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, 2020

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 May 1, 2020: 190,778,387.

HORIZON THERAPEUTICS PLC

INDEX

PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	As of March 31, 2020	As of December 31, 2019
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 754,638	$ 1,076,287
Restricted cash	3,624	3,752
Accounts receivable, net	425,405	408,685
Inventories, net	68,170	53,802
Prepaid expenses and other current assets	161,903	143,577
Total current assets	**1,413,740**	**1,686,103**
Property and equipment, net	142,420	30,159
Developed technology, net	1,745,625	1,698,808
Other intangible assets, net	3,619	3,820
Goodwill	413,669	413,669
Deferred tax assets, net	552,722	555,165
Other assets	42,925	48,310
Total assets	**$ 4,314,720**	**$ 4,436,034**
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 50,124	$ 21,514
Accrued expenses	205,988	235,234
Accrued trade discounts and rebates	336,320	466,421
Total current liabilities	**592,432**	**723,169**
LONG-TERM LIABILITIES:		
Exchangeable notes, net	356,551	351,533
Long-term debt, net	1,001,809	1,001,308
Deferred tax liabilities, net	89,721	94,247
Other long-term liabilities	85,868	80,328
Total long-term liabilities	**1,533,949**	**1,527,416**
COMMITMENTS AND CONTINGENCIES		
SHAREHOLDERS' EQUITY:		
Ordinary shares, $0.0001 nominal value; 600,000,000 shares authorized at March 31, 2020 and December 31, 2019; 190,962,613 and 188,402,040 shares issued at March 31, 2020 and December 31, 2019, respectively, and 190,578,247 and 188,017,674 shares outstanding at March 31, 2020 and December 31, 2019, respectively	19	19
Treasury stock, 384,366 ordinary shares at March 31, 2020 and December 31, 2019	(4,585)	(4,585)
Additional paid-in capital	2,814,408	2,797,602
Accumulated other comprehensive loss	(2,230)	(1,905)
Accumulated deficit	(619,273)	(605,682)
Total shareholders' equity	**2,188,339**	**2,185,449**
Total liabilities and shareholders' equity	**$ 4,314,720**	**$ 4,436,034**

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,	
	2020	**2019**
Net sales	$ 355,909	$ 280,371
Cost of goods sold	97,416	88,142
Gross profit	**258,493**	**192,229**
OPERATING EXPENSES:		
Research and development	27,209	21,725
Selling, general and administrative	247,775	172,299
Total operating expenses	**274,984**	**194,024**
Operating loss	**(16,491)**	**(1,795)**
OTHER EXPENSE, NET:		
Interest expense, net	(17,344)	(27,530)
Loss on debt extinguishment	—	(5,586)
Foreign exchange gain (loss)	776	(61)
Other income, net	442	189
Total other expense, net	**(16,126)**	**(32,988)**
Loss before benefit for income taxes	**(32,617)**	**(34,783)**
Benefit for income taxes	(19,026)	(1,920)
Net loss	**$ (13,591)**	**$ (32,863)**
Net loss per ordinary share—basic and diluted	$ (0.07)	$ (0.19)
Weighted average ordinary shares outstanding—basic and diluted	190,072,112	172,789,209
OTHER COMPREHENSIVE LOSS, NET OF TAX		
Foreign currency translation adjustments	$ (325)	$ (487)
Other comprehensive loss	**(325)**	**(487)**
Comprehensive loss	**$ (13,916)**	**$ (33,350)**

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, 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**

	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, 2018	**169,244,520**	**$ 17**	**384,366**	**$ (4,585)**	**$ 2,374,966**	**$ (1,523)**	**$ (1,178,769)**	**$ 1,190,106**
Cumulative effect adjustments from adoption of ASU 2016-02	—	—	—	—	—	—	64	64
Issuance of ordinary shares - public offering	14,081,632	1	—	—	326,848	—	—	326,849
Issuance of ordinary shares in conjunction with vesting of restricted stock units and stock option exercises	1,804,196	—	—	—	10,042	—	—	10,042
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(17,171)	—	—	(17,171)
Share-based compensation	—	—	—	—	27,548	—	—	27,548
Currency translation adjustment	—	—	—	—	—	(487)	—	(487)
Net loss	—	—	—	—	—	—	(32,863)	(32,863)
Balances at March 31, 2019	**185,130,348**	**$ 18**	**384,366**	**$ (4,585)**	**$ 2,722,233**	**$ (2,010)**	**$ (1,211,568)**	**$ 1,504,088**

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,	
	2020	**2019**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net loss	$ (13,591)	$ (32,863)
Adjustments to reconcile net loss to net cash (used in) provided by operating activities:		
Depreciation and amortization expense	65,741	58,891
Equity-settled share-based compensation	56,421	27,548
Amortization of debt discount and deferred financing costs	5,569	5,851
Loss on debt extinguishment	—	5,586
Deferred income taxes	(2,082)	1,502
Foreign exchange and other adjustments	(190)	404
Changes in operating assets and liabilities:		
Accounts receivable	(16,869)	60,769
Inventories	(14,444)	(847)
Prepaid expenses and other current assets	(24,953)	111
Accounts payable	28,551	6,416
Accrued trade discounts and rebates	(129,940)	(50,904)
Accrued expenses	(28,087)	(21,336)
Deferred revenues	—	(67)
Other non-current assets and liabilities	11,281	(4,893)
Net cash (used in) provided by operating activities	**(62,593)**	**56,168**
CASH FLOWS FROM INVESTING ACTIVITIES:		
Payments for acquisition	(105,200)	—
Purchases of property and equipment	(119,004)	(1,849)
Change in escrow deposit for property purchase	6,000	—
Net cash used in investing activities	**(218,204)**	**(1,849)**
CASH FLOWS FROM FINANCING ACTIVITIES:		
Proceeds from the issuance of ordinary shares in connection with stock option exercises	7,050	10,042
Payment of employee withholding taxes relating to share-based awards	(46,664)	(17,171)
Net proceeds from the issuance of ordinary shares	—	327,750
Repayment of term loans	—	(300,000)
Net cash (used in) provided by financing activities	**(39,614)**	**20,621**
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	(1,366)	(518)
Net (decrease) increase in cash, cash equivalents and restricted cash	**(321,777)**	**74,422**
Cash, cash equivalents and restricted cash, beginning of the period	1,080,039	962,117
Cash, cash equivalents and restricted cash, end of the period	**$ 758,262**	**$ 1,036,539**
SUPPLEMENTAL CASH FLOW INFORMATION:		
Cash paid for interest	$ 26,636	$ 15,842
Cash paid for income taxes, net of refunds received	266	856
Cash paid for amounts included in the measurement of lease liabilities	1,812	1,611
SUPPLEMENTAL NON-CASH FLOW INFORMATION:		
Purchases of property and equipment included in accounts payable and accrued expenses	539	2,759
Transaction costs related to issuance of ordinary shares included in accrued expenses	—	902

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

NOTE 1 – BASIS OF PRESENTATION AND BUSINESS OVERVIEW

Basis of Presentation

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, 2020 are not necessarily indicative of the results that may be expected for the year ending December 31, 2020. The December 31, 2019 condensed consolidated balance sheet was derived from audited financial statements, but does not include all disclosures required by GAAP.

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.

During the three months ended March 31, 2020, the Company recorded out of period adjustments that decreased income tax benefit by $3.2 million and increased share-based compensation expense by $1.9 million to correct for expenses that should have been recorded in the year ended December 31, 2019. The Company evaluated the materiality of the adjustments on prior period financial statements and making the adjustments in the current period, and concluded the effect of the adjustments were immaterial to both the current and prior period financial statements.

Business Overview

Horizon is focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare and rheumatic 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 currently markets eleven medicines in the areas of rare diseases, gout, ophthalmopathy and inflammation.

Effective in the first quarter of 2020, the Company (i) reorganized its commercial operations and moved responsibility for and reporting of RAYOS® to the inflammation segment and (ii) renamed the orphan and rheumatology segment the orphan segment. Net sales generated by TEPEZZA™, which was approved on January 21, 2020, are reported as part of the renamed orphan segment.

As of March 31, 2020, the Company's marketed medicines consisted of the following:

Orphan
KRYSTEXXA® (pegloticase injection), for intravenous infusion
RAVICTI® (glycerol phenylbutyrate) oral liquid
PROCYSBI® (cysteamine bitartrate) delayed-release capsules, for oral use
ACTIMMUNE® (interferon gamma-1b) injection, for subcutaneous use
TEPEZZA (teprotumumab-trbw), for intravenous infusion
BUPHENYL® (sodium phenylbutyrate) Tablets and Powder
QUINSAIR™ (levofloxacin) solution for inhalation
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
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 June 2016, the FASB issued Accounting Standards Update No. 2016-13, *Financial Instruments – Credit Losses (Topic 326): Measurement of Credit Losses on Financial Instruments* ("ASU 2016-13"), which modifies the measurement of expected credit losses on certain financial instruments and became effective for the Company as of January 1, 2020. The adoption of ASU 2016-13 did not have a material impact to the Company's condensed consolidated financial statements and related disclosures.

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 is effective for the Company as of January 1, 2021. The Company is currently evaluating the impact of ASU 2019-12.

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, 2019, with the exception of the change to the accounting policy related to property and equipment due to the purchase of land and buildings as described below.

Property and Equipment

Land is stated at cost. Property and equipment, other than land, are stated at cost less accumulated depreciation. Depreciation is recognized using the straight-line method over the estimated useful lives of the related assets for financial reporting purposes and an accelerated method for income tax reporting purposes. Upon retirement or sale of an asset, the cost and related accumulated depreciation and amortization are removed from the balance sheet and the resulting gain or loss is reflected in operations. Repair and maintenance costs are charged to expenses as incurred and improvements are capitalized.

Leasehold improvements are amortized on a straight-line basis over the term of the applicable lease, or the useful life of the assets, whichever is shorter.

Depreciation and amortization periods for the Company's property and equipment are as follows:

Buildings	40 years
Machinery and equipment	5 to 7 years
Furniture and fixtures	3 to 5 years
Computer equipment	3 years
Software	3 years
Trade show equipment	3 years

The Company capitalizes software development costs associated with internal use software, including external direct costs of materials and services and payroll costs for employees devoting time to a software project. Costs incurred during the preliminary project stage, as well as costs for maintenance and training, are expensed as incurred.

Software includes internal-use software acquired and modified to meet the Company's internal requirements. Amortization commences when the software is ready for its intended use.

NOTE 3 – NET LOSS PER SHARE

The following table presents basic and diluted net loss per share for the three months ended March 31, 2020 and 2019 (in thousands, except share and per share data):

	For the Three Months Ended March 31,	
	2020	2019
Basic and diluted net loss per share calculation:		
Numerator - net loss	$ (13,591)	$ (32,863)
Denominator - weighted average ordinary shares outstanding	190,072,112	172,789,209
Basic and diluted net loss per share	**$ (0.07)**	**$ (0.19)**

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, 2020 excluded 9.3 million shares subject to equity awards and 14.0 million shares (based on the if-converted method) related to its 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.

The computation of diluted net loss per share for the three months ended March 31, 2019, excluded 8.2 million shares subject to equity awards because their inclusion would have had an anti-dilutive effect on diluted net loss per share.

