, under which our board of directors will not be permitted to take any action which might frustrate an offer for our ordinary shares once it has received an approach which may lead to an offer or has reason to believe an offer is imminent.

A transfer of our ordinary shares may be subject to Irish stamp duty.

In certain circumstances, the transfer of shares in an Irish incorporated company will be subject to Irish stamp duty, which is a legal obligation of the buyer. This duty is currently charged at the rate of 1.0 percent of the price paid or the market value of the shares acquired, if higher. Because our ordinary shares are traded on a recognized stock exchange in the United States, an exemption from this stamp duty is available to transfers by shareholders who hold ordinary shares beneficially through brokers, which in turn hold those shares through the Depositary Trust Company, or DTC, to holders who also hold through DTC. However, a transfer by or to a record holder who holds ordinary shares directly in his, her or its own name could be subject to this stamp duty. We, in our absolute discretion and insofar as the Irish Companies Act 2014 (as amended) or any other applicable law permit, may, or may provide that one of our subsidiaries will pay Irish stamp duty arising on a transfer of our ordinary shares on behalf of the transferee of such ordinary shares. If stamp duty resulting from the transfer of ordinary shares which would otherwise be payable by the transferee is paid by us or any of our subsidiaries on behalf of the transferee, then in those circumstances, we will, on our behalf or on behalf of such subsidiary (as the case may be), be entitled to (i) seek reimbursement of the stamp duty from the transferee, (ii) set-off the stamp duty against any dividends payable to the transferee of those ordinary shares and (iii) claim a first and permanent lien on the ordinary shares on which stamp duty has been paid by us or such subsidiary for the amount of stamp duty paid. Our lien shall extend to all dividends paid on those ordinary shares.

Dividends paid by us may be subject to Irish dividend withholding tax.

In certain circumstances, as an Irish tax resident company, we will be required to deduct Irish dividend withholding tax (currently at the rate of 25%) from dividends paid to our shareholders. Shareholders that are resident in the United States, EU countries (other than Ireland) or other countries with which Ireland has signed a tax treaty (whether the treaty has been ratified or not) generally should not be subject to Irish withholding tax so long as the shareholder has provided its broker, for onward transmission to our qualifying intermediary or other designated agent (in the case of shares held beneficially), or our or its transfer agent (in the case of shares held directly), with all the necessary documentation by the appropriate due date prior to payment of the dividend. However, some shareholders may be subject to withholding tax, which could adversely affect the price of our ordinary shares.

General Risk Factors

We have incurred and will continue to incur significant increased costs as a result of operating as a public company and our management will be required to devote substantial time to compliance initiatives.

As a public company, we have incurred and will continue to incur significant legal, accounting and other expenses that we did not incur as a private company. In particular, the Sarbanes-Oxley Act of 2000, or the Sarbanes-Oxley Act, as well as rules subsequently implemented by the SEC and the Nasdaq Stock Market, Inc., or Nasdaq, impose significant requirements on public companies, including requiring establishment and maintenance of effective disclosure and financial controls and changes in corporate governance practices. These rules and regulations have substantially increased our legal and financial compliance costs and have made some activities more time-consuming and costly. These effects are exacerbated by our transition to an Irish company and the integration of numerous acquired businesses and operations into our historical business and operating structure. If these requirements divert the attention of our management and personnel from other business concerns, they could have a material adverse effect on our business, financial condition and results of operations. The increased costs will continue to decrease our net income or increase our net income (loss), and may require us to reduce costs in other areas of our business or increase the prices of our medicines or services. For example, these rules and regulations make it more difficult and more expensive for us to obtain and maintain director and officer liability insurance. We cannot predict or estimate the amount or timing of additional costs that we may incur to respond to these requirements. The impact of these requirements could also make it more difficult for us to attract and retain qualified persons to serve on our board of directors, our board committees or as executive officers. If we fail to comply with the continued listing requirements of Nasdaq, our ordinary shares could be delisted from The Nasdaq Global Select Market, which would adversely affect the liquidity of our ordinary shares and our ability to obtain future financing.

The Sarbanes-Oxley Act requires, among other things, that we maintain effective internal controls for financial reporting and disclosure controls and procedures. In particular, we are required to perform annual system and process evaluation and testing of our internal controls over financial reporting to allow management to report on the effectiveness of our internal controls over financial reporting, as required by Section 404 of the Sarbanes-Oxley Act, or Section 404. Our independent registered public accounting firm is also required to deliver a report on the effectiveness of our internal control over financial reporting. Our testing, or the testing by our independent registered public accounting firm, may reveal deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses. Our compliance with Section 404 requires that we incur substantial expense and expend significant management efforts, particularly because of our Irish parent company structure and international operations. If we are not able to comply with the requirements of Section 404 or if we or our independent registered public accounting firm identify deficiencies in our internal controls over financial reporting that are deemed to be material weaknesses, the market price of our ordinary shares could decline and we could be subject to sanctions or investigations by Nasdaq, the SEC or other regulatory authorities, which would require additional financial and management resources.

New laws and regulations as well as changes to existing laws and regulations affecting public companies, including the provisions of the Sarbanes-Oxley Act and rules adopted by the SEC and by Nasdaq, would likely result in increased costs as we respond to their requirements.

Securities class action litigation could divert our management's attention and harm our business and could subject us to significant liabilities.

The stock markets have from time to time experienced significant price and volume fluctuations that have affected the market prices for the equity securities of pharmaceutical companies. These broad market fluctuations may cause the market price of our ordinary shares to decline. In the past, securities class action litigation has often been brought against a company following a decline in the market price of its securities. This risk is especially relevant for us because biotechnology and biopharma companies have experienced significant stock price volatility in recent years. For example, following declines in our stock price, two federal securities class action lawsuits were filed in March 2016 against us and certain of our current and former officers alleging violations of the Securities Exchange Act of 1934, as amended, which lawsuits were dismissed by the plaintiffs in June 2018. Even if we are successful in defending any similar claims that may be brought in the future, such litigation could result in substantial costs and may be a distraction to our management and may lead to an unfavorable outcome that could adversely impact our financial condition and prospects.

Our employees, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in misconduct or other improper activities, including noncompliance with regulatory standards and requirements.

We are exposed to the risk that our employees, independent contractors, principal investigators, consultants, vendors, distributors and CROs may engage in fraudulent or other illegal activity. Misconduct by these parties could include intentional, reckless and/or negligent conduct or unauthorized activities that violate FDA regulations, including those laws that require the reporting of true, complete and accurate information to the FDA, manufacturing standards, federal and state healthcare fraud and abuse laws and regulations, and laws that require the true, complete and accurate reporting of financial information or data. In particular, sales, marketing and business arrangements in the healthcare industry are subject to extensive laws and regulations intended to prevent fraud, misconduct, kickbacks, self-dealing and other abusive practices. These laws and regulations may restrict or prohibit a wide range of pricing, discounting, marketing and promotion, sales commission, customer incentive programs and other business arrangements. Misconduct by our employees and other third parties may also include the improper use of information obtained in the course of clinical trials, which could result in regulatory sanctions and serious harm to our reputation. We have adopted a Code of Conduct and Ethics, but it is not always possible to identify and deter misconduct by our employees and other third parties, and the precautions we take to detect and prevent this activity may not be effective in controlling unknown or unmanaged risks or losses or in protecting us from governmental investigations or other actions or lawsuits stemming from a failure to be in compliance with such laws or regulations. If any such actions are instituted against us, and we are not successful in defending ourselves or asserting our rights, those actions could have a significant impact on our business, including the imposition of significant civil and criminal penalties, damages, fines, the curtailment or restructuring of our operations, the exclusion from participation in federal and state healthcare programs and imprisonment.

Third-party claims of intellectual property infringement may prevent or delay our development and commercialization efforts.

Our commercial success depends in part on us avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biotechnology and pharmaceutical industries, including patent infringement lawsuits, interferences, oppositions and inter party reexamination proceedings before the United States Patent and Trademark Office, or the U.S. PTO. Numerous U.S. and foreign issued patents and pending patent applications, which are owned by third parties, exist in the fields in which our collaborators are developing medicine candidates. As the biotechnology and pharmaceutical industries expand and more patents are issued, the risk increases that our medicine candidates may be subject to claims of infringement of the patent rights of third parties.

Third parties may assert that we are employing their proprietary technology without authorization. There may be third-party patents or patent applications with claims to materials, formulations, methods of manufacture or methods for treatment related to the use or manufacture of our medicines and/or any other medicine candidates. Because patent applications can take many years to issue, there may be currently pending patent applications, which may later result in issued patents that our medicine candidates may infringe. In addition, third parties may obtain patents in the future and claim that use of our technologies infringes upon these patents. If any third-party patents were held by a court of competent jurisdiction to cover the manufacturing process of any of our medicine candidates, any molecules formed during the manufacturing process or any final medicine itself, the holders of any such patents may be able to block our ability to commercialize such medicine candidate unless we obtained a license under the applicable patents, or until such patents expire. Similarly, if any third-party patent were held by a court of competent jurisdiction to cover aspects of our formulations, processes for manufacture or methods of use, including combination therapy, the holders of any such patent may be able to block our ability to develop and commercialize the applicable medicine candidate unless we obtained a license or until such patent expires. In either case, such a license may not be available on commercially reasonable terms or at all.

Parties making claims against us may obtain injunctive or other equitable relief, which could effectively block our ability to further develop and commercialize one or more of our medicine candidates. Defense of these claims, regardless of their merit, would involve substantial litigation expense and would be a substantial diversion of employee resources from our business. In the event of a successful claim of infringement against us, we may have to pay substantial damages, including treble damages and attorneys' fees for willful infringement, obtain one or more licenses from third parties, pay royalties or redesign our infringing medicines, which may be impossible or require substantial time and monetary expenditure. We cannot predict whether any such license would be available at all or whether it would be available on commercially reasonable terms. Furthermore, even in the absence of litigation, we may need to obtain licenses from third parties to advance our research or allow commercialization of our medicine candidates, and we have done so from time to time. We may fail to obtain any of these licenses at a reasonable cost or on reasonable terms, if at all. In that event, we would be unable to further develop and commercialize one or more of our medicine candidates, which could harm our business significantly. We cannot provide any assurances that third-party patents do not exist which might be enforced against our medicines, resulting in either an injunction prohibiting our sales, or, with respect to our sales, an obligation on our part to pay royalties and/or other forms of compensation to third parties.

We may be involved in lawsuits to protect or enforce our patents or the patents of our licensors, which could be expensive, time consuming and unsuccessful.

Competitors may infringe our patents or the patents of our licensors. To counter infringement or unauthorized use, we may be required to file infringement claims, which can be expensive and time-consuming. In addition, in an infringement proceeding, a court may decide that one of our patents, or a patent of one of our licensors, is not valid or is unenforceable, or may refuse to stop the other party from using the technology at issue on the grounds that our patents do not cover the technology in question. An adverse result in any litigation or defense proceedings could put one or more of our patents at risk of being invalidated or interpreted narrowly and could put our patent applications at risk of not issuing.

There are numerous post grant review proceedings available at the U.S. PTO (including inter partes review, post-grant review and ex-parte reexamination) and similar proceedings in other countries of the world that could be initiated by a third-party that could potentially negatively impact our issued patents.

Interference proceedings provoked by third parties or brought by us may be necessary to determine the priority of inventions with respect to our patents or patent applications or those of our collaborators or licensors. An unfavorable outcome could require us to cease using the related technology or to attempt to license rights to it from the prevailing party. Our business could be harmed if the prevailing party does not offer us a license on commercially reasonable terms. Our defense of litigation or interference proceedings may fail and, even if successful, may result in substantial costs and distract our management and other employees. We may not be able to prevent, alone or with our licensors, misappropriation of our intellectual property rights, particularly in countries where the laws may not protect those rights as fully as in the United States.

Furthermore, because of the substantial amount of discovery required in connection with intellectual property litigation, there is a risk that some of our confidential information could be compromised by disclosure during this type of litigation. There could also be public announcements of the results of hearings, motions or other interim proceedings or developments. If securities analysts or investors perceive these results to be negative, it could have a material adverse effect on the price of our ordinary shares.

Obtaining and maintaining our patent protection depends on compliance with various procedural, document submission, fee payment and other requirements imposed by governmental patent agencies, and our patent protection could be reduced or eliminated for non-compliance with these requirements.

Periodic maintenance fees on any issued patent are due to be paid to the U.S. PTO and foreign patent agencies in several stages over the lifetime of the patent. The U.S. PTO and various foreign governmental patent agencies require compliance with a number of procedural, documentary, fee payment and other similar provisions during the patent application process. While an inadvertent lapse can in many cases be cured by payment of a late fee or by other means in accordance with the applicable rules, there are situations in which noncompliance can result in abandonment or lapse of the patent or patent application, resulting in partial or complete loss of patent rights in the relevant jurisdiction. Non-compliance events that could result in abandonment or lapse of a patent or patent application include, but are not limited to, failure to respond to official actions within prescribed time limits, non-payment of fees and failure to properly legalize and submit formal documents. If we or licensors that control the prosecution and maintenance of our licensed patents fail to maintain the patents and patent applications covering our medicine candidates, our competitors might be able to enter the market, which would have a material adverse effect on our business.

We may be subject to claims that our employees, consultants or independent contractors have wrongfully used or disclosed confidential information of third parties.

We employ individuals who were previously employed at other biotechnology or pharmaceutical companies. We may be subject to claims that we or our employees, consultants or independent contractors have inadvertently or otherwise used or disclosed confidential information of our employees' former employers or other third parties. We may also be subject to claims that former employers or other third parties have an ownership interest in our patents. Litigation may be necessary to defend against these claims. There is no guarantee of success in defending these claims, and even if we are successful, litigation could result in substantial cost and be a distraction to our management and other employees.

Sales of a substantial number of our ordinary shares in the public market could cause our share price to decline.

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of such ordinary shares could decline. In addition, our ordinary shares that are either subject to outstanding options and restricted stock units or reserved for future issuance under our employee benefit plans are or may become eligible for sale in the public market to the extent permitted by the provisions of various vesting schedules and the Securities Act of 1933, as amended, or the Securities Act. If these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

If securities or industry analysts do not publish research or publish inaccurate or unfavorable research about our business, our share price and trading volume could decline.

The trading market for our ordinary shares will depend in part on the research and reports that securities or industry analysts publish about us or our business. If one or more of the analysts who cover us downgrade our rating or publish inaccurate or unfavorable research about our business, our share price could decline. If one or more of these analysts cease coverage of our company or fail to publish reports on our company regularly, demand for our ordinary shares could decrease, which might cause our share price and trading volume to decline.

ITEM 6. EXHIBITS

Exhibit Number	Description of Document
2.1#	Agreement and Plan of Merger, dated January 31, 2021, by and among Horizon Therapeutics USA, Inc., Teiripic Merger Sub, Inc., Viela Bio, Inc. and solely for purposes of Sections 6.7 and 9.12 of the Merger Agreement, Horizon Therapeutics plc (incorporated by reference to Exhibit 2.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on February 1, 2021).
3.1	Memorandum and Articles of Association of Horizon Therapeutics Public Limited Company, as amended (incorporated by reference to Exhibit 3.1 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 8, 2019).
4.1	Indenture dated as of July 16, 2019 by and between Horizon Therapeutics USA, Inc., the guarantors party thereto and U.S. Bank National Association, as trustee (incorporated by reference to Exhibit 4.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on July 16, 2019).
4.2	Form of 5.500% Senior Note due 2027 (incorporated by reference to Exhibit 4.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on July 16, 2019).
4.3	First Supplemental Indenture, dated November 19, 2019, by and between HZNP Finance Limited and U.S. Bank National Association (incorporated by reference to Exhibit 4.5 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 6, 2020).
4.4	Second Supplemental Indenture, dated April 23, 2020, by and among Horizon Properties Holding LLC, Curzion Pharmaceuticals, Inc. and U.S. Bank National Association (incorporated by reference to Exhibit 4.6 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 6, 2020).
4.5	Third Supplemental Indenture, dated March 15, 2021, by and between Viela Bio, Inc. and U.S. Bank National Association.
10.1*	Second Amendment to Supply Agreement, effective as of January 22, 2021, by and between NOF Corporation and Horizon Therapeutics Ireland DAC (incorporated by reference to Exhibit 10.70 to Horizon Therapeutics Public Limited Company's Annual Report on Form 10-K, filed on February 24, 2021).
10.2	Amendment No. 9, dated March 15, 2021, to the Credit Agreement, dated May 7, 2015, by and among Horizon Therapeutics USA, Inc., as borrower, Horizon Therapeutics plc, as Irish Holdco and a guarantor, the subsidiary guarantors party thereto, as subsidiary guarantors, the lenders party thereto and Citibank, N.A., as administrative agent and collateral agent (incorporated by reference to Exhibit 99.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on March 15, 2021).
10.3+	Horizon Therapeutics Public Limited Company Amended and Restated 2020 Equity Incentive Plan and Form of Option Agreement, Form of Stock Option Grant Notice, Forms of Restricted Stock Unit Agreement and Forms of Restricted Stock Unit Grant Notice thereunder (incorporated by reference to Exhibit 99.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on April 30, 2021).
10.4+	Horizon Therapeutics Public Limited Company Amended and Restated 2018 Equity Incentive Plan (assumed from Viela Bio, Inc.) and Form of RSU Award Grant Notice and Form of Award Agreement (RSU Award) thereunder (incorporated by reference to Exhibit 99.1 to Horizon Therapeutics Public Limited Company's Registration Statement on Form S-8, filed on April 30, 2021).
10.5+	Executive Employment Agreement, effective as of March 15, 2021, by and among Horizon Therapeutics Public Limited Company, Horizon Therapeutics USA, Inc. and Elizabeth H.Z. Thompson.
31.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.
31.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(a) or 15d-14(a) of the Exchange Act.
32.1	Certification of Principal Executive Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350.
32.2	Certification of Principal Financial Officer pursuant to Rule 13a-14(b) or 15d-14(b) of the Exchange Act and 18 U.S.C. Section 1350.