During the three months ended March 31, 2019, the potentially dilutive impact of the Exchangeable Senior Notes was determined using a method similar to the treasury stock method. Under this method, no numerator or denominator adjustments arose from the principal and interest components of the Exchangeable Senior Notes because the Company had the intent, at that time, and ability to settle the Exchangeable Senior Notes' principal and interest in cash. Instead, the Company was required to increase the diluted net loss per share denominator by the variable number of shares that would be issued upon conversion if it settled the conversion spread obligation with shares. For diluted net loss per share purposes, the conversion spread obligation was calculated based on whether the average market price of the Company's ordinary shares over the reporting period was in excess of the exchange price of the Exchangeable Senior Notes. There was no calculated spread added to the denominator for the three months ended March 31, 2019. Beginning in the fourth quarter of 2019, with the ordinary share price significantly above the $28.66 exchange price, the Company decided that it no longer had the intent to settle the notes for cash and, as a result, began to prospectively apply the if-converted method to the Exchangeable Senior Notes when determining the diluted net income (loss) per share.

NOTE 4 – ACQUISITIONS, DIVESTITURES AND OTHER ARRANGEMENTS

Sale of MIGERGOT rights

On June 28, 2019, the Company sold its rights to MIGERGOT to Cosette Pharmaceuticals, Inc., for $6.0 million and total potential contingent consideration payments of $4.0 million (the "MIGERGOT transaction").

Pursuant to ASC 805 (as amended by ASU No. 2017-01, Business *Combinations (Topic 805): Clarifying the Definition of a Business* ("ASU No. 2017-01")), the Company accounted for the MIGERGOT transaction as a sale of assets, specifically a sale of intellectual property rights, and a sale of inventory.

The loss on sale of assets recorded to the consolidated statement of comprehensive income (loss) during the year ended December 31, 2019, was determined as follows (in thousands):

Cash proceeds	$ 6,000
Less net assets sold:	
Developed technology	(16,999)
Inventory	(236)
Release of contingent consideration liability	272
Loss on sale of assets	**$ (10,963)**

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. Pursuant to ASU No. 2017-01, the Company accounted for the River Vision acquisition as the purchase of an in-process research and development asset (teprotumumab, now known as TEPEZZA) and, pursuant to ASC Topic 730, *Research and Development*, recorded the purchase price as research and development expense during the year ended December 31, 2017. Further, the Company recognized approximately $32.4 million of federal net operating losses, $2.2 million of state net operating losses and $9.5 million of federal tax credits. The acquired tax attributes were set up as deferred tax assets which were further netted within the net deferred tax liabilities of the U.S. group, offset by a deferred credit recorded in long-term liabilities.

Under the agreement for the acquisition of 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.

Refer to Note 15 for further detail on TEPEZZA milestone payments.

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.

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, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020	December 31, 2019
Raw materials	$ 16,557	$ 6,750
Work-in-process	27,839	22,465
Finished goods	23,774	24,587
Inventories, net	**$ 68,170**	**$ 53,802**

NOTE 6 – PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets as of March 31, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020	December 31, 2019
Deferred charge for taxes on intra-company profit	$ 46,344	$ 46,388
Prepaid income taxes and income tax receivable	36,380	12,583
Advance payments for inventory	30,338	31,203
Rabbi trust assets	12,653	12,704
Other prepaid expenses and other current assets	36,188	40,699
Prepaid expenses and other current assets	**$ 161,903**	**$ 143,577**

Prepaid income taxes and income tax receivable as of March 31, 2020, includes a benefit for income taxes recognized during the three months ended March 31, 2020. This benefit primarily arises due to the mix of pre-tax income and losses incurred in various tax jurisdictions.

Advance payments for inventory as of March 31, 2020 and December 31, 2019, primarily represented payments made to the manufacturer of TEPEZZA drug substance.

NOTE 7 – PROPERTY AND EQUIPMENT

Property and equipment as of March 31, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020	December 31, 2019
Buildings	$ 80,431	$ —
Land	38,076	—
Leasehold improvements	26,250	25,985
Software	15,051	14,890
Machinery and equipment	5,001	5,217
Computer equipment	3,489	3,316
Construction in process	703	265
Other	6,246	6,334
	175,247	**56,007**
Less accumulated depreciation	(32,827)	(25,848)
Property and equipment, net	**$ 142,420**	**$ 30,159**

Depreciation expense was $7.2 million and $1.5 million for the three months ended March 31, 2020 and 2019, respectively. The increase in depreciation expense primarily relates to the reduction in the useful lives of leasehold improvements relating to the Company's Lake Forest office.

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. The Company expects to move to the Deerfield campus in the second half of 2020 and market its Lake Forest office for sub-lease.

NOTE 8 – GOODWILL AND INTANGIBLE ASSETS

Goodwill

The gross carrying amount of goodwill as of March 31, 2020 and December 31, 2019 was $413.7 million.

Effective in the first quarter of 2020, the Company (i) reorganized its commercial operations and moved responsibility for and reporting of RAYOS to the inflammation segment and (ii) renamed the orphan and rheumatology segment the orphan segment. As of March 31, 2020, this resulted in a $3.2 million increase in the Company's allocation of goodwill to its inflammation segment and a corresponding decrease in the goodwill allocated to the orphan segment. The Company allocated goodwill to its new reporting units using a relative fair value approach. In addition, the Company completed an assessment of any potential goodwill impairment for all reporting units immediately prior to the allocation and determined that no impairment existed.

The table below presents goodwill for the Company's reportable segments as of March 31, 2020 (in thousands):

	Orphan	Inflammation	Total
Goodwill	$ 357,498	$ 56,171	$ 413,669

As of March 31, 2020, there were no accumulated goodwill impairment losses.

Intangible Assets

As of March 31, 2020, the Company's finite-lived intangible assets consisted of developed technology related to ACTIMMUNE, BUPHENYL, KRYSTEXXA, PENNSAID 2%, PROCYSBI, RAVICTI, RAYOS and TEPEZZA as well as customer relationships for ACTIMMUNE. The intangible asset related to VIMOVO developed technology was fully amortized as of December 31, 2019.

During the three months ended March 31, 2020, in connection with the acquisition of River Vision, the Company capitalized payments of $105.2 million related to TEPEZZA developed technology. See Note 4 for further details.

During the year ended December 31, 2019, in connection with the MIGERGOT transaction, the Company wrote off the remaining net book value of developed technology related to MIGERGOT of $17.0 million. See Note 4 for further details.

Intangible assets as of March 31, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020			December 31, 2019		
	Cost Basis	Accumulated Amortization	Net Book Value	Cost Basis	Accumulated Amortization	Net Book Value
Developed technology	$ 2,863,593	$ (1,117,968)	$ 1,745,625	$ 2,758,403	$ (1,059,595)	$ 1,698,808
Customer relationships	8,100	(4,481)	3,619	8,100	(4,280)	3,820
Total intangible assets	**$ 2,871,693**	**$ (1,122,449)**	**$ 1,749,244**	**$ 2,766,503**	**$ (1,063,875)**	**$ 1,702,628**

Amortization expense for the three months ended March 31, 2020 and 2019 was $58.6 million and $57.4 million, respectively. As of March 31, 2020, estimated future amortization expense was as follows (in thousands):

2020 (April to December)	$ 178,217
2021	230,012
2022	228,839
2023	228,222
2024	226,790
Thereafter	657,164
Total	**$ 1,749,244**

NOTE 9 – ACCRUED EXPENSES

Accrued expenses as of March 31, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020	December 31, 2019
Payroll-related expenses	$ 55,865	$ 84,516
Allowances for returns	49,118	45,082
Consulting and professional services	35,801	32,423
Accrued royalties	20,557	19,985
Pricing review liability	11,661	9,831
Accrued interest	6,945	18,709
Accrued other	26,041	24,688
Accrued expenses	**$ 205,988**	**$ 235,234**

NOTE 10 – ACCRUED TRADE DISCOUNTS AND REBATES

Accrued trade discounts and rebates as of March 31, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020	December 31, 2019
Accrued government rebates and chargebacks	$ 156,492	$ 164,508
Accrued co-pay and other patient assistance	90,465	163,641
Accrued commercial rebates and wholesaler fees	89,363	138,272
Accrued trade discounts and rebates	**$ 336,320**	**$ 466,421**
Invoiced commercial rebates and wholesaler fees, co-pay and other patient assistance costs, and government rebates and chargebacks in accounts payable	14,204	489
Total customer-related accruals and allowances	**$ 350,524**	**$ 466,910**

The following table summarizes changes in the Company's customer-related accruals and allowances from December 31, 2019 to March 31, 2020 (in thousands):

	Wholesaler Fees and Commercial Rebates	Co-Pay and Other Patient Assistance	Government Rebates and Chargebacks	Total
Balance at December 31, 2019	$ 138,761	$ 163,641	$ 164,508	$ 466,910
Current provisions relating to sales during the three months ended March 31, 2020	73,581	230,094	137,840	441,515
Adjustments relating to prior-year sales	(14,103)	—	(1,648)	(15,751)
Payments relating to sales during the three months ended March 31, 2020	(5,911)	(143,570)	(30,807)	(180,288)
Payments relating to prior-year sales	(101,990)	(157,988)	(101,884)	(361,862)
Balance at March 31, 2020	**$ 90,338**	**$ 92,177**	**$ 168,009**	**$ 350,524**

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.

Effective in the first quarter of 2020, the Company (i) reorganized its commercial operations and moved responsibility for and reporting of RAYOS to the inflammation segment and (ii) renamed the orphan and rheumatology segment the orphan segment. Net sales generated by TEPEZZA, which was approved in the first quarter of 2020, are reported as part of the renamed orphan segment.

The orphan segment includes the marketed medicines KRYSTEXXA, RAVICTI, PROCYSBI, ACTIMMUNE, TEPEZZA, BUPHENYL and QUINSAIR. The inflammation segment includes the marketed medicines PENNSAID 2%, DUEXIS, RAYOS, VIMOVO and previously included MIGERGOT prior to the MIGERGOT transaction.

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, 2020 and 2019 (in thousands):

	Three Months Ended March 31	
	2020	**2019**
KRYSTEXXA	$ 93,248	$ 52,257
RAVICTI	61,189	49,903
PROCYSBI	38,343	39,571
ACTIMMUNE	26,541	21,746
TEPEZZA	23,452	—
BUPHENYL	2,313	2,770
QUINSAIR	277	168
Orphan segment net sales	**$ 245,363**	**$ 166,415**
PENNSAID 2%	41,563	50,189
DUEXIS	31,346	29,457
VIMOVO	19,428	14,043
RAYOS	18,209	19,424
MIGERGOT	—	843
Inflammation segment net sales	**$ 110,546**	**$ 113,956**
Total net sales	**$ 355,909**	**$ 280,371**

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, 2020 and 2019 (in thousands):

	For the Three Months Ended March 31,	
	2020	2019
Segment operating income:		
Orphan	$ 54,356	$ 36,704
Inflammation	51,942	51,419
Reconciling items:		
Amortization and step-up:		
Intangible amortization expense	(58,575)	(57,417)
Inventory step-up expense	—	(115)
Share-based compensation	(56,421)	(27,548)
Interest expense, net	(17,344)	(27,530)
Depreciation	(7,165)	(1,473)
Drug substance harmonization costs	(290)	(80)
Acquisition/divestiture-related costs	(284)	(1,202)
Fees related to refinancing activities	(54)	(142)
Restructuring and realignment costs	—	(20)
Loss on debt extinguishment	—	(5,586)
Upfront and milestone payments related to license and collaboration agreements	—	(2,000)
Charges relating to discontinuation of Friedreich's ataxia program	—	79
Foreign exchange loss	776	(61)
Other income, net	442	189
Loss before benefit for income taxes	**$ (32,617)**	**$ (34,783)**

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, 2020 and 2019 (in thousands, except percentages):