Exhibit Number	Description of Document
101. INS	Inline 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 Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

Schedules have been omitted pursuant to Item 601(a)(5) of Regulation S-K. The registrant hereby undertakes to furnish supplemental copies of any of the omitted schedules upon request by the U.S. Securities and Exchange Commission.

+ Indicates management contract or compensatory plan.

* Certain portions of this exhibit (indicated by "[***]") have been omitted as the Registrant has determined (i) the omitted information is not material and (ii) the omitted information would likely cause harm to the Registrant if publicly disclosed.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

HORIZON THERAPEUTICS PLC

Date: May 5, 2021

By: /s/ Timothy P. Walbert
Timothy P. Walbert
Chairman, President and Chief Executive Officer
(Principal Executive Officer)

Date: May 5, 2021

By: /s/ Paul W. Hoelscher
Paul W. Hoelscher
Executive Vice President, Chief Financial Officer
(Principal Financial Officer)

Exhibit 4.5

THIRD SUPPLEMENTAL INDENTURE

THIRD SUPPLEMENTAL INDENTURE (this "*Supplemental Indenture*"), dated as of March 15, 2021, between Viela Bio, Inc., a Delaware corporation (the "*Guaranteeing Entity*"), which is a subsidiary of the Issuer (as defined below), and U.S. Bank National Association, as trustee under the Indenture referred to below (the "*Trustee*").

W I T N E S S E T H

WHEREAS, Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc.), a Delaware corporation (the "*Issuer*"), has heretofore executed and delivered to the Trustee an indenture (the "*Indenture*"), dated as of July 16, 2019, providing for the issuance of 5.500% Senior Notes due 2027 (the "*Notes*");

WHEREAS, the Indenture provides that under certain circumstances the Guaranteeing Entity shall execute and deliver to the Trustee a supplemental indenture pursuant to which the Guaranteeing Entity shall unconditionally guarantee all of the Issuer's Obligations under the Notes and the Indenture on the terms and conditions set forth herein (the "*Note Guarantee*"); and

WHEREAS, pursuant to Section 9.01 of the Indenture, the Trustee is authorized to execute and deliver this Supplemental Indenture.

NOW, THEREFORE, in consideration of the foregoing and for other good and valuable consideration, the receipt of which is hereby acknowledged, the Guaranteeing Entity and the Trustee mutually covenant and agree for the equal and ratable benefit of the Holders of the Notes as follows:

1. CAPITALIZED TERMS. Capitalized terms used herein without definition shall have the meanings assigned to them in the Indenture.

2. AGREEMENT TO GUARANTEE. The Guaranteeing Entity hereby agrees to provide an unconditional Guarantee on the terms and subject to the conditions set forth in the Note Guarantee of the Indenture including but not limited to Article 10 thereof.

3. NO RECOURSE AGAINST OTHERS. No director, officer, employee, incorporator or stockholder of the Issuer or any Guarantor (including, for the avoidance of doubt, the Guaranteeing Entity), as such, will have any liability for any obligations of the Issuer or the Guarantors under the Notes, the Indenture, the Note Guarantees or for any claim based on, in respect of, or by reason of, such obligations or their creation. Each Holder of Notes by accepting a Note waives and releases all such liability. The waiver and release are part of the consideration for issuance of the Notes. The waiver may not be effective to waive liabilities under the federal securities laws.

4. NEW YORK LAW TO GOVERN; WAIVER OF JURY TRIAL. THIS SUPPLEMENTAL INDENTURE SHALL BE GOVERNED BY, AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK. THE TRUSTEE AND THE GUARANTEEING ENTITY CONSENTS AND IRREVOCABLY SUBMITS TO THE JURISDICTION OF ANY NEW YORK STATE OR U.S. FEDERAL COURT LOCATED IN THE BOROUGH OF MANHATTAN, CITY OF NEW YORK, COUNTY OF NEW YORK, STATE OF NEW YORK IN RELATION TO ANY LEGAL ACTION OR PROCEEDING (I) ARISING OUT OF, RELATING TO OR IN CONNECTION WITH THIS INDENTURE, AS SUPPLEMENTED, THE NOTES, THE GUARANTEES AND ANY RELATED DOCUMENTS AND/OR

(II) ARISING UNDER ANY U.S. FEDERAL OR U.S. STATE SECURITIES LAWS IN RESPECT OF THE NOTES, THE GUARANTEES AND ANY SECURITIES ISSUED PURSUANT TO THE TERMS OF THE INDENTURE, AS SUPPLEMENTED. THE TRUSTEE AND THE GUARANTEEING ENTITY WAIVES ANY OBJECTION TO PROCEEDINGS IN ANY SUCH COURTS, WHETHER ON THE GROUND OF VENUE OR ON THE GROUND THAT THE PROCEEDINGS HAVE BEEN BROUGHT IN AN INCONVENIENT FORUM. THE TRUSTEE AND THE GUARANTEEING ENTITY, TO THE EXTENT ORGANIZED OUTSIDE OF THE UNITED STATES, SHALL APPOINT HORIZON PHARMA USA, INC. (HORIZON PHARMA USA, INC., 150 S SAUNDERS ROAD, LAKE FOREST, IL 60045), AS ITS AGENT FOR SERVICE OF PROCESS IN ANY SUCH SUIT, ACTION OR PROCEEDING AND AGREES THAT SERVICE OF PROCESS UPON SAID AUTHORIZED AGENT SHALL BE DEEMED IN EVERY RESPECT EFFECTIVE SERVICE OF PROCESS UPON IT IN ANY SUCH SUIT, ACTION OR PROCEEDING. THE GUARANTEEING ENTITY AGREES TO DELIVER, UPON THE EXECUTION AND DELIVERY OF THIS SUPPLEMENTAL INDENTURE, A WRITTEN ACCEPTANCE BY SUCH AGENT OF ITS APPOINTMENT AS SUCH AGENT. THE GUARANTEEING ENTITY, TO THE EXTENT ORGANIZED OUTSIDE OF THE UNITED STATES, FURTHER AGREES TO TAKE ANY AND ALL ACTION, INCLUDING THE FILING OF ANY AND ALL SUCH DOCUMENTS AND INSTRUMENTS, AS MAY BE REASONABLY NECESSARY TO CONTINUE SUCH DESIGNATION AND APPOINTMENT OF CT CORPORATION SYSTEM IN FULL FORCE AND EFFECT FOR SO LONG AS THE INDENTURE, AS SUPPLEMENTED, REMAINS IN FORCE. THE ISSUER, THE TRUSTEE AND THE GUARANTEEING ENTITY HEREBY IRREVOCABLY WAIVES, TO THE FULLEST EXTENT PERMITTED BY APPLICABLE LAW, ANY AND ALL RIGHT TO TRIAL BY JURY IN ANY LEGAL PROCEEDING ARISING OUT OF OR RELATING TO THIS SUPPLEMENTAL INDENTURE OR THE TRANSACTIONS CONTEMPLATED HEREBY.

5. COUNTERPARTS. The parties may sign any number of copies of this Supplemental Indenture. Each signed copy (which may be provided via facsimile or other electronic transmission) shall be an original, but all of them together represent the same agreement.

6. EFFECT OF HEADINGS. The Section headings herein are for convenience only and shall not affect the construction hereof.

7. THE TRUSTEE. The Trustee shall not be responsible in any manner whatsoever for or in respect of the validity or sufficiency of this Supplemental Indenture or for or in respect of the recitals contained herein, all of which recitals are made solely by the Guaranteeing Entity and the Issuer.

8. RATIFICATION OF INDENTURE; SUPPLEMENTAL INDENTURE PART OF INDENTURE. Except as expressly amended hereby, the Indenture is in all respects ratified and confirmed and all the terms, conditions and provisions thereof shall remain in full force and effect. This Supplemental Indenture shall form a part of the Indenture for all purposes.