	For the Three Months Ended March 31,			
	2020		2019	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Customer A	$ 246,775	31%	$ 345,247	36%
Customer B	207,277	26%	122,057	13%
Customer C	133,876	17%	184,869	20%
Customer D	84,788	10%	74,986	8%
Other Customers	130,806	16%	218,007	23%
Gross Sales	**$ 803,522**	**100%**	**$ 945,166**	**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, 2020 and 2019 (in thousands, except percentages):

	Three Months Ended March 31, 2020		Three Months Ended March 31, 2019	
	Amount	% of Total Net Sales	Amount	% of Total Net Sales
United States	$ 354,016	100%	$ 279,209	100%
Rest of world	1,893	*	1,162	*
Net sales	**$ 355,909**		**$ 280,371**	

***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, 2020 and December 31, 2019 (in thousands):

	March 31, 2020			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 641,225	$ —	$ —	$ 641,225
Other current assets	12,638	—	—	12,638
Total assets at fair value	**$ 653,863**	**$ —**	**$ —**	**$ 653,863**
Liabilities:				
Other long-term liabilities	(12,638)	—	—	(12,638)
Total liabilities at fair value	**$ (12,638)**	**$ —**	**$ —**	**$ (12,638)**

	December 31, 2019			
	Level 1	Level 2	Level 3	Total
Assets:				
Money market funds	$ 1,029,725	—	—	$ 1,029,725
Other current assets	12,704	—	—	12,704
Total assets at fair value	**$ 1,042,429**	**$ —**	**$ —**	**$ 1,042,429**
Liabilities:				
Other long-term liabilities	(12,704)	—	—	(12,704)
Total liabilities at fair value	**$ (12,704)**	**$ —**	**$ —**	**$ (12,704)**

NOTE 13 – DEBT AGREEMENTS

The Company's outstanding debt balances as of March 31, 2020 and December 31, 2019 consisted of the following (in thousands):

	March 31, 2020	December 31, 2019
Term Loan Facility due 2026	$ 418,026	$ 418,026
Senior Notes due 2027	600,000	600,000
Exchangeable Senior Notes due 2022	400,000	400,000
Total face value	**1,418,026**	**1,418,026**
Debt discount	(54,567)	(59,922)
Deferred financing fees	(5,099)	(5,263)
Total long-term debt and exchangeable notes	**1,358,360**	**1,352,841**
Less: long-term debt—current portion	—	—
Long-term debt and exchangeable notes, net	**$ 1,358,360**	**$ 1,352,841**

Term Loan Facility and Revolving Credit Facility

On December 18, 2019, Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc.) (the "Borrower"), a wholly owned subsidiary of the Company, borrowed approximately $418.0 million aggregate principal amount of loans (the "December 2019 Refinancing Loans") pursuant to an amendment (the "December 2019 Refinancing 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 and Amendment No. 6, dated May 22, 2019 (the "Term Loan Facility"). Pursuant to Amendment No. 5, the Borrower received $200.0 million aggregate principal amount of revolving commitments (the "Incremental Revolving Commitments"). The Incremental Revolving Commitments were established pursuant to an incremental facility (the "Revolving Credit Facility") and provide the Borrower with $200.0 million of additional borrowing capacity, which 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, 2020, 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 December 2019 Refinancing Amendment.

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 the London Inter-Bank Offered Rate ("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 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 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 December 2019 Refinancing Loans, (ii) the Revolving Credit Facility, (iii) one or more uncommitted additional incremental loan facilities subject to the satisfaction of certain financial and other conditions, and (iv) 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 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 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 Company elected to exercise its reinvestment rights under the mandatory prepayment provisions of the Credit Agreement with respect to the net proceeds from the Company's sale of its rights to PROCYSBI and QUINSAIR in the Europe, Middle East and Africa regions to Chiesi Farmaceutici S.p.A. To the extent the Company had not applied such net proceeds to permitted acquisitions (including the acquisition of rights to products and products lines) and/or the acquisition of capital assets within 365 days of the receipt thereof (or committed to so apply and then applied within 180 days after the end of such 365-day period), the Company was required to make a mandatory prepayment under the Credit Agreement in an amount equal to the unapplied net proceeds. In June 2018, the Company repaid $23.5 million under the mandatory prepayment provisions of the Credit Agreement.

On March 18, 2019, the Company completed the repayment of $300.0 million of the outstanding principal amount of term loans under the Credit Agreement following the closing of its underwritten public equity offering on March 11, 2019. In July 2019, the Company repaid an additional $100.0 million of term loans under the Credit Agreement following the private placement of the Company's 5.500% Senior Notes due 2027 (the "2027 Senior Notes"). Following these repayments, the outstanding principal balance of term loans under the Credit Agreement was $418.0 million.

Additionally, the Company elected to exercise its reinvestment rights under the mandatory prepayment provisions of the Credit Agreement with respect to the net proceeds from the Company's sale of its rights to RAVICTI and AMMONAPS (known as BUPHENYL in the United States) outside of North America and Japan to Medical Need Europe AB, part of the Immedica Group (the "Immedica transaction"). To the extent the Company had not applied such net proceeds to permitted acquisitions (including the acquisition of rights to products and products lines) and/or the acquisition of capital assets within 365 days of the receipt of proceeds from the Immedica transaction (or commit to so apply and then apply within 180 days after the end of such 365-day period), the Company was required to make a mandatory prepayment under the Credit Agreement in an amount equal to the unapplied net proceeds. In March 2019, the Company repaid $35.0 million under the mandatory prepayment provisions of the Credit Agreement which was included in the $300.0 million repayment referred to above.

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 December 2019 Refinancing Loans, a 1% premium will apply to a repayment of the December 2019 Refinancing 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 the date that is six months following December 18, 2019. 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 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 Term Loan Facility is variable and as of March 31, 2020 the interest rate on the Term Loan Facility was 3.94% and the effective interest rate was 4.25%.

As of March 31, 2020, the fair value of the amounts outstanding under the Term Loan Facility was approximately $390.9 million, categorized as a Level 2 instrument, as defined in Note 12.

2027 Senior Notes

On July 16, 2019, Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc.), the Company's wholly owned subsidiary ("HTUSA"), completed a private placement of $600.0 million aggregate principal amount of 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, 2020 the interest rate on the 2027 Senior Notes was 5.50% and the effective interest rate was 5.76%.

As of March 31, 2020 the fair value of the 2027 Senior Notes was approximately $582.0 million, categorized as a Level 2 instrument, as defined in Note 12.

Exchangeable Senior Notes

On March 13, 2015, Horizon Therapeutics Investment Limited (formerly known as Horizon Pharma Investment Limited) ("Horizon Investment"), a wholly owned subsidiary of the Company, completed a private placement of $400.0 million aggregate principal amount of Exchangeable Senior Notes to certain investment banks acting as initial purchasers who subsequently resold the Exchangeable Senior Notes to qualified institutional buyers as defined in Rule 144A under the Securities Act of 1933, as amended. The net proceeds from the offering of the Exchangeable Senior Notes were approximately $387.2 million, after deducting the initial purchasers' discount and offering expenses payable by Horizon Investment.

The Exchangeable Senior Notes are fully and unconditionally guaranteed, on a senior unsecured basis, by the Company (the "Guarantee"). The Exchangeable Senior Notes and the Guarantee are Horizon Investment's and the Company's senior unsecured obligations. The Exchangeable Senior Notes accrue interest at an annual rate of 2.50% payable semiannually in arrears on March 15 and September 15 of each year, beginning on September 15, 2015. The Exchangeable Senior Notes will mature on March 15, 2022, unless earlier exchanged, repurchased or redeemed. The initial exchange rate is 34.8979 ordinary shares of the Company per $1,000 principal amount of the Exchangeable Senior Notes (equivalent to an initial exchange price of approximately $28.66 per ordinary share). The exchange rate will be subject to adjustment in some events but will not be adjusted for any accrued and unpaid interest. In addition, following certain corporate events that occur prior to the maturity date or upon a tax redemption, Horizon Investment will increase the exchange rate for a holder who elects to exchange its Exchangeable Senior Notes in connection with such a corporate event or a tax redemption in certain circumstances.

Other than as described below, the Exchangeable Senior Notes may not be redeemed by the Company.

Issuer Redemptions:

Optional Redemption for Changes in the Tax Laws of a Relevant Taxing Jurisdiction: Horizon Investment may redeem the Exchangeable Senior Notes at its option, prior to March 15, 2022, in whole but not in part, in connection with certain tax-related events.

Provisional Redemption: Horizon Investment may redeem for cash all or a portion of the Exchangeable Senior Notes if the last reported sale price of ordinary shares of the Company has been at least 130% of the exchange price then in effect for at least twenty trading days whether or not consecutive) during any thirty consecutive trading day period ending on, and including, the trading day immediately preceding the date on which Horizon Investment provide written notice of redemption. The redemption price will be equal to 100% of the principal amount of the Exchangeable Senior Notes to be redeemed, plus accrued and unpaid interest to, but not including, the redemption date; provided that if the redemption date occurs after a regular record date and on or prior to the corresponding interest payment date, Horizon Investment will pay the full amount of accrued and unpaid interest due on such interest payment date to the record holder of the Exchangeable Senior Notes on the regular record date corresponding to such interest payment date, and the redemption price payable to the holder who presents an Exchangeable Senior Note for redemption will be equal to 100% of the principal amount of such Exchangeable Senior Note.

Holder Exchange Rights:

Holders may exchange all or any portion of their Exchangeable Senior Notes at their option at any time prior to the close of business on the business day immediately preceding December 15, 2021 only upon satisfaction of one or more of the following conditions:

1. Exchange upon Satisfaction of Sale Price Condition – During any calendar quarter, if the last reported sale price of ordinary shares of the Company for at least twenty trading days (whether or not consecutive) during the period of thirty consecutive trading days ending on the last trading day of the immediately preceding calendar quarter is greater than or equal to 130% of the applicable exchange price on each applicable trading day.
2. Exchange upon Satisfaction of Trading Price Condition – During the five business day period after any ten consecutive trading day period in which the trading price per $1,000 principal amount of Exchangeable Senior Notes for each trading day of such period was less than 98% of the product of the last reported sale price of ordinary shares of the Company and the applicable exchange rate on such trading day.
3. Exchange upon Notice of Redemption – Prior to the close of business on the business day immediately preceding December 15, 2021, if Horizon Investment provides a notice of redemption, at any time prior to the close of business on the second scheduled trading day immediately preceding the redemption date.

As of March 31, 2020, none of the above conditions had been satisfied and no exchange of Exchangeable Senior Notes had been triggered.

On or after December 15, 2021, a holder may exchange all or any portion of its Exchangeable Senior Notes at any time prior to the close of business on the second scheduled trading day immediately preceding the maturity date regardless of the foregoing conditions.

Upon exchange, Horizon Investment will settle exchanges of the Exchangeable Senior Notes by paying or causing to be delivered, as the case may be, cash, ordinary shares or a combination of cash and ordinary shares, at its election.

The Company recorded the Exchangeable Senior Notes under the guidance in ASC Topic 470-20, *Debt with Conversion and Other Options*, and separated them into a liability component and equity component. The carrying amount of the liability component of $268.9 million was determined by measuring the fair value of a similar liability that does not have an associated equity component. The carrying amount of the equity component of $119.1 million represented by the embedded conversion option was determined by deducting the fair value of the liability component of $268.9 million from the initial proceeds of $387.2 million ascribed to the convertible debt instrument as a whole. The initial debt discount of $131.1 million is being charged to interest expense over the life of the Exchangeable Senior Notes using the effective interest rate method.

As of March 31, 2020, the interest rate on the Exchangeable Senior Notes was 2.50% and the effective interest rate was 8.88%.

As of March 31, 2020, the fair value of the Exchangeable Senior Notes was approximately $460.0 million, categorized as a Level 2 instrument, as defined in Note 12.

NOTE 14 – LEASE OBLIGATIONS

The Company has 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
Chicago, Illinois	9,200	December 31, 2028
Mannheim, Germany	4,800	December 31, 2020
Other	12,400	May 31, 2020 to September 15, 2022

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 incur leasehold improvement costs during 2020 and 2021 in order to prepare the building for occupancy.

As of March 31, 2020 and December 31, 2019, the Company had right-of-use lease assets included in other assets of $38.9 million and $39.8 million, respectively; current lease liabilities included in accrued expenses of $4.6 million and $4.4 million, respectively; and non-current lease liabilities included in other long-term liabilities of $45.2 million and $46.5 million, respectively, in its condensed consolidated balance sheets.

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, 2020 and 2019.

The table below reconciles the undiscounted cash flows for each of the first five years and total of the remaining years to the operating lease liabilities recorded on the Company's condensed consolidated balance sheet as of March 31, 2020 (in thousands):

2020 (April to December)	$	5,972
2021		7,097
2022		5,922
2023		5,849
2024		6,466
Thereafter		39,522
Total lease payments		70,828
Imputed interest		(21,001)
Total operating lease liabilities	**$**	**49,827**

The weighted-average discount rate and remaining lease term for operating leases as of March 31, 2020 was 7.11% and 10.28 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. 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. At March 31, 2020, the Company had binding purchase commitments with AGC Biologics for TEPEZZA drug substance of €58.3 million ($64.3 million converted at an exchange rate as of March 31, 2020 of 1.1034), to be delivered through March 2022. In addition, the Company had binding purchase commitments with Catalent for TEPEZZA drug product of $8.4 million, to be delivered through March 2021.

Patheon Pharmaceuticals Inc. (“Patheon”) is obligated to manufacture PROCYSBI for the Company through December 31, 2021. The Company must provide Patheon with rolling, non-binding forecasts of PROCYSBI, with a portion of the forecast being a firm written order. Cambrex Profarmaco Milano (“Cambrex”) is obligated to manufacture PROCYSBI active pharmaceutical ingredient (“API”) for the Company through November 2, 2020. The Company must provide Cambrex with rolling, non-binding forecasts, with a portion of the forecast being the minimum floor of the firm order that must be placed. At March 31, 2020, the Company had a binding purchase commitment with Patheon for PROCYSBI of $1.4 million, to be delivered through April 2020 and with Cambrex for PROCYSBI API of $0.7 million, to be delivered through October 2020.

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, 2020, the minimum binding purchase commitment to Boehringer Ingelheim Biopharmaceuticals was $15.4 million (converted using a Dollar-to-Euro exchange rate of 1.1034 as of March 31, 2020) through June 2024. As of March 31, 2020, the Company also committed to incur an additional $0.4 million for the harmonization of the drug substance manufacturing process with Boehringer Ingelheim Biopharmaceuticals.

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, 2020, the Company had a binding purchase commitment with BTG Israel for KRYSTEXXA of $38.0 million, to be delivered through December 2026. Additionally, there were other purchase orders relating to the manufacture of KRYSTEXXA of $1.2 million outstanding at March 31, 2020.

Nuvo Pharmaceuticals Inc. (formerly known as Nuvo Research Inc.) (“Nuvo”) is obligated to manufacture and supply PENNSAID 2% to the Company. The term of the supply agreement is through December 31, 2029, but the agreement may be terminated earlier by either party for any uncured material breach by the other party of its obligations under the supply agreement or upon the bankruptcy or similar proceeding of the other party. At least ninety days prior to the first day of each calendar month during the term of the supply agreement, the Company submits a binding written purchase order to Nuvo for PENNSAID 2% in minimum batch quantities. At March 31, 2020, the Company had a binding purchase commitment with Nuvo for PENNSAID 2% of $3.8 million, to be delivered through August 2020.

Sanofi-Aventis U.S. LLC (“Sanofi-Aventis U.S.”) is obligated to manufacture and supply DUEXIS to the Company in final, packaged form and the Company is obligated to purchase DUEXIS exclusively from Sanofi-Aventis U.S. for the commercial requirements of DUEXIS in North America, South America and certain countries and territories in Europe, including the European Union (“EU”) member states and Scandinavia. The agreement term extends until May 2021 and automatically renews for successive two-year terms unless terminated by either party upon two years’ prior written notice. At March 31, 2020, the Company had a binding purchase commitment to Sanofi-Aventis U.S. for DUEXIS of $9.0 million, to be delivered through October 2020.

Excluding the above, additional purchase orders and other commitments relating to the manufacture of RAVICTI, BUPHENYL, RAYOS and QUINSAIR of $8.8 million were outstanding at March 31, 2020.

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.

Other Agreements

Under the agreement for the acquisition of 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 (if any).

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 will be recorded as TEPEZZA developed technology intangible assets in the second quarter of 2020.

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 transactions with S.R. One and Lundbeckfond, the Company's remaining net obligations to make TEPEZZA payments to the former stockholders of River Vision will be reduced by approximately 71.32%.

Under the Company's license agreement with Roche, the Company is required to pay Roche up to CHF103.0 million ($107.2 million when converted using a CHF-to-Dollar exchange rate at March 31, 2020 of 1.0406) upon the attainment of various development, regulatory and sales milestones for TEPEZZA. During the years ended December 31, 2019 and 2017, CHF3.0 million ($3.0 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.0023) and CHF2.0 million ($2.0 million when converted using a CHF-to-Dollar exchange rate at the date of payment of 1.0169), respectively, was paid in relation to these milestones. 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.

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.

Under the Company's license agreement with Boehringer Ingelheim Biopharmaceuticals, the Company is required to pay Boehringer Ingelheim Biopharmaceuticals milestone payments totaling low-single-digit million Euros upon the achievement of certain TEPEZZA sales milestones.

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 November 13, 2014, the Company received a Paragraph IV Patent Certification from Watson Laboratories, Inc., now known as Actavis Laboratories UT, Inc. ("Actavis UT"), advising that Actavis UT had filed an Abbreviated New Drug Application ("ANDA") with the FDA for a generic version of PENNSAID 2%. On December 23, 2014, June 30, 2015, August 11, 2015 and September 17, 2015, the Company filed four separate suits against Actavis UT and Actavis plc (collectively "Actavis"), in the United States District Court for the District of New Jersey, with each of the suits seeking an injunction to prevent approval of the ANDA. The lawsuits alleged that Actavis has infringed nine of the Company's patents covering PENNSAID 2% by filing an ANDA seeking approval from the FDA to market a generic version of PENNSAID 2% prior to the expiration of certain of the Company's patents listed in the FDA's Orange Book (the "Orange Book"). These four suits were consolidated into a single suit. On October 27, 2015 and on February 5, 2016, the Company filed two additional suits against Actavis, in the United States District Court for the District of New Jersey, for patent infringement of three additional Company patents covering PENNSAID 2%.

On August 17, 2016, the District Court issued a *Markman* opinion holding certain of the asserted claims of seven of the Company's patents covering PENNSAID 2% invalid as indefinite. On March 16, 2017, the Court granted Actavis' motion for summary judgment of non-infringement of the asserted claims of three of the Company's patents covering PENNSAID 2%. In view of the *Markman* and summary judgment decisions, a bench trial was held from March 21, 2017 through March 30, 2017, regarding a claim of one of the Company's patents covering PENNSAID 2%. On May 14, 2017, the Court issued its opinion upholding the validity of claim of the patent, which Actavis had previously admitted its proposed generic diclofenac sodium topical solution product would infringe. Actavis filed its Notice of Appeal on June 16, 2017. The Company also filed its Notice of Appeal of the District Court's rulings on certain claims of the Company's patents covering PENNSAID 2%. On October 10, 2019, the Federal Circuit Court affirmed the District Court's judgment of validity of U.S Patent No. 9,066,913 (the "'913 patent"), and its finding that the Actavis generic product would infringe the '913 patent. The Federal Circuit also affirmed the District Court's summary judgment finding that certain patents are invalid for indefiniteness and would not be infringed. The Company filed a Petition for Rehearing, asking the Federal Circuit to reconsider the latter order invalidating certain patents.

On August 18, 2016, the Company filed suit in the United States District Court for the District of New Jersey against Actavis for patent infringement of four of the Company's newly issued patents covering PENNSAID 2%. All four of such patents are listed in the Orange Book. This litigation is currently stayed by agreement of the parties. The Company received from Actavis a Paragraph IV Patent Certification notice, dated September 27, 2016, against an additional newly issued patent covering PENNSAID 2%, advising that Actavis had filed an ANDA with the FDA for a generic version of PENNSAID 2%. The subject patent is listed in the Orange Book.

DUEXIS

On May 29, 2018, the Company received notice from Alkem Laboratories, Inc. ("Alkem") 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 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 is scheduled for a bench trial beginning on September 14, 2020.

VIMOVO

Currently, patent litigation is pending in the United States District Court for the District of New Jersey and the Court of Appeals for the Federal Circuit against Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd. (collectively, "Dr. Reddy's") which seeks to market VIMOVO prior to the expiration of certain of the Company's patents listed in the Orange Book. Settlements have been reached with four other generic companies: (i) Teva Pharmaceuticals Industries Limited (formerly known as Actavis Laboratories FL, Inc., which itself was formerly known as Watson Laboratories, Inc. – Florida) and Actavis Pharma, Inc. (collectively, "Actavis Pharma"), (ii) Lupin Limited and Lupin Pharmaceuticals, Inc., (iii) Mylan Pharmaceuticals Inc., Mylan Laboratories Limited, and Mylan Inc. (collectively, "Mylan"), and (iv) Ajanta Pharma Ltd. and Ajanta Pharma USA Inc. (collectively, "Ajanta"). Under the settlement agreements, the license entry date was August 1, 2024; however, the entry date under all four licenses was accelerated and the licenses became effective upon Dr. Reddy's launch of its generic version of VIMOVO on February 27, 2020, as described below.

The VIMOVO cases were filed on April 21, 2011, July 25, 2011, October 28, 2011, January 4, 2013, May 10, 2013, June 28, 2013, October 23, 2013, May 13, 2015 and November 24, 2015 and collectively include allegations of infringement of certain of the Company's patents covering VIMOVO.

The District Court consolidated all of the cases pending against the generic companies into two separate cases for purposes of discovery. The District Court entered final judgment for one of the consolidated cases on July 21, 2017, upholding the validity of U.S. Patent No. 6,926,907 (the "'907 patent") and U.S. Patent No. 8,557,285 (the "'285 patent"), and finding the generic products would infringe one or both of the two patents. Both sides appealed the District Court's judgment to the Court of Appeals for the Federal Circuit. On May 15, 2019, the Federal Circuit reversed the District Court's judgment in favor of the Company, and entered judgment that the '285 and '907 patents are invalid for lack of a sufficient written description. On July 30, 2019, the Federal Circuit Court of Appeals denied the Company's request for a rehearing of the Court's invalidity ruling against the '285 and '907 patents for VIMOVO coordinated-release tablets. As a result, the District Court entered judgment invalidating the '285 and '907 patents in September 2019. On February 18, 2020, the FDA granted final approval for 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 (the "'996 patent") and U.S. Patent No. 9,161,920 (the "'920 patent") in the District Court.