Notwithstanding anything to the contrary in the Indenture, this Supplemental Indenture and any notice or other communication sent to the Trustee hereunder requiring a signature must be signed manually or by way of a digital signature provided by DocuSign (or such other digital signature provider as specified in writing by the Trustee from time to time). Issuer agrees to assume all risks arising out of the use of using digital signatures and electronic methods to submit communications to the Bank, including without limitation the risk of the Bank acting on unauthorized instructions, and the risk of interception and misuse by third parties.

IN WITNESS WHEREOF, the parties hereto have caused this Supplemental Indenture to be duly executed and attested, all as of the date first above written.

VIELA BIO, INC.

By: /s/ Paul W. Hoelscher
Name: Paul W. Hoelscher
Title: Treasurer

U.S. BANK NATIONAL ASSOCIATION,
as Trustee

By: /s/ Joshua A. Hahn_
Name: Joshua A. Hahn
Title: Vice President

EXECUTIVE EMPLOYMENT AGREEMENT BY AND BETWEEN HORIZON THERPEUTICS PUBLIC PLC AND HORIZON THERAPEUTICS USA, INC. AND ELIZABETH H. Z. THOMPSON

This Executive Employment Agreement (hereinafter referred to as the ***"Agreement"***), is entered into by and between Horizon Therapeutics PLC., an Irish Public Limited Company, and its wholly owned subsidiary, Horizon Therapeutics USA, Inc., a Delaware corporation, having a principal place of business at 1 Horizon Way, Deerfield IL 60015, (hereinafter referred to together as the ***"Company"***) and Elizabeth H. Z. Thompson (hereinafter referred as to the ***"Executive"***). The terms of this Agreement shall be effective commencing March 15, 2021 (the "***Effective Date***").

RECITALS

WHEREAS, the Company desires assurance of the continued association and services of the Executive in order to continue to retain the Executive's experience, skills, abilities, background and knowledge, and is willing to continue to engage the Executive's services on the terms and conditions set forth in this Agreement; and

WHEREAS, Executive desires to be in the continued employ of the Company, and is willing to accept such continuing employment on the terms and conditions set forth in this Agreement.

AGREEMENT

1. Employment.

1.1 Term. The Company hereby agrees to continue to employ the Executive, and the Executive hereby accepts employment by the Company, upon the terms and conditions set forth in this Agreement. The Executive originally commenced employment with the Company on June 6, 2018. Executive's employment shall be governed under the terms set forth in this Agreement beginning on the Effective Date and shall continue until it is terminated pursuant to Section 4 herein (hereinafter referred to as the ***"Term"***).

1.2 Title. From and after the Effective Date the Executive will have the title of Executive Vice President, Research and Development (such position held by Executive during such period is hereinafter referred to as ***"EVP, R&D")*** and Executive shall serve in such other capacity or capacities commensurate with her position as EVP, R&D as the President and CEO of the Company may from time to time prescribe.

1.3 Duties. The Executive shall do and perform all services, acts or things necessary or advisable to manage and conduct the business of the Company and shall have the authority and responsibilities which are generally associated with the position of EVP, R&D. The Executive shall report to the President and CEO.

1.4 Policies and Practices. The employment relationship between the Parties shall be governed by this Agreement and the policies and practices established by the Company and the Board of Directors (hereinafter referred to as the ***"Board"***). In the event that the terms of this Agreement differ from or are in conflict with the Company's policies or practices or the Company's Employee Handbook, this Agreement shall control.

1.5 Location. The Executive shall perform the services the Executive is required to perform pursuant to this Agreement in at the Company's location in South San Francisco, California. The Company may from time to time require the Executive to travel temporarily to other locations outside of South San Francisco, California area in connection with the Company's business.

2. Loyalty of Executive.

2.1 Loyalty. During the Executive's employment by the Company, the Executive shall devote the Executive's business energies, interest, abilities and productive time to the proper and efficient performance of Executive's duties under this Agreement. Subject to the prior written consent of the President and CEO, the Executive is permitted to serve on the board of directors of one other company, so long as the other company does not compete with the Company.

2.2 Exclusive Employment. Except with the prior written consent of the Chief Executive Officer, Executive shall not, during the term of this Agreement, undertake or engage in any other employment, occupation or business enterprise, other than ones in which Executive is a passive investor. Executive may engage in any civic and not-for-profit activities so long as such activities do not materially interfere with the performance of her duties hereunder or present a conflict of interest with the Company.

2.3 Agreement not to Participate in Company's Competitors. During the Term of this Agreement, the Executive agrees not to acquire, assume or participate in, directly or indirectly, any position, investment or interest known by Executive to be adverse or antagonistic to the Company, its business or prospects, financial or otherwise or in any company, person or entity that is, directly or indirectly, in competition with the business of the Company or any of its affiliates. Notwithstanding the foregoing, Executive may invest and/or maintain investments in any public or private entity up to an amount of 2% of an entity's fully diluted shares and on a passive basis.

3. Compensation to Executive.

3.1 Base Salary. The Company shall pay the Executive a base salary at the initial annualized rate of Five Hundred Seventy-Five Thousand Dollars ($575,000.00) per year, subject to standard deductions and withholdings, or such higher rate as may be determined from time to time by the Board or the compensation committee thereof (hereinafter referred to as the ***"Base Salary"***). Such Base Salary shall be paid in accordance with the Company's standard payroll practice. Payments of salary installments shall be made no less frequently than once per month. Executive's Base Salary will be reviewed annually. If increased, the new salary shall become the Base Salary for purposes of this Agreement and shall not be

reduced without the Executive's written consent. Any material reduction in the Base Salary of the Executive, without her written consent, may be deemed Good Reason as set forth in and subject to Section 4.5.2 of this Agreement.

3.2 Discretionary Bonus. Provided the Executive meets the conditions stated in this Section 3.2, the Executive shall be eligible for an annual discretionary bonus (hereinafter referred to as the ***"Bonus"***) with a target amount of sixty percent (60%) of the Executive's Base Salary, subject to standard deductions and withholdings, based on the Board's determination, in good faith, and based upon the Executive's individual achievement and company performance objectives as set by the Board or the compensation committee thereof, of whether the Executive has met such performance milestones as are established for the Executive by the Board or the compensation committee thereof, in good faith, in consultation with the Executive (hereinafter referred to as the ***"Performance Milestones"***). The Performance Milestones will be based on certain factors including, but not limited to, the Executive's performance and the Company's financial performance. The Executive's Bonus target will be reviewed annually and may be adjusted by the Board or the compensation committee thereof in its discretion, provided however, that the Bonus target may only be materially reduced upon Executive's written consent. The Executive must be employed on the date the Bonus is awarded to be eligible for the Bonus, subject to the termination provisions hereof. The Bonus shall be paid during the calendar year following the performance calendar year.

3.3 Equity Awards.

3.3.1 Prior Equity Grants. All Company equity awards previously granted to Executive shall continue in effect from and following the Effective Date in accordance with their existing terms. Executive may be eligible to receive additional grants of Company equity awards in the sole discretion and subject to the approval of the Board.

3.3.2 Annual Long-Term Incentive Plan. Executive will participate in the Annual Long-Term Incentive Plan ("ALTIP") adopted by the Board of Directors for executives, and all applicable terms which may apply. The annual grant for the Executive shall be at the discretion of the Board of Directors and may be in a mix of RSUs and PSUs. The final target amount, vesting schedule and other terms and criteria for the ALTIP are to be determined at the sole discretion of the Board of Directors and may be subject to shareholder approval.

3.4 Legal Review. Upon the Executive's submission of appropriate itemized proof and verification of reasonable and customary legal fees incurred by the Executive in obtaining legal advice associated with the review, preparation, approval, and execution of this Agreement, the Company shall pay for up to $10,000.00 of such legal fees subject to receipt of appropriate proof and verification of such legal fees no later than sixty (60) days of receipt of an invoice for legal services from the Executive and/or her attorneys. To be eligible for reimbursement, the invoice must be submitted no later than ninety (90) days after the legal fees are incurred.

3.5 Changes to Compensation. The Executive's compensation may be changed from time to time by mutual agreement of the Executive and the Company. In the event that the Executive's base salary is materially decreased without her written consent, said decrease will be Good Reason for the Executive to terminate the Agreement as set forth in and subject to Section 4.5.2 of this Agreement.

3.6 Taxes. All amounts paid under this Agreement to the Executive by the Company will be paid less applicable tax withholdings and any other withholdings required by law or authorized by the Executive.