On November 19, 2018, the District Court granted Dr. Reddy's and Mylan'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, '208, 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 December 4, 2017, Mylan filed a Petition for inter partes review ("IPR") against the '208 patent. The Patent Trial and Appeals Board ("PTAB") instituted an IPR proceeding on Mylan's Petition on June 14, 2018. On July 2, 2018, Dr. Reddy's filed a motion seeking to join Mylan's '208 IPR. On April 1, 2019, the PTAB granted Dr. Reddy's request to join the Mylan '208 IPR. On September 6, 2019, the PTAB issued a Final Written Decision invalidating the '208 patent on the basis of obviousness. On November 18, 2019, the Company filed an appeal with the Federal Circuit Court of Appeals to review the PTAB's ruling invalidating the '208 patent.

On August 20, 2019, the Company received notice from Ajanta that it had filed an ANDA with the FDA seeking approval of a generic version of VIMOVO. The ANDA contained a Paragraph IV Patent Certification alleging that the patents covering VIMOVO are invalid and/or will not be infringed by Ajanta'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 Ajanta on September 30, 2019, seeking an injunction to prevent the approval of Ajanta's ANDA and/or to prevent Ajanta from selling a generic version of VIMOVO. Ajanta and the Company settled and dismissed the litigation on March 9, 2020.

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

The Company's equity incentive plans at March 31, 2020 included its 2005 Stock Plan, 2011 Equity Incentive Plan, as amended, 2014 Employee Share Purchase Plan, as amended ("2014 ESPP"), Amended and Restated 2014 Equity Incentive Plan ("2014 EIP") and 2014 Non-Employee Equity Plan, as amended ("2014 Non-Employee Plan"). As of March 31, 2020, an aggregate of 1,236,775 ordinary shares were authorized and available for future issuance under the 2014 ESPP, an aggregate of 5,612,651 ordinary shares were authorized and available for future grants under the 2014 EIP (of which 532,737 shares are to be used exclusively for grants of awards to individuals who were not previously employees or non-employee directors of the Company (or following a bona fide period of non-employment with the Company)) and an aggregate of 698,491 ordinary shares were authorized and available for future grants under the 2014 Non-Employee Plan.

On February 19, 2020, the Compensation Committee of the Company's Board of Directors (the "Compensation Committee") adopted, subject to shareholder approval, the Company's 2020 Equity Incentive Plan ("2020 EIP"), as successor to and continuation of the 2014 EIP, including increasing the number of ordinary shares available for the grant of equity awards to the Company's employees by an additional 6,900,000 shares. On April 30, 2020, the shareholders of the Company approved the 2020 EIP.

On February 19, 2020, the Compensation Committee adopted, subject to shareholder approval, the Company's 2020 Employee Share Purchase Plan ("2020 ESPP"), as successor to and continuation of the 2014 ESPP, increasing the number of ordinary shares available for issuance to the Company's employees pursuant to the exercise of purchase rights by an additional 2,500,000 shares. On April 30, 2020, the shareholders of the Company approved the 2020 ESPP.

Stock Options

The following table summarizes stock option activity during the three months ended March 31, 2020:

	Options	Weighted Average Exercise Price	Weighted Average Contractual Term Remaining (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2019	9,564,202	$ 19.85	5.43	$ 156,270
Exercised	(498,753)	14.66	—	—
Forfeited	(54,098)	15.96	—	—
Expired	(20,442)	23.32	—	—
Outstanding as of March 31, 2020	**8,990,909**	**20.16**	**5.15**	**85,351**
Exercisable as of March 31, 2020	**8,616,016**	**$ 20.22**	**5.05**	**$ 81,226**

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

Restricted Stock Units

The following table summarizes restricted stock unit activity for the three months ended March 31, 2020:

	Number of Units	Weighted Average Grant-Date Fair Value Per Unit
Outstanding as of December 31, 2019	6,541,224	$ 18.77
Granted	2,298,993	35.44
Vested	(1,963,611)	17.91
Forfeited	(265,953)	23.85
Outstanding as of March 31, 2020	**6,610,653**	**$ 24.62**

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, 2020:

	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, 2019	3,558,900			
Granted	587,802	$ 42.38	8.1%	$ 38.94
Forfeited	(201,645)	25.73	4.3%	24.62
Vested	(1,380,312)	20.85	0.0%	20.85
Performance Based Adjustment (1)	89,941	20.24	0.0%	20.24
Outstanding as of March 31, 2020	**2,654,686**			

(1) Represents adjustment based on the net sales performance criteria meeting 119.2% of target as of December 31, 2019 for the 2019 PSUs (as defined below).

On January 4, 2019, the Company awarded PSUs to key executive participants ("2019 PSUs"). The 2019 PSUs utilize two performance metrics, a short-term component tied to business performance and a long-term component tied to relative compounded annual shareholder rate of return ("TSR"), as follows:

- 30% of the granted 2019 PSUs that may vest (such portion of the PSU award, the "2019 Relative TSR PSUs") are determined by reference to the level of the Company's relative TSR over the three-year period ending December 31, 2021, 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 2019 Relative TSR PSUs, the participant must also remain in continuous service with the Company through the earlier of January 1, 2022 or the date immediately prior to a change in control. If a change in control occurs prior to December 31, 2021, the level of the Company's relative TSR will be measured through the date of the change in control.

- 70% of the granted 2019 PSUs that may vest (such portion of the PSU award, the "2019 Net Sales PSUs"), are determined by reference to the Company's net sales performance for its rare disease business unit (formerly named the orphan business unit) and KRYSTEXXA. The rare disease business unit and KRYSTEXXA are part of the orphan segment. During the year ended December 31, 2019, the net sales performance criteria was met at 119.2% of target. Accordingly, one-third of the net sales PSUs portion have vested and the remaining two-thirds will vest in equal installments in January 2021 and January 2022, subject to the participant's continued service with the Company through the applicable vesting dates.

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.

All PSUs outstanding at March 31, 2020 may vest in a range of between 0% and 200%, based on the performance metrics described above. The Company accounts for the 2019 PSUs and 2020 PSUs as equity-settled awards in accordance with ASC 718. Because the value of the 2019 Relative TSR PSUs and 2020 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 2019 Relative TSR PSUs and 2020 Relative TSR PSUs. As a result, the Monte Carlo model is applied and the most significant valuation assumptions used related to the 2020 PSUs during the three months ended March 31, 2020, include:

Valuation date stock price	$	36.10
Expected volatility		47.3%
Risk free rate		1.5%

The value of the 2020 Net Sales 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, 2020, there were 724,490 TEPEZZA PSUs outstanding. For members of the executive committee, one-third of the TEPEZZA PSUs vested on the FDA approval date and one-third will vest on each of the first two anniversaries of the FDA approval date, subject to the employee's continued service through the applicable vesting dates. For all other participants, one-half of the TEPEZZA PSUs vested on the FDA approval date and one-half will vest 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, 2020 and 2019 (in thousands):

	For the Three Months Ended March 31,	
	2020	2019
Share-based compensation expense		
Cost of goods sold	$ 2,689	$ 1,039
Research and development	6,376	2,636
Selling, general and administrative	47,356	23,873
Total share-based compensation expense	**$ 56,421**	**$ 27,548**

During the three months ended March 31, 2020 and 2019, the Company recognized $14.1 million and $2.5 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, 2020, the Company estimates that pre-tax unrecognized compensation expense of $178.1 million for all unvested share-based awards, including stock options, restricted stock units and PSUs, will be recognized through the third quarter of 2022. 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 2014 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 will vest and become payable in January 2021, subject to the participant's continued services with the Company through such vesting date, the date of any earlier change in control, or a termination due to death or disability.

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, 2020 and 2019, the Company recorded an expense of $1.0 million and $1.2 million, respectively, to the condensed consolidated statement of comprehensive loss related to the Cash Incentive Program.

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, 2020 and 2019 (in thousands):

	For the Three Months Ended March 31,	
	2020	2019
Loss before benefit for income taxes	$ (32,617)	$ (34,783)
Benefit for income taxes	(19,026)	(1,920)
Net loss	**$ (13,591)**	**$ (32,863)**

During the three months ended March 31, 2020, the Company recorded a benefit for income taxes of $19.0 million. During the three months ended March 31, 2019, the Company recorded a benefit for income taxes of $1.9 million. The increase in benefit for income taxes recorded during the three months ended March 31, 2020 compared to the three months ended March 31, 2019, resulted primarily from the increase in the tax benefits recognized on share-based compensation and the mix of pre-tax income and losses incurred in various tax jurisdictions.

NOTE 19 – SUBSEQUENT EVENTS

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 (LPAR1) antagonist, CZN001 (renamed HZN-825).

Under terms of the agreement, the Company acquired Curzion for a $45.0 million upfront cash payment with additional payments contingent on the achievement of development and regulatory milestones. The $45.0 million payment will be recorded as an in-process research and development expense in the second quarter of 2020. HZN-825 was originally discovered and developed by Sanofi, 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.

Agreement with S.R. One and Lundbeckfond

In April 2020, a subsidiary of the Company entered into an agreement with S.R. One and an agreement with 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 will be recorded as TEPEZZA developed technology intangible assets in the second quarter of 2020. Refer to Note 15 for further detail of the contingent future milestone and royalty payments related to TEPEZZA and the agreements with S.R. One and Lundbeckfond.

Final Regulations for Section 267A (commonly referred to as the “Anti-Hybrid Rules”)

On April 8, 2020, the U.S. Treasury published in the Federal Register the Final Regulations for Section 267A of the Internal Revenue Code of 1986, as amended (commonly referred to as the “Anti-Hybrid Rules”). The Final Regulations for Section 267A provide several rules expanding the reach and scope of Section 267A particularly involving the payment of interest and royalties to certain branches, reverse hybrid entities, and other hybrid mismatch arrangements. The Company is in the process of assessing the impact, if any, of the provisions of the Final Regulations for Section 267A on the Company’s financial statements. If the Anti-Hybrid Rules under the Final Regulations for Section 267A are applicable to the Company, the Company will recognize a one-time tax provision of $15.2 million during the three months ended June 30, 2020.

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 and rheumatic 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.

On January 21, 2020, the U.S. Food and Drug Administration, or FDA, approved TEPEZZA™ (teprotumumab-trbw), for the treatment of thyroid eye disease, or TED, a serious, progressive and vision-threatening rare autoimmune condition.

We have two reportable segments, (i) the orphan segment (previously the orphan and rheumatology segment), our strategic growth business, and (ii) the inflammation segment, and we report net sales and segment operating income for each segment. Effective in the first quarter of 2020, we (i) reorganized our commercial operations and moved responsibility for and reporting of RAYOS® to the inflammation segment and (ii) renamed the orphan and rheumatology segment the orphan segment. Net sales generated by TEPEZZA, which was approved in the first quarter of 2020, are reported as part of the renamed orphan segment.

As of March 31, 2020, our marketed medicine portfolio consisted of the following:

Orphan
KRYSTEXXA® (pegloticase injection), for intravenous infusion
RAVICTI® (glycerol phenylbutyrate) oral liquid
PROCYSBI® (cysteamine bitartrate) delayed-release capsules, for oral use
ACTIMMUNE® (interferon gamma-1b) injection, for subcutaneous use
TEPEZZA (teprotumumab-trbw), for intravenous infusion
BUPHENYL® (sodium phenylbutyrate) Tablets and Powder
QUINSAIR™ (levofloxacin) solution for inhalation
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
VIMOVO® (naproxen/esomeprazole magnesium) delayed-release tablets, for oral use

Acquisitions and Divestitures

Since January 1, 2019, we completed the following acquisitions and divestitures:

- 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.