3.7 Benefits. The Executive shall, in accordance with Company policy and the terms of the applicable plan documents, be eligible to participate in benefits under any executive benefit plan or arrangement which may be in effect from time to time and made available to the Company's executives or key management employees; provided, however, that the Executive shall be entitled to at least four (4) weeks of paid vacation annually.

4. Termination.

4.1 Termination by the Company. The Executive's employment with the Company may be terminated only under the following conditions:

4.1.1 Termination for Death or Disability. The Executive's employment with the Company shall terminate effective upon the date of the Executive's death or "Complete Disability" (as defined in Section 4.5.1), provided, however, that this Section 4.1.1 shall in no way limit the Company's obligations to provide such reasonable accommodations to the Executive and/or her heirs as may be required by law.

4.1.2 **Termination by the Company For Cause**. The Company may terminate the Executive's employment under this Agreement for "Cause" (as defined in Section 4.5.3) by delivery of written notice to the Executive specifying the Cause or Causes relied upon for such termination, provided that such notice is delivered within two (2) months following the occurrence or discovery of any event or events constituting "Cause". Any notice of termination given pursuant to this Section 4.1.2 shall effect termination as of the date of the notice or such date as specified in the notice. The Executive shall have the right to appear before the CEO before any termination for Cause becomes effective and binding upon the Executive.

4.1.3 **Termination by the Company Without Cause**. The Company may terminate the Executive's employment under this Agreement at any time and for any reason or no reason subject to the requirements set out in Section 4.4 of this Agreement. Such termination shall be effective on the date the Executive is so informed or as otherwise specified by the Company, pursuant to notice requirements set forth in Section 6 of this Agreement.

4.2 Termination By The Executive. The Executive may terminate her employment with the Company at any time and for any reason or no reason, including, but not limited, to the following conditions:

4.2.1 Good Reason. The Executive may terminate her employment under this Agreement for "Good Reason" (as defined below in Section 4.5.2) by delivery of written notice to the Company specifying the Good Reason relied upon by the Executive for such termination in accordance with the requirements of such section.

4.2.2 Without Good Reason. The Executive may terminate the Executive's employment hereunder for other than Good Reason upon thirty (30) days written notice to the Company.

4.3 Termination by Mutual Agreement of the Parties. The Executive's employment pursuant to this Agreement may be terminated at any time upon a mutual agreement in writing of the Parties. Any such termination of employment shall have the consequences specified in such mutual agreement.

4.4 Compensation to Executive Upon Termination. In connection with any termination of the Executive's employment for any reason, the Executive or the Executive's estate, as applicable, shall be entitled to any amounts payable to the Executive or the Executive's beneficiaries subject to and in accordance with the terms of the Company's employee welfare benefit plans or policies (excluding any severance pay).

4.4.1 Death or Complete Disability. If the Executive's employment shall be terminated by death or Complete Disability as provided in Section 4.1.1, the Company shall pay to Executive, and/or Executive's heirs, all earned but unpaid Base Salary, any earned but unpaid discretionary bonuses for any prior period at such time as bonuses would have been paid if the Executive remained employed, all accrued but unpaid business expenses, and all accrued but unused vacation time earned through the date of termination at the rate in effect at the time of termination (hereinafter referred to as the ***"Accrued Amounts"***), less standard deductions and withholdings. The Executive shall also be eligible to receive a pro-rated bonus for the year of termination, as determined by the Board or the Compensation Committee of the Board based on actual performance and the period of the year she was employed (hereinafter referred to as the ***"Pro-rata Bonus"***), less standard deductions and withholdings, to be paid as a lump sum within thirty (30) days after the date of termination.

4.4.2 With Cause or Without Good Reason. If the Executive's employment shall be terminated by the Company for Cause, or if the Executive terminates employment hereunder without Good Reason, the Company shall pay the Executive's Base Salary, accrued but unpaid business expenses and accrued and unused vacation benefits earned through the date of termination at the rate in effect at the time of termination, less standard deductions and withholdings.

4.4.3 Without Cause or For Good Reason.

(i) Not in Connection With a Change in Control. If the Company terminates the Executive's employment without Cause or the Executive terminates her employment for Good Reason, and Section 4.4.3(ii) below does not apply, the Company shall pay the Accrued Amounts subject to standard deductions and withholdings, to be paid as a lump sum

no later than thirty (30) days after the date of termination. In addition, subject to the limitations stated in this Agreement and upon the Executive's furnishing to the Company an executed waiver and release of claims (the form of which is attached hereto as Exhibit A) (the "***Release***") within the applicable time period set forth therein, but in no event later than forty-five days following termination of employment and permitting such Release to become effective in accordance with its terms (the "***Release Effective Date***"), and subject to Executive entering into no later than the Release Effective Date a non-competition agreement to be effective during the Severance Period (as defined below), substantially similar to Section 2.3, and continuing to abide by its terms during the Severance Period, the Executive shall be entitled to:

(a) the equivalent of the Executive's Base Salary in effect at the time of termination will continue to be paid for a period of twelve (12) months following the date of termination (hereinafter referred to as the "***Non Change in Control Severance Period***"), less standard deductions and withholdings, to be paid during the Non Change in Control Severance Period according to the Company's regular payroll practices, subject to any delay in payment required by Section 4.6 in connection with the Release Effective Date; and

(b) in the event the Executive timely elects continued coverage under COBRA, the Company will continue to pay the same portion of Executive's COBRA health insurance premium as the percentage of health insurance premiums that it paid during the Executive's employment, including any amounts that Company paid for benefits to the qualifying family members of the Executive, following the date of termination up until the earlier of either (i) the last day of the Non Change in Control Severance Period or, (ii) the date on which the Executive begins full-time employment with another company or business entity which offers comparable health insurance coverage to the Executive (such period, the "***Non Change in Control COBRA Payment Period***"). Notwithstanding the foregoing, if the Company determines, in its sole discretion, that the Company cannot provide the COBRA premium benefits without potentially incurring financial costs or penalties under applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof pay Executive a taxable cash amount, which payment shall be made regardless of whether the Executive or her qualifying family members elect COBRA continuation coverage (the "***Health Care Benefit Payment***"). The Health Care Benefit Payment shall be paid in monthly or bi-weekly installments on the same schedule that the COBRA premiums would otherwise have been paid to the insurer. The Health Care Benefit Payment shall be equal to the amount that the Company otherwise would have paid for COBRA insurance premiums (which amount shall be calculated based on the premium for the first month of coverage), and shall be paid until the expiration of the Non Change in Control COBRA Payment Period.

(ii) In Connection With a Change in Control. If the Company (or its successor) terminates the Executive's employment without Cause or the Executive terminates her employment for Good Reason within the period commencing three (3) months immediately prior to a Change in Control of the Company and ending eighteen (18) months immediately

following a Change in Control of the Company (as defined in Section 4.5.4 of this Agreement), the Executive shall receive the Accrued Amounts subject to standard deductions and withholdings, to be paid as a lump sum no later than thirty (30) days after the date of termination. In addition, subject to the limitations stated in this Agreement and upon the Executive's furnishing to the Company (or its successor) an executed Release within the applicable time period set forth therein, but in no event later than forty-five days following termination of employment and permitting such Release to become effective in accordance with its terms, and subject to Executive entering into no later than the Release Effective Date a non-competition agreement to be effective during the Severance Period, substantially similar to Section 2.3, and continuing to abide by its terms during the Severance Period, then in lieu of (and not additional to) the benefits provided pursuant to Section 4.4.3(i) above, the Executive shall be entitled to:

(a) the equivalent of the Executive's Base Salary in effect at the time of termination will continue to be paid for a period of eighteen (18) months following the date of termination (hereinafter referred to as the "***Change in Control Severance Period***"), less standard deductions and withholdings, to be paid during the Change in Control Severance Period according to the Company's regular payroll practices, subject to any delay in payment required by Section 4.6 in connection with the Release Effective Date;

(b) one and half (1.5) times Executive's target Bonus in effect at the time of termination, or if none, one and half (1.5) times the last target Bonus in effect for Executive, less standard deductions and withholdings, to be paid in a lump sum within ten (10) days following the later of (i) the Release Effective Date, or (ii) the effective date of the Change in Control; and

(c) in the event the Executive timely elects continued coverage under COBRA, the Company will continue to pay the same portion of Executive's COBRA health insurance premium as the percentage of health insurance premiums that it paid during the Executive's employment, including any amounts that Company paid for benefits to the qualifying family members of the Executive, following the date of termination until the expiration of the Change in Control Severance Period. Notwithstanding the foregoing, if the Company determines, in its sole discretion, that the Company cannot provide the COBRA premium benefits without potentially incurring financial costs or penalties under applicable law (including, without limitation, Section 2716 of the Public Health Service Act), the Company shall in lieu thereof pay Executive the Health Care Benefit Payment, which payment shall be made regardless of whether the Executive or her qualifying family members elect COBRA continuation coverage. The Health Care Benefit Payment shall be paid in monthly or bi-weekly installments on the same schedule that the COBRA premiums would otherwise have been paid to the insurer. The Health Care Benefit Payment shall be equal to the amount that the Company otherwise would have paid for COBRA insurance premiums (which amount shall be calculated based on the premium for the first month of coverage), and shall be paid until the expiration of the Change in Control Severance Period.