- On June 28, 2019, we sold our rights to MIGERGOT to Cosette Pharmaceuticals, Inc., for an upfront payment and potential additional contingent consideration payments.

- Effective January 1, 2019, we amended our license and supply agreements with Jagotec AG and Skyepharma AG, which are affiliates of Vectura Group plc, or Vectura. Under these amendments, we agreed to transfer all economic benefits of LODOTRA® in Europe to Vectura during an initial transition period, with full rights transferring to Vectura when certain transfer activities have been completed. We no longer recorded LODOTRA net sales beginning January 1, 2019.

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, can be characterized as a pandemic. The President of the United States declared the COVID-19 pandemic a national emergency and many states and municipalities in the Unites States have announced 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 have moved to a “virtual” model with respect to our physician, patient and partner support activities. While our financial results during the three months ended March 31, 2020 were strong and we continue to have a significant amount of available liquidity, we anticipate the COVID-19 pandemic to have a negative impact on net sales during the remaining quarters of 2020.

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. We believe we have sufficient inventory of raw materials and finished goods for all of our medicines. We expect patients to be able to continue to receive their medicines from their current pharmacies, alternative pharmacies or, if necessary, by direct shipment from our third-party providers that have such capability.

In regard to our orphan segment, the first-quarter launch of our new infused medicine for TED, TEPEZZA, has significantly exceeded our expectations. In early 2019, we initiated our pre-launch disease awareness, market development and market access efforts with the multi-functional field-based teams beginning to engage with key stakeholders in July of 2019. These pre-launch efforts, the severity and acute nature of TED, and a highly motivated patient population have generated significant demand for the medicine that was well in excess of our initial expectations. While we anticipate a much higher number of new patients in 2020 than our prior estimates, the impact from COVID-19 has slowed the generation of patient enrollment forms for TEPEZZA, which drive new patient starts. 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, due to shelter-in-place guidelines, many new patients have delayed infusions. Patient visits to physicians have substantially declined, which has resulted in a reduction of new patient generation. We expect this deferred demand to begin to return with the return of healthcare activity. Our other rare disease 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 we expect these three medicines to be relatively stable, with the least impact from COVID-19 of all of our medicines.

In regard to the inflammation segment, we are experiencing 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. This impact is somewhat mitigated by the virtual engagement efforts of our sales representatives, as well as the use of telemedicine by many physicians, which allow 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.

In addition, our clinical trials may be affected by COVID-19. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital 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 to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Some clinical sites in the United States have started to slow or stop 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.

It is too early to determine the ultimate impact of the COVID-19 pandemic on any of our medicines. 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 is a best estimate based on the information available as of today's date.

Strategy

Horizon today is a leading biopharma company focused on rare diseases, delivering innovative therapies to patients and generating value for our shareholders. Our strategy is to maximize the benefit and value of our key growth drivers KRYSTEXXA and TEPEZZA, both rare disease medicines, and expand our pipeline for sustainable growth. We believe our strategy allows more patients to benefit from our on-market medicines, as well as from medicines we develop as part of our pipeline. Our vision is to build healthier communities, urgently and responsibly, which in turn, we believe, generates value to our many stakeholders, including our shareholders.

Orphan

As of March 31, 2020, our orphan segment consisted of our medicines KRYSTEXXA, RAVICTI, PROCYSBI, ACTIMMUNE, TEPEZZA, BUPHENYL and QUINSAIR. Effective in the first quarter of 2020, we (i) reorganized our commercial operations and moved responsibility for and reporting of RAYOS to the inflammation segment and (ii) renamed the orphan and rheumatology segment the orphan segment.

TEPEZZA is the first and only FDA-approved medicine for the treatment of TED, a serious, progressive and vision-threatening rare autoimmune condition. TEPEZZA was launched commercially shortly after receiving FDA approval for the treatment of TED on January 21, 2020. The FDA approval was obtained well in advance of the TEPEZZA Prescription User Fee Act (PDUFA) action date of March 8, 2020, after an accelerated review of the medicine and its statistically significant Phase 3 data. We believe TEPEZZA represents a significant driver of growth for Horizon.

Our commercialization strategy for TEPEZZA has four components: (i) driving early uptake by continuing to define the role of TEPEZZA in the treatment of TED and getting uptake from treating physicians; (ii) continuing to develop the TED market by driving awareness of the disease severity and benefits of treatment, educating the appropriate treating physicians on the urgency to diagnose and treat TED and continuing to drive patients' awareness of TED; (iii) supporting TEPEZZA with our comprehensive approach that includes a high-touch, patient-centric model; and (iv) facilitating patient and physician access to TEPEZZA. Our launch followed our significant investment in TEPEZZA in 2019 to prepare for the then potential U.S. approval, driving awareness about TED in the medical and patient community and establishing a potential pathway for treatment.

Our clinical strategy for TEPEZZA is to maximize the potential of TED for patients. We have announced three new TEPEZZA development programs in the first quarter of 2020 in this respect: the evaluation of TEPEZZA in the later fibrotic phase of the disease to support the expanded indication received upon approval; the assessment of a subcutaneous route of administration; and an exploratory trial for TEPEZZA in the treatment of diffuse cutaneous systemic sclerosis (dcSSc), a rare, autoimmune rheumatic disease, given that scientific literature suggests that the mechanism of action of TEPEZZA could have an impact on fibrotic processes.

KRYSTEXXA is the only approved medicine indicated for the treatment of uncontrolled gout, or gout that is refractory (unresponsive) to conventional therapies. We are focused on optimizing and maximizing the peak sales potential of KRYSTEXXA through our patient-centric commercialization efforts, through the clinical evaluation of the use of immunomodulation with KRYSTEXXA and investing in education, patient and physician outreach that demonstrates the benefits KRYSTEXXA offers in treating uncontrolled gout. We believe KRYSTEXXA represents a significant driver of growth for Horizon.

Three areas are driving growth for KRYSTEXXA: an increase in new and existing accounts; accelerating uptake by nephrologists; and growth in the adoption of the use of KRYSTEXXA with immunomodulators such as methotrexate to improve the KRYSTEXXA response rate in patients with uncontrolled gout.

Immunomodulation is one of the clinical development programs we are investing in to evaluate ways to increase the number of patients who can benefit from KRYSTEXXA. Our registrational MIRROR randomized controlled trial, or RCT, is evaluating the co-administration of KRYSTEXXA with methotrexate, the immunomodulator most often used by rheumatologists, to increase the durability of response for uncontrolled gout patients. The MIRROR RCT, which we initiated in mid-2019, was preceded by the MIRROR open-label study, which was initiated in 2018 and completed in 2019. The positive topline results of the MIRROR open-label trial, announced in January 2020, signify to us the value of continuing our research into the benefits of this immunomodulation approach. We are also investing to expand the use of KRYSTEXXA among nephrologists by providing additional data about the effectiveness of KRYSTEXXA in treating uncontrolled gout with its kidney-friendly mechanism of action. In October 2019, we initiated our PROTECT open-label trial to evaluate the use of KRYSTEXXA in adult uncontrolled gout patients who have undergone a kidney transplant, a population that was not originally studied in the KRYSTEXXA pivotal trials. We have also announced plans to initiate a proof of concept trial to evaluate the impact of administering KRYSTEXXA over a shorter infusion time, which could improve the experience and convenience for patients. We currently expect to initiate the KRYSTEXXA shorter-infusion trial in 2020.

The RECIPE trial, an investigator-initiated study partially supported by Horizon, recently completed. The trial was a randomized, double-blind, placebo-controlled study to assess preliminary efficacy and safety of administering the immunomodulator mycophenolate mofetil, or MMF, with KRYSTEXXA to enhance the KRYSTEXXA response rate. Thirty-two patients with chronic refractory gout were randomized 3:1 in the study design to receive MMF versus placebo in addition to all patients receiving KRYSTEXXA. The primary efficacy endpoint was the proportion of participants achieving and maintaining serum uric acid levels less than or equal to 6 mg/dL through 12 weeks. The trial also assessed the incidence and types of adverse events and infusion reactions. After 12 weeks of co-administration, all participants continued on KRYSTEXXA alone for an additional 12 weeks without combination MMF therapy to evaluate the longer-term efficacy and safety of this approach. The results are consistent with previously reported open label studies of KRYSTEXXA with methotrexate in which response rates were greater than the rates observed for KRYSTEXXA alone in the Phase 3 program, further supporting the KRYSTEXXA immunomodulation strategy. We anticipate that the full results and data set will be released at a future scientific meeting.

Our strategy for RAVICTI, our medicine for the treatment of urea cycle disorders, is to drive growth through increased awareness and diagnosis of urea cycle disorders; to drive conversion to RAVICTI from older-generation nitrogen scavengers, such as generic forms of sodium phenylbutyrate based on the medicine's differentiated benefits; to position RAVICTI as the first line of therapy; and to increase compliance rates.

Our strategy for PROCYSBI, our medicine for the treatment of nephropathic cystinosis, is to drive conversion of patients from older-generation immediate-release capsules of cysteamine bitartrate; to increase the use of the medicine by diagnosed but untreated patients; to identify previously undiagnosed patients who are suitable for treatment; to position PROCYSBI as a first line of therapy; and to increase compliance rates.

In February 2020, the FDA approved PROCYSBI Delayed-Release Oral Granules in Packets for adults and children one year of age and older living with nephropathic cystinosis. The PROCYSBI Delayed-Release Oral Granules in Packets product is the same as the currently available PROCYSBI capsules product except in respect of the packaging format. This new dosage form provides another administration option for patients, in addition to the PROCYSBI capsules. PROCYSBI Delayed-Release Oral Granules in Packets became commercially available in April 2020.

Our strategy with respect to ACTIMMUNE, our medicine for the treatment of chronic granulomatous disease, includes increasing awareness and diagnosis of chronic granulomatous disease and increasing compliance rates.

Inflammation

As of March 31, 2020, our inflammation segment consisted of our medicines PENNSAID 2%, DUEXIS, RAYOS and VIMOVO. Our strategy for our inflammation segment medicines is to educate physicians about these clinically differentiated medicines and the benefits they offer. Patients are able to fill prescriptions for these medicines through pharmacies participating in our HorizonCares patient assistance program, as well as other pharmacies. We offer discount card and other programs to patients under which the patient receives a discount on his or her prescription. In certain circumstances when a patient's prescription is rejected by a managed care vendor, we will pay for the full cost of the prescription. In addition, we have entered into business arrangements with pharmacy benefit managers, or PBMs, and other payers to secure formulary status and reimbursement of our inflammation segment medicines. The business arrangements with the PBMs generally require us to pay administrative fees and rebates to the PBMs and other payers for qualifying prescriptions. Effective in the first quarter of 2020, we reorganized our commercial operations and moved responsibility for and reporting of RAYOS to the inflammation segment.

On February 18, 2020, the FDA granted final approval for Dr. Reddy's Laboratories Inc. and Dr. Reddy's Laboratories Ltd., or 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 we now face generic competition with respect to VIMOVO. Patent litigation against Dr. Reddy's for infringement continues with respect to certain patents in the New Jersey District Court. We have repositioned our promotional efforts previously made on VIMOVO to the other inflammation segment medicines and expect that our VIMOVO net sales will decrease in future periods.

We market all of our medicines in the United States through our field sales forces, which numbered approximately 455 representatives as of March 31, 2020.

RESULTS OF OPERATIONS

Comparison of Three Months Ended March 31, 2020 and 2019

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, 2020, compared to the three months ended March 31, 2019.