(iii) No Duplication of Benefits. For the avoidance of doubt, in no event will Executive be entitled to benefits under both Section 4.4.3(i) and Section 4.4.3(ii). If Executive commences to receive benefits under Section 4.4.3(i) due to a qualifying termination prior to a Change in Control and thereafter becomes entitled to benefits under Section 4.4.3(ii), any benefits provided to Executive under Section 4.4.3(i) shall offset the benefits to be provided to Executive under Section 4.4.3(ii) and shall be deemed to have been provided to Executive pursuant to Section 4.4.3(ii).

4.4.4 Equity Award Acceleration.

(i) Not in Connection With a Change in Control. In the event that the Executive's employment is terminated without Cause or for Good Reason and Section 4.4.4 **(ii)** below does not apply, the vesting of any equity awards granted to Executive that vest solely subject to Executive's continued services to the Company (the "***Time-Based Vesting Equity Awards***") shall be deemed vested and immediately exercisable (if applicable) by the Executive with respect to such number of shares as determined in accordance with their applicable vesting schedules as if Executive had provided an additional twelve (12) months of services as of the date of termination. Treatment of any performance based vesting equity awards will be governed solely by the terms of the agreements under which such awards were granted and will not be eligible to accelerate vesting pursuant to the foregoing provision.

(ii) In Connection With a Change in Control. In the event that the Executive's employment is terminated without Cause or for Good Reason within the three (3) months immediately preceding or during the eighteen (18) months immediately following a Change in Control of the Company (as defined in Section 4.5.4 of this Agreement), the vesting of any Time-Based Vesting Equity Awards granted to Executive shall be fully accelerated such that on the effective date of such termination (or if later, the date of the Change in Control) one hundred percent (100%) of any Time-Based Vesting Equity Awards granted to Executive prior to such termination shall be fully vested and immediately exercisable, if applicable, by the Executive. Treatment of any performance based vesting equity awards will be governed solely by the terms of the agreements under which such awards were granted and will not be eligible to accelerate vesting pursuant to the foregoing provision.

(iii) Release and Waiver. Any equity vesting acceleration pursuant to this Section 4.4.4 shall be conditioned upon and subject to the Executive's delivery to the Company of a fully effective Release in accordance with the terms specified by Section 4.4.3 hereof and such vesting acceleration benefit shall be in addition to the benefits provided by Section 4.4.3 hereof.

4.5 Definitions. For purposes of this Agreement, the following terms shall have the following meanings:

4.5.1 Complete Disability. ***"Complete Disability"*** shall mean the inability of the Executive to perform the Executive's duties under this Agreement, whether with or without reasonable accommodation, because the Executive has become permanently disabled

within the meaning of any policy of disability income insurance covering employees of the Company then in force. In the event the Company has no policy of disability income insurance covering employees of the Company in force when the Executive becomes disabled, the term "Complete Disability" shall mean the inability of the Executive to perform the Executive's duties under this Agreement, whether with or without reasonable accommodation, by reason of any incapacity, physical or mental, which the Board, based upon medical advice or an opinion provided by a licensed physician, determines to have incapacitated the Executive from satisfactorily performing all of the Executive's usual services for the Company, with or without reasonable accommodation, for a period of at least one hundred eighty (180) days during any twelve (12) month period that need not be consecutive.

4.5.2 Good Reason. ***"Good Reason"*** for the Executive to terminate the Executive's employment hereunder shall mean the occurrence of any of the following events without the Executive's consent:

(i) a material reduction in the Executive's duties, authority, or responsibilities relative to the duties, authority, or responsibilities in effect immediately prior to such reduction, including by way of example, having the same title, duties, authority and responsibilities at a subsidiary level following a Change in Control;

(ii) the relocation of the Executive's primary work location to a point more than twenty-five (25) miles from the Executive's current work location set forth in Section 1.5 that requires a material increase in Executive's one-way driving distance;

(iii) a material reduction by the Company of the Executive's base salary or annual target Bonus opportunity, without the written consent of the Executive, as initially set forth herein or as the same may be increased from time to time pursuant to this Agreement; and

(iv) a material breach by the Company of Section 1.2 of this Agreement.

Provided, however that, such termination by the Executive shall only be deemed for Good Reason pursuant to the foregoing definition if (i) the Company is given written notice from the Executive within sixty (60) days following the first occurrence of the condition that she considers to constitute Good Reason describing the condition and the Company fails to satisfactorily remedy such condition within thirty (30) days following such written notice, and (ii) the Executive terminates employment within thirty (30) days following the end of the period within which the Company was entitled to remedy the condition constituting Good Reason but failed to do so.

4.5.3 Cause. ***"Cause"*** for the Company to terminate Executive's employment hereunder shall mean the occurrence of any of the following events, as determined reasonably and in good faith by the Board or a committee designated by the Board:

(i) the Executive's gross negligence or willful failure to substantially perform her duties and responsibilities to the Company or willful and deliberate violation of a Company policy;

(ii) the Executive's conviction of a felony or the Executive's commission of any act of fraud, embezzlement or dishonesty against the Company or involving moral turpitude that is likely to inflict or has inflicted material injury on the business of the Company, to be determined by the sole discretion of the Company;

(iii) the Executive's unauthorized use or disclosure of any proprietary information or trade secrets of the Company or any other party that the Executive owes an obligation of nondisclosure as a result of the Executive's relationship with the Company; and

(iv) the Executive's willful and deliberate breach of the obligations under this Agreement that causes material injury to the business of the Company.

4.5.4 Change in Control. For purposes of this Agreement, ***"Change in Control"*** means: (i) a sale of all or substantially all of the assets of the Company; (ii) a merger or consolidation in which the Company is not the surviving entity and in which the holders of the Company's outstanding voting stock immediately prior to such transaction own, immediately after such transaction, securities representing less than fifty percent (50%) of the voting power of the entity surviving such transaction or, where the surviving entity is a wholly-owned subsidiary of another entity, the surviving entity's parent; (iii) a reverse merger in which the Company is the surviving entity but the shares of Common Stock outstanding immediately preceding the merger are converted by virtue of the merger into other property, whether in the form of securities of the surviving entity's parent, cash or otherwise, and in which the holders of the Company's outstanding voting stock immediately prior to such transaction own, immediately after such transaction, securities representing less than fifty percent (50%) of the voting power of the Company or, where the Company is a wholly-owned subsidiary of another entity, the Company's parent; or (iv) an acquisition by any person, entity or group (excluding any employee benefit plan, or related trust, sponsored or maintained by the Company or subsidiary of the Company or other entity controlled by the Company) of the beneficial ownership of securities of the Company representing at least seventy-five percent (75%) of the combined voting power entitled to vote in the election of Directors; provided, however, that nothing in this paragraph shall apply to a sale of assets, merger or other transaction effected exclusively for the purpose of changing the domicile of the Company.

4.6 **Application of Internal Revenue Code Section 409A**. Notwithstanding anything to the contrary set forth herein, any payments and benefits provided under this Agreement (the ***"Severance Benefits"***) that constitute "deferred compensation" within the meaning of Section 409A of the Internal Revenue Code of 1986, as amended (the ***"Code"***) and the regulations and other guidance thereunder and any state law of similar effect (collectively ***"Section 409A"***) shall not commence in connection with Executive's termination of employment unless and until Executive has also incurred a "separation from service" (as such term is defined in Treasury Regulation Section 1.409A-1(h) (***"Separation***

From Service"), unless the Company reasonably determines that such amounts may be provided to Executive without causing Executive to incur the additional 20% tax under Section 409A.

It is intended that each installment of the Severance Benefits payments provided for in this Agreement is a separate "payment" for purposes of Treasury Regulation Section 1.409A-2(b)(2)(i). For the avoidance of doubt, it is intended that payments of the Severance Benefits set forth in this Agreement satisfy, to the greatest extent possible, the exemptions from the application of Section 409A provided under Treasury Regulation Sections 1.409A- 1(b)(4), 1.409A-1(b)(5) and 1.409A-1(b)(9). However, if the Company (or, if applicable, the successor entity thereto) determines that the Severance Benefits constitute "deferred compensation" under Section 409A and Executive is, on the termination of service, a "specified employee" of the Company or any successor entity thereto, as such term is defined in Section 409A(a)(2)(B)(i) of the Code, then, solely to the extent necessary to avoid the incurrence of the adverse personal tax consequences under Section 409A, the timing of the Severance Benefit payments shall be delayed until the earlier to occur of: (i) the date that is six months and one day after Executive's Separation From Service, or (ii) the date of Executive's death (such applicable date, the ***"Specified Employee Initial Payment Date"***), the Company (or the successor entity thereto, as applicable) shall (A) pay to Executive a lump sum amount equal to the sum of the Severance Benefit payments that Executive would otherwise have received through the Specified Employee Initial Payment Date if the commencement of the payment of the Severance Benefits had not been so delayed pursuant to this Section and (B) commence paying the balance of the Severance Benefits in accordance with the applicable payment schedules set forth in this Agreement.

Notwithstanding anything to the contrary set forth herein, Executive shall receive the Severance Benefits described above, if and only if Executive duly executes and returns to the Company within the applicable time period set forth therein, but in no event more than forty- five days following Separation From Service, the Company's standard form of release of claims in favor of the Company (attached to this Agreement as Exhibit A) (the "***Release***") and permits the release of claims contained therein to become effective in accordance with its terms (such latest permitted date, the ***"Release Deadline"***). If the severance benefits are not covered by one or more exemptions from the application of Section 409A and the Release could become effective in the calendar year following the calendar year in which Executive separates from service, the Release will not be deemed effective any earlier than the Release Deadline. Notwithstanding any other payment schedule set forth in this Agreement, none of the Severance Benefits will be paid or otherwise delivered prior to the effective date (or deemed effective date) of the Release. Except to the extent that payments may be delayed until the Specified Employee Initial Payment Date pursuant to the preceding paragraph, on the first regular payroll pay day following the effective date of the Release, the Company will pay Executive the Severance Benefits Executive would otherwise have received under the Agreement on or prior to such date but for the delay in payment related to the effectiveness of the Release, with the balance of the Severance Benefits being paid as originally scheduled.

The severance benefits are intended to qualify for an exemption from application of Section 409A or comply with its requirements to the extent necessary to avoid adverse personal tax consequences under Section 409A, and any ambiguities herein shall be interpreted accordingly.

4.7 Application of Internal Revenue Code Section 280G. If any payment or benefit Executive would receive pursuant to a Change in Control from the Company or otherwise (***"Payment"***) would (i) constitute a "parachute payment" within the meaning of Section 280G of the Code, and (ii) but for this sentence, be subject to the excise tax imposed by Section 4999 of the Code (the ***"Excise Tax"***), then such Payment shall be equal to the Reduced Amount. The "**Reduced Amount**" shall be either (x) the largest portion of the Payment that would result in no portion of the Payment being subject to the Excise Tax or (y)the largest portion, up to and including the total, of the Payment, whichever amount, after taking into account all applicable federal, state and local employment taxes, income taxes, and the Excise Tax (all computed at the highest applicable marginal rate), results in Executive's receipt, on an after-tax basis, of the greater economic benefit notwithstanding that all or some portion of the Payment may be subject to the Excise Tax. If a reduction in payments or benefits constituting "parachute payments" is necessary so that the Payment equals the Reduced Amount, reduction shall occur in the manner that results in the greatest economic benefit for Executive. If more than one method of reduction will result in the same economic benefit, the items so reduced will be reduced pro rata.

In the event it is subsequently determined by the Internal Revenue Service that some portion of the Reduced Amount as determined pursuant to clause (x) in the preceding paragraph is subject to the Excise Tax, Executive agrees to promptly return to the Company a sufficient amount of the Payment so that no portion of the Reduced Amount is subject to the Excise Tax. For the avoidance of doubt, if the Reduced Amount is determined pursuant to clause (y) in the preceding paragraph, Executive will have no obligation to return any portion of the Payment pursuant to the preceding sentence.

Unless Executive and the Company agree on an alternative accounting firm, the accounting firm engaged by the Company for general tax compliance purposes as of the day prior to the effective date of the Change in Control shall perform the foregoing calculations. If the accounting firm so engaged by the Company is serving as accountant or auditor for the individual, entity or group effecting the Change in Control, the Company shall appoint a nationally recognized accounting firm to make the determinations required hereunder. The Company shall bear all expenses with respect to the determinations by such accounting firm required to be made hereunder.

The Company shall use commercially reasonable efforts to cause the accounting firm engaged to make the determinations hereunder to provide its calculations, together with detailed supporting documentation, to Executive and the Company within fifteen (15) calendar days after the date on which Executive's right to a Payment is triggered (if requested at that time by Executive or the Company) or such other time as requested by Executive or the Company.

4.8 Indemnification Agreements. Concurrently with the execution of this Agreement, the Company and the Executive shall enter into indemnification agreements, copies of which are attached hereto as Exhibit B-1 and Exhibit B-2.

4.9 Confidential Information and Invention Assignment Agreement. The Executive shall execute the Company's Confidential Information and Invention Assignment Agreement the terms of which shall govern the terms of Executive's employment following the Effective Date, and a copy of which is attached as Exhibit C.

4.10 No Mitigation or Offset. The Executive shall not be required to seek or accept other employment, or otherwise to mitigate damages, as a condition to receipt of the Severance Benefits, and the Severance Benefits shall not be offset by any amounts received by the Executive from any other source, except to the extent that the Executive's rights to the benefits described in Sections 4.4.3(i)(b) or 4.4.3(ii)(c), as applicable, are terminated by reason of the Executive obtaining full-time employment with another company or business entity which offers comparable health insurance coverage.

5. Assignment and Binding Effect.

This Agreement shall be binding upon the Executive and the Company and inure to the benefit of the Executive and the Executive's heirs, executors, personal representatives, assigns, administrators and legal representatives. Because of the unique and personal nature of the Executive's duties under this Agreement, neither this Agreement nor obligations under this Agreement shall be assignable by the Executive. This Agreement shall be binding upon and inure to the benefit of the Company and its successors, assigns and legal representatives, provided that the Agreement may only be assigned to an acquirer of all or substantially all of the Company's assets. Any such successor of the Company will be deemed substituted for the Company under the terms of this Agreement for all purposes. For this purpose, "successor" means any person, firm, corporation or other business entity which at any time, whether by purchase, merger or otherwise, directly or indirectly acquires all or substantially all of the assets or business of the Company.

6. Notice.

For the purposes of this Agreement, notices, demands, and all other forms of communication provided for in this Agreement shall be in writing and shall be deemed to have been duly given when delivered or (unless otherwise specified) mailed by registered mail, return receipt requested, postage prepaid, or by confirmed facsimile, addressed as set forth below, or to such other address as any party may have furnished to the other in writing in accordance herewith, except that notices of address shall be effective only upon receipt, as follows:

If to the Company:

Horizon Therapeutics plc
Horizon Therapeutics USA, Inc.
1 Horizon Way
Deerfield, IL 60015
Attention: Timothy P. Walbert, Chairman, President & CEO
Fax: 847-572-1372

If to the Executive:

Elizabeth H. Z. Thompson

Any such written notice shall be deemed given on the earlier of the date on which such notice is personally delivered or five (5) days after its deposit in the United States mail as specified above. Either Party may change its address for notices by giving written notice to the other Party in the manner specified in this section.

7. Choice of Law.

This Agreement shall be governed by the laws of the State of Illinois, without regard to any conflicts of law principals thereof that would call for the application of the laws of any other jurisdiction. The Parties consent to the exclusive jurisdiction and venue of the federal court in the Northern District of Illinois, and state courts located in the state of Illinois, county of Cook. Nothing in this Section 7 limits the rights of the Parties to seek appeal of a decision of an Illinois court outside of Illinois that has proper jurisdiction over the decision of a court sitting in Illinois.

8. Integration.

This Agreement, including Exhibit A, Exhibit B, Exhibit C, the 2014 Equity Incentive Plan and the Equity Plan Documents, contains the complete, final and exclusive agreement of the Parties relating to the terms and conditions of the Executive's employment and the termination of Executive's employment, and supersedes all prior and contemporaneous oral and written employment agreements or arrangements between the Parties.

9. Amendment.

This Agreement cannot be amended or modified except by a written agreement signed by the Executive and the Company.

10. Waiver.

No term, covenant or condition of this Agreement or any breach thereof shall be deemed waived, except with the written consent of the Party against whom the wavier is claimed, and any waiver or any such term, covenant, condition or breach shall not be deemed to be a waiver of any preceding or succeeding breach of the same or any other term, covenant, condition or breach.