	For the Three Months Ended March 31,		
	2020	2019	Change
	(in thousands)		
Net sales	$ 355,909	$ 280,371	$ 75,538
Cost of goods sold	97,416	88,142	9,274
Gross profit	**258,493**	**192,229**	**66,264**
Operating expenses:			
Research and development	27,209	21,725	5,484
Selling, general and administrative	247,775	172,299	75,476
Total operating expenses	**274,984**	**194,024**	**80,960**
Operating loss	**(16,491)**	**(1,795)**	**(14,696)**
Other expense, net:			
Interest expense, net	(17,344)	(27,530)	10,186
Loss on debt extinguishment	—	(5,586)	5,586
Foreign exchange gain (loss)	776	(61)	837
Other income, net	442	189	253
Total other expense, net	**(16,126)**	**(32,988)**	**16,862**
Loss before benefit for income taxes	**(32,617)**	**(34,783)**	**2,166**
Benefit for income taxes	(19,026)	(1,920)	(17,106)
Net loss	**$ (13,591)**	**$ (32,863)**	**$ 19,272**

Net sales. Net sales increased $75.5 million, or 26.9%, to $355.9 million during the three months ended March 31, 2020, from $280.4 million during the three months ended March 31, 2019. The increase in net sales during the three months ended March 31, 2020 was due to an increase in net sales in our orphan segment of $78.9 million primarily due to post-launch sales of TEPEZZA of $23.5 million and higher net sales of KRYSTEXXA and RAVICTI when compared to the three months ended March 31,2019, partially offset by a decrease in net sales in our inflammation segment of $3.4 million.

The following table reflects net sales by medicine for the three months ended March 31, 2020 and 2019 (in thousands, except percentages):

	Three Months Ended March 31,		Change $	Change %
	2020	2019		
KRYSTEXXA	$ 93,248	$ 52,257	$ 40,991	78%
RAVICTI	61,189	49,903	11,286	23%
PROCYSBI	38,343	39,571	(1,228)	(3)%
ACTIMMUNE	26,541	21,746	4,795	22%
TEPEZZA	23,452	—	23,452	100%
BUPHENYL	2,313	2,770	(457)	(16)%
QUINSAIR	277	168	109	65%
Orphan segment net sales	**$ 245,363**	**$ 166,415**	**$ 78,948**	**47%**
PENNSAID 2%	41,563	50,189	(8,626)	(17)%
DUEXIS	31,346	29,457	1,889	6%
VIMOVO	19,428	14,043	5,385	38%
RAYOS	18,209	19,424	(1,215)	(6)%
MIGERGOT	—	843	(843)	(100)%
Inflammation segment net sales	**$ 110,546**	**$ 113,956**	**$ (3,410)**	**(3)%**
Total net sales	**$ 355,909**	**$ 280,371**	**$ 75,538**	**27%**

Orphan

KRYSTEXXA. Net sales increased $41.0 million, or 78%, to $93.2 million during the three months ended March 31, 2020 from $52.2 million during the three months ended March 31, 2019. Net sales increased by approximately $23.6 million due to volume growth and $17.4 million due to higher net pricing.

RAVICTI. Net sales increased $11.3 million, or 23%, to $61.2 million during the three months ended March 31, 2020, from $49.9 million during the three months ended March 31, 2019. Net sales in the United States increased by approximately $10.9 million, which was composed of an increase of approximately $7.4 million resulting from higher net pricing and an increase of approximately $3.5 million due to higher sales volume. Net sales outside the United States increased by approximately $0.4 million due to higher sales volume.

PROCYSBI. Net sales decreased $1.2 million, or 3%, to $38.3 million during the three months ended March 31, 2020, from $39.5 million during the three months ended March 31, 2019. The decrease in net sales was composed of a decrease of approximately $0.8 million due to lower sales volume and a decrease of $0.4 million resulting from lower net pricing.

ACTIMMUNE. Net sales increased $4.8 million, or 22%, to $26.5 million during the three months ended March 31, 2020, from $21.7 million during the three months ended March 31, 2019. Net sales increased by approximately $2.7 million due to higher net pricing and by approximately $2.1 million resulting from higher sales volume.

TEPEZZA. On January 21, 2020, the FDA approved TEPEZZA for the treatment of TED. Net sales generated for TEPEZZA during the three months ended March 31, 2020 were $23.5 million.

BUPHENYL. Net sales decreased $0.5 million, or 16%, to $2.3 million during the three months ended March 31, 2020, from $2.8 million during the three months ended March 31, 2019. Net sales decreased by approximately $2.1 million due to lower net pricing, partially offset by an increase of approximately $1.6 million resulting from higher sales volume.

Inflammation

PENNSAID 2%. Net sales decreased $8.6 million, or 17%, to $41.6 million during the three months ended March 31, 2020, from $50.2 million during the three months ended March 31, 2019. Net sales decreased by approximately $15.3 million due to lower sales volume, partially offset by an increase of approximately $6.7 million resulting from higher net pricing primarily due to lower utilization of our patient assistance programs.

DUEXIS. Net sales increased $1.8 million, or 6%, to $31.3 million during the three months ended March 31, 2020, from $29.5 million during the three months ended March 31, 2019. Net sales increased by approximately $11.1 million resulting from higher net pricing primarily due to lower utilization of our patient assistance programs, partially offset by a decrease of approximately $9.3 million resulting from lower sales volume.

VIMOVO. Net sales increased $5.3 million, or 38%, to $19.4 million during the three months ended March 31, 2020, from $14.1 million during the three months ended March 31, 2019. Of the $5.3 million increase in net sales, $1.6 million relates to authorized generic VIMOVO sales in the first quarter of 2020. The remaining net sales increase of $3.7 million was due to higher net pricing of $11.9 million primarily due to lower utilization of our patient assistance programs, partially offset by a decrease of approximately $8.2 million resulting from lower sales volume.

On February 18, 2020, the FDA granted final approval for 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 we now face generic competition with respect to VIMOVO. Patent litigation against Dr. Reddy's for infringement continues with respect to certain patents in the New Jersey District Court. We have repositioned our promotional efforts previously made on VIMOVO to the other inflammation segment medicines and expect that our VIMOVO net sales will decrease in future periods.

RAYOS. Net sales decreased $1.2 million, or 6%, to $18.2 million during the three months ended March 31, 2020, from $19.4 million during the three months ended March 31, 2019. Net sales decreased by approximately $7.5 million due to lower sales volume, partially offset by an increase of $6.3 million resulting from higher net pricing primarily due to lower utilization of our patient assistance programs.

MIGERGOT. On June 28, 2019, we sold our rights to MIGERGOT.

The table below reconciles our gross to net sales for the three months ended March 31, 2020 and 2019 (in millions, except percentages):

	Three Months Ended March 31, 2020		Three Months Ended March 31, 2019	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Gross sales	$ 803.5	100.0%	$ 945.2	100.0%
Adjustments to gross sales:				
Prompt pay discounts	(13.0)	(1.6)%	(17.8)	(1.9)%
Medicine returns	(8.8)	(1.1)%	(5.1)	(0.5)%
Co-pay and other patient assistance	(230.1)	(28.6)%	(417.8)	(44.2)%
Commercial rebates and wholesaler fees	(59.5)	(7.4)%	(110.4)	(11.7)%
Government rebates and chargebacks	(136.2)	(17.0)%	(113.7)	(12.0)%
Total adjustments	**(447.6)**	**(55.7)%**	**(664.8)**	**(70.3)%**
Net sales	**$ 355.9**	**44.3%**	**$ 280.4**	**29.7%**

During the three months ended March 31, 2020, co-pay and other patient assistance costs, as a percentage of gross sales, decreased to 28.6% from 44.2% during the three months ended March 31, 2019, primarily due to lower utilization of our patient assistance programs and the impact of generic competition on VIMOVO sales.

During the three months ended March 31, 2020, commercial rebates and wholesaler fees, as a percentage of gross sales, decreased to 7.4% from 11.7% during the three months ended March 31, 2019, primarily as a result of an increased proportion of orphan segment medicines sold and the impact of generic competition on VIMOVO sales.

During the three months ended March 31, 2020, government rebates and chargebacks, as a percentage of gross sales, increased to 17.0% from 12.0% during the three months ended March 31, 2019, primarily as a result of an increased proportion of orphan segment medicines sold. Government rebates and chargebacks as a percentage of gross sales are typically higher for medicines in the orphan segment compared to medicines in the inflammation segment.

Cost of Goods Sold. Cost of goods sold increased $9.2 million to $97.4 million during the three months ended March 31, 2020, from $88.2 million during the three months ended March 31, 2019. The increase in cost of goods sold during the three months ended March 31, 2020 compared to three months ended March 31, 2019, was primarily due to a $4.5 million increase in royalty expense, a $2.4 million increase in employee-related costs and a $1.3 million increase in depreciation and amortization expense. As a percentage of net sales, cost of goods sold was 27.4% during the three months ended March 31, 2020, compared to 31.4% during the three months ended March 31, 2019. The decrease in cost of goods sold as a percentage of net sales was primarily due to change in the mix of medicines sold.

Research and Development Expenses. Research and development expenses increased $5.5 million to $27.2 million during the three months ended March 31, 2020, from $21.7 million during the three months ended March 31, 2019. The increase was primarily attributable to a $3.7 million increase in share-based compensation primarily due to company-wide grant of performance stock unit awards related to TEPEZZA, or TEPEZZA PSUs, that vested in January 2020 upon FDA approval for TEPEZZA, a $2.1 million increase in clinical trial costs and a $1.6 million increase in employee-related costs, partially offset by an upfront payment of $2.0 million made under our collaboration agreement with HemoShear Therapeutics, LLC, or HemoShear, during the three months ended March 31, 2019.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased $75.5 million to $247.8 million during the three months ended March 31, 2020, from $172.3 million during the three months ended March 31, 2019. The increase was primarily attributable to an increase of $47.9 million in employee costs of which $23.5 million relates to an increase in share-based compensation primarily due to the TEPEZZA PSUs and an increase of $14.6 million related to marketing program costs.

Interest Expense, Net. Interest expense, net, decreased $10.2 million to $17.3 million during the three months ended March 31, 2020, from $27.5 million during the three months ended March 31, 2019. The decrease was primarily due to a decrease in debt interest expense of $12.6 million, primarily related to the decrease in the principal amount of our term loans in March 2019 and July 2019, repayment of our 6.625% Senior Notes due 2023 in May 2019 and in August 2019, repayment of our 8.750% Senior Notes due 2024 in August 2019, and an increase in interest income of $2.8 million.

Benefit for Income Taxes. During the three months ended March 31, 2020, we recorded a benefit for income taxes of $19.0 million compared to a benefit for income taxes of $1.9 million during the three months ended March 31, 2019. The benefit for income taxes recorded during the three months ended March 31, 2020 resulted primarily from tax benefits recognized on share-based compensation and the mix of pre-tax income and losses incurred in various tax jurisdictions.

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, 2020 and 2019.

Orphan

The following table reflects our orphan net sales and segment operating income for the three months ended March 31, 2020 and 2019 (in thousands, except percentages).

	For the Three Months Ended March 31,			
	2020	2019	Change	% Change
Net sales	$ 245,363	$ 166,415	$ 78,948	47%
Segment operating income	54,356	36,704	17,652	48%

The increase in orphan net sales during the three months ended March 31, 2020 is described in the *Consolidated Results* section above.

Segment operating income. Orphan segment operating income increased $17.6 million to $54.3 million during the three months ended March 31, 2020, from $36.7 million during the three months ended March 31, 2019. The increase was primarily attributable to an increase in net sales of $78.9 million as described above, partially offset by an increase in selling, general and administrative expenses of $49.9 million. The increase in selling, general and administrative expenses was mainly due to an increase in costs to prepare for the U.S. launch of TEPEZZA.