11. Severability.

The finding by a court of competent jurisdiction of the unenforceability, invalidity or illegality of any provision of this Agreement shall not render any other provision of this

Agreement unenforceable, invalid or illegal. Such court shall have the authority to modify or replace the invalid or unenforceable term or provision with a valid and enforceable term or provision, which most accurately represents the Parties' intention with respect to the invalid, unenforceable, or illegal term or provision.

12. Interpretation; Construction.

The headings set forth in this Agreement are for convenience of reference only and shall not be used in interpreting this Agreement. This Agreement has been drafted and negotiated by legal counsel representing the Company and the Executive. The Parties acknowledge that each Party and its counsel has reviewed and revised, or had an opportunity to review and revise, this Agreement, and any rule of construction to the effect that any ambiguities are to be resolved against the drafting party shall not be employed in the interpretation of this Agreement.

13. Execution by Facsimile Signatures or .PDF Signatures and in Counterparts.

The parties agree that facsimile signatures and .pdf-signatures shall have the same force and effect as original signatures. This Agreement may be executed in one or more counterparts, each of which shall be deemed an original but all of which together shall constitute one and the same instrument.

14. Survival.

The provisions of this Agreement, and of all other agreements referenced herein, shall survive the termination of this Agreement, and of the Executive's employment by the Company for any reason, to the extent necessary to enable the parties to enforce their respective rights hereunder.

[Remainder of Page Intentionally Left Blank]

IN WITNESS WHEREFORE, the parties have signed this Agreement on the date first written above.

COMPANY:

HORIZON THERAPEUTICS PLC and
HORIZON THERAPEUTICS USA, INC.

By:

Title: Chairman, President & CEO

Print Name: Timothy P. Walbert

/s/ Timothy P. Walbert
Signature:

As authorized agent of the Company

EXECUTIVE:

Elizabeth H. Z. Thompson

/s/ Elizabeth H. Z. Thompson
Elizabeth H. Z. Thompson, individually

EXHIBIT A

RELEASE AND WAIVER OF CLAIMS

In consideration of the payments and other benefits set forth in Section 4.4 of the Executive Employment Agreement dated , (the ***"Employment Agreement"***), to which this form is attached, I, Elizabeth H. Z. Thompson, hereby furnish Horizon Therapeutics, Inc. and Horizon Therapeutics USA, Inc. (together the ***"Company"***), with the following release and waiver (***"Release and Waiver"***).

In exchange for the consideration provided to me by the Employment Agreement that I am not otherwise entitled to receive, I hereby generally and completely release the Company and its directors, officers, employees, shareholders, partners, agents, attorneys, predecessors, successors, parent and subsidiary entities, insurers, Affiliates, and assigns from any and all claims, liabilities and obligations, both known and unknown, that arise out of or are in any way related to events, acts, conduct, or omissions occurring relating to my employment or the termination thereof prior to my signing this Release and Waiver. This general release includes, but is not limited to: (1) all claims arising out of or in any way related to my employment with the Company or the termination of that employment; (2) all claims related to my compensation or benefits from the Company, including, but not limited to, salary, bonuses, commissions, vacation pay, expense reimbursements, severance pay, fringe benefits, stock, stock options, or any other ownership interests in the Company; (3) all claims for breach of contract, wrongful termination, and breach of the implied covenant of good faith and fair dealing; (4) all tort claims, including, but not limited to, claims for fraud, defamation, emotional distress, and discharge in violation of public policy; and (5) all federal, state, and local statutory claims, including, but not limited to, claims for discrimination, harassment, retaliation, attorneys' fees, or other claims arising under the federal Civil Rights Act of 1964 (as amended), the federal Americans with Disabilities Act of 1990, the federal Age Discrimination in Employment Act of 1967 (as amended) (***"ADEA"***), the Illinois Human Rights Act, the Illinois Equal Pay Act, the Illinois Religious Freedom Restoration Act, and the Illinois Genetic Information Privacy Act. Notwithstanding the foregoing, this Release and Waiver, shall not release or waive my rights: to indemnification under the articles and bylaws of the Company or applicable law; to payments under Sections of the Employment Agreement; under any provision of the Employment Agreement that survives the termination of that agreement; under any applicable workers' compensation statute; under any option, restricted share or other agreement concerning any equity interest in the Company; as a shareholder of the Company or any other right that is not waivable under applicable law.

I acknowledge that, among other rights, I am waiving and releasing any rights I may have under ADEA, that this Release and Waiver is knowing and voluntary, and that the consideration given for this Release and Waiver is in addition to anything of value to which I was already entitled as an executive of the Company. If I am 40 years of age or older upon execution of this Release and Waiver, I further acknowledge that I have been advised, as required by the Older Workers Benefit Protection Act, that: (a) the release and waiver granted herein does not relate to claims under the ADEA which may arise after this Release

and Waiver is executed; (b) I should consult with an attorney prior to executing this Release and Waiver; and (c) I have twenty-one (21) days from the date of termination of my employment with the Company in which to consider this Release and Waiver (although I may choose voluntarily to execute this Release and Waiver earlier); (d) I have seven (7) days following the execution of this Release and Waiver to revoke my consent to this Release and Waiver; and (e) this Release and Waiver shall not be effective until the seven (7) day revocation period has expired unexercised. If I am less than 40 years of age upon execution of this Release and Waiver, I acknowledge that I have the right to consult with an attorney prior to executing this Release and Waiver (although I may choose voluntarily not to do so), and I have five (5) days from the date of termination of my employment with the Company in which to consider this Release and Waiver (although I may choose voluntarily to execute this Release and Waiver earlier).

I acknowledge my continuing obligations under my Confidential Information and Inventions Agreement dated , . Pursuant to the Confidential Information and Inventions Agreement I understand that among other things, I must not use or disclose any confidential or proprietary information of the Company and I must immediately return all Company property and documents (including all embodiments of proprietary information) and all copies thereof in my possession or control. I understand and agree that my right to the payments and other benefits I am receiving in exchange for my agreement to the terms of this Release and Waiver is contingent upon my continued compliance with my Confidential Information and Inventions Agreement.

This Release and Waiver, including my Confidential Information and Inventions Agreement dated , , constitutes the complete, final and exclusive embodiment of the entire agreement between the Company and me with regard to the subject matter hereof. I am not relying on any promise or representation by the Company that is not expressly stated herein. This Release and Waiver may only be modified by a writing signed by both me and a duly authorized officer of the Company.

Date:

By:
Elizabeth H. Z. Thompson

Exhibit 31.1

Certification of Principal Executive Officer

I, Timothy P. Walbert, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Horizon Therapeutics PLC (the "registrant");

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 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 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: May 5, 2021

/s/ Timothy P. Walbert
Timothy P. Walbert
Chairman, President and Chief Executive Officer
(Principal Executive Officer)

Exhibit 31.2

Certification of Principal Financial Officer

I, Paul W. Hoelscher, certify that:

1. I have reviewed this quarterly report on Form 10-Q of Horizon Therapeutics PLC (the "registrant");

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 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 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: May 5, 2021

/s/ Paul W. Hoelscher
Paul W. Hoelscher
Executive Vice President, Chief Financial Officer
(Principal Financial Officer)

Exhibit 32.1

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), I, Timothy P. Walbert, President, Chief Executive Officer and Chairman of the Board of Horizon Therapeutics PLC (the "Company"), certify to the best of my knowledge that:

1. the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2021 (the "Report"), to which this Certification is attached as Exhibit 32.1, fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 5, 2021

/s/ Timothy P. Walbert
Timothy P. Walbert
Chairman, President and Chief Executive Officer
(Principal Executive Officer)

This certification accompanies the 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 the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.

Exhibit 32.2

CERTIFICATION

Pursuant to the requirement set forth in Rule 13a-14(b) of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), and Section 1350 of Chapter 63 of Title 18 of the United States Code (18 U.S.C. Section 1350), I, Paul W. Hoelscher, Executive Vice President and Chief Financial Officer of Horizon Therapeutics PLC (the "Company"), certify to the best of my knowledge that:

1. the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2021 (the "Report"), to which this Certification is attached as Exhibit 32.2, fully complies with the requirements of Section 13(a) or 15(d) of the Exchange Act; and

2. the information contained in the Report fairly presents, in all material respects, the financial condition and results of operations of the Company.

Date: May 5, 2021

/s/ Paul W. Hoelscher
Paul W. Hoelscher
Executive Vice President, Chief Financial Officer
(Principal Financial Officer)

This certification accompanies the 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 the Company under the Securities Act of 1933, as amended, or the Exchange Act (whether made before or after the date of the Form 10-Q), irrespective of any general incorporation language contained in such filing.