Inflammation

The following table reflects our inflammation net sales and segment operating income for the three months ended March 31, 2020 and 2019 (in thousands, except percentages).

	For the Three Months Ended March 31,			
	2020	2019	Change	% Change
Net sales	$ 110,546	$ 113,956	$ (3,410)	(3%)
Segment operating income	51,942	51,419	523	1%

The decrease in inflammation net sales during the three months ended March 31, 2020 is described in the *Consolidated Results* section above.

Segment operating income. Inflammation segment operating income increased $0.5 million to $51.9 million during the three months ended March 31, 2020, from $51.4 million during the three months ended March 31, 2019. The increase was primarily attributable to a decrease in selling, general and administrative expenses of $3.5 million and a decrease in research and development expense of $0.2 million, partially offset by a decrease in net sales of $3.4 million as described above.

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, litigation settlements and charges related to discontinuation of the Friedreich's ataxia program, 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,	
	2020	2019
GAAP net loss	**$ (13,591)**	**$ (32,863)**
Depreciation (1)	7,165	1,473
Amortization and step-up:		
Intangible amortization expense (2)	58,575	57,417
Inventory step-up expense	—	115
Interest expense, net (including amortization of debt discount and deferred financing costs)	17,344	27,530
Benefit for income taxes	(19,026)	(1,920)
EBITDA	**50,467**	**51,752**
Other non-GAAP adjustments:		
Share-based compensation (3)	56,421	27,548
Drug substance harmonization costs (4)	290	80
Fees related to refinancing activities (5)	54	142
Acquisition/divestiture-related costs (6)	(6)	1,345
Restructuring and realignment costs (7)	—	20
Loss on debt extinguishment (8)	—	5,586
Charges related to discontinuation of Friedreich's ataxia program (9)	—	(79)
Upfront and milestones payments related to license and collaboration agreements (10)	—	2,000
Total of other non-GAAP adjustments	**56,759**	**36,642**
Adjusted EBITDA	**$ 107,226**	**$ 88,394**

	For the Three Months Ended March 31,	
	2020	2019
GAAP net loss	**$ (13,591)**	**$ (32,863)**
Non-GAAP adjustments:		
Depreciation (1)	7,165	1,473
Amortization and step-up:		
Intangible amortization expense (2)	58,575	57,417
Amortization of debt discount and deferred financing costs (11)	5,569	5,912
Inventory step-up expense	—	115
Share-based compensation (3)	56,421	27,548
Drug substance harmonization costs (4)	290	80
Fees related to refinancing activities (5)	54	142
Acquisition/divestiture-related costs (6)	(6)	1,345
Restructuring and realignment costs (7)	—	20
Loss on debt extinguishment (8)	—	5,586
Charges relating to discontinuation of Friedreich's ataxia program (9)	—	(79)
Upfront and milestone payments related to license and collaboration agreements (10)	—	2,000
Total of pre-tax non-GAAP adjustments	**128,068**	**101,559**
Income tax effect of pre-tax non-GAAP adjustments (12)	(31,262)	(14,751)
Total non-GAAP adjustments	**96,806**	**86,808**
Non-GAAP Net Income	**$ 83,215**	**$ 53,945**
Non-GAAP Earnings Per Share:		
Weighted average ordinary shares – Basic	**190,072,112**	**172,789,209**
Non-GAAP Earnings Per Share – Basic		
GAAP loss per share – Basic	**$ (0.07)**	**$ (0.19)**
Non-GAAP adjustments	0.51	0.50
Non-GAAP earnings per share – Basic	**$ 0.44**	**$ 0.31**
Non-GAAP Net Income	**$ 83,215**	**$ 53,945**
Effect of assumed conversion of Exchangeable Senior Notes, net of tax	1,875	—
Numerator - non-GAAP Net Income	**$ 85,090**	**$ 53,945**
Weighted average ordinary shares – Diluted		
Weighted average ordinary shares – Basic	190,072,112	172,789,209
Ordinary share equivalents	22,984,847	7,496,024
Denominator - weighted average ordinary shares – Diluted	**213,056,959**	**180,285,233**
Non-GAAP Earnings Per Share – Diluted		
GAAP loss per share – Diluted	**$ (0.07)**	**$ (0.19)**
Non-GAAP adjustments	0.51	0.50
Diluted earnings per share effect of ordinary share equivalents	(0.04)	(0.01)
Non-GAAP earnings per share – Diluted	**$ 0.40**	**$ 0.30**

(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 KRYSTEXXA, RAVICTI, PROCYSBI, ACTIMMUNE, TEPEZZA, BUPHENYL, RAYOS, PENNSAID 2%, VIMOVO and MIGERGOT.

(3) 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.

(4) 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 FA 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.

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

(6) Represents expenses, including legal and consulting fees, 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.

(7) Represents expenses, including severance costs and consulting fees, related to restructuring and realignment activities.

(8) During the three months ended March 31, 2019, we recorded a loss on debt extinguishment of $5.6 million in the condensed consolidated statement of comprehensive loss, which reflects the write-off of the deferred financing and debt discount fees related to the $300.0 million term loan repayment.

(9) Represents expenses incurred relating to discontinuation of Friedreich's ataxia program and a reduction to previous charges recorded.

(10) During the three months ended March 31, 2019, we recorded an upfront cash payment of $2.0 million in relation to the collaboration agreement with HemoShear.

(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, 2020, we had an accumulated deficit of $619.3 million. We expect that our sales and marketing expenses will continue to increase as a result of the commercialization of our medicines, including as a result of the commercial launch of TEPEZZA, 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.

As a result of the COVID-19 pandemic and actions taken to slow its spread, the global credit and financial markets have recently 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 continue to deteriorate, it may make any additional debt or equity financing more difficult, more costly or more dilutive.

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. We expect to move to the Deerfield campus in the second half of 2020 and market our Lake Forest office for sub-lease. We expect to make significant capital expenditures during 2020 in order to prepare the Deerfield campus for occupancy. In addition, if we are unable to sub-lease our existing Lake Forest office at rental rates similar to the rates under our existing lease or at all, we would be obligated to continue paying substantial rental payments through the end of the lease term in 2031.

As a result of the FDA approval of TEPEZZA in January 2020, we made a milestone payment of $100.0 million under the agreement for the acquisition of River Vision Development Corp, or River Vision, during the first quarter of 2020.

On April 1, 2020, we acquired Curzion, a privately held development-stage biopharma company, for a $45.0 million upfront cash payment and are obligated to make additional payments contingent on the achievement of development and regulatory milestones. The $45.0 million will be recorded as an in-process research and development expense in the second quarter of 2020.

In April 2020, we entered into an agreement with S.R. One, Limited, or S.R. One, and an agreement with Lundbeckfond Invest A/S, or Lundbeckfond pursuant to which we 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 will be recorded as TEPEZZA developed technology intangible assets in the second quarter of 2020.

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, 2020, we had $754.6 million in cash and cash equivalents and total debt with a book value of $1,358.4 million and face value of $1,418.0 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 twelve 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 could 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 5.500% Senior Notes due 2027, or 2027 Senior Notes, 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, 2020, we issued an aggregate of 2.6 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 $7.0 million in proceeds in connection with such stock option exercises.

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, 2020 and 2019 (in thousands):

	For the Three Months Ended March 31, 2020	2019
Cash, cash equivalents and restricted cash	$ 758,262	$ 1,036,539
Cash (used in) provided by:		
Operating activities	(62,593)	56,168
Investing activities	(218,204)	(1,849)
Financing activities	(39,614)	20,621

Operating Cash Flows

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.

During the three months ended March 31, 2019, net cash provided by operating activities of $56.2 million was primarily attributable to cash collections from net sales, partially offset by payments made during the first quarter of 2019 related to patient assistance costs and commercial rebates for our inflammation segment medicines.

Investing Cash Flows

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 agreement for the acquisition of River Vision, we made a milestone payment of $100.0 million related to FDA approval, during the first quarter of 2020.

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 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.

During the three months ended March 31, 2019, net cash used in investing activities of $1.8 million was primarily attributable to the purchases of property and equipment.

Financing Cash Flows

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.

During the three months ended March 31, 2019, net cash provided by financing activities of $20.6 million was primarily attributable to net proceeds from the issuance of ordinary shares of $327.8 million, partially offset by the repayment of term loans of $300.0 million.

Financial Condition as of March 31, 2020 compared to December 31, 2019

Accounts receivable, net. Accounts receivable, net, increased $16.7 million, from $408.7 million as of December 31, 2019 to $425.4 million as of March 31, 2020. The increase was due to the timing of receipts of accounts receivable.

Inventories, net. Inventories, net, increased $14.4 million, from $53.8 million as of December 31, 2019 to $68.2 million as of March 31, 2020. The increase was primarily related to the increase in production of TEPEZZA.

Prepaid expenses and other current assets. Prepaid expenses and other current assets increased $18.3 million, from $143.6 million as of December 31, 2019 to $161.9 million as of March 31, 2020. The increase was primarily due to a benefit for income taxes recognized during the three months ended March 31, 2020.

Property and equipment, net. Property and equipment, net, increased $112.3 million, from $30.1 million as of December 31, 2019 to $142.4 million as of March 31, 2020. In February 2020, we purchased a three-building campus in Deerfield, Illinois, for total consideration and directly attributable transaction costs of $118.5 million.

Developed technology, net. Developed technology, net, increased $46.8 million, from $1,698.8 million as of December 31, 2019 to $1,745.6 million as of March 31, 2020. During the three months ended March 31, 2020, in connection with the acquisition of River Vision and our license agreement with Roche, we capitalized $105.2 million of developed technology related to TEPEZZA. This was partially offset by amortization of developed technology of $58.6 million during the three months ended March 31, 2020.

Accounts payable. Accounts payable increased $28.6 million, from $21.5 million as of December 31, 2019 to $50.1 million as of March 31, 2020. This increase was primarily due to the timing of invoices received including an increase of $11.5 million in accounts payable related to government rebates.

Accrued expenses. Accrued expenses decreased $29.2 million, from $235.2 million as of December 31, 2019 to $206.0 million as of March 31, 2020. This was primarily due to a decrease in payroll-related accrued expenses of $28.6 million primarily due to payments under compensation plans and lower accrued interest of $11.8 million, partially offset by an increase of $4.0 million in allowance for returns and $3.4 million in accrued consulting and professional service fees.

Accrued trade discounts and rebates. Accrued trade discounts and rebates decreased $130.1 million, from $466.4 million as of December 31, 2019 to $336.3 million as of March 31, 2020. This was primarily due to a decrease of $73.2 million in accrued co-pay and other patient assistance costs primarily due lower utilization of our patient assistance programs, the impact of generic competition on VIMOVO sales and the timing of co-pay payments, a $48.9 million decrease in accrued commercial rebates and wholesaler fees primarily due to an increased proportion of orphan segment medicines sold and the impact of generic competition on VIMOVO sales and $8.0 million decrease in accrued government rebates and chargebacks.

Contractual Obligations

During the three months ended March 31, 2020, 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, 2019, except for our obligations described in Note 19, Subsequent Events, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q.

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. A summary of our significant accounting policies is included in Note 2 to our Annual Report on Form 10-K for the year ended December 31, 2019.

During the three months ended March 31, 2020, there have been no significant changes in our application of our critical accounting policies.

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. Term loans under our Credit Agreement 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%. The loans under our incremental revolving credit facility (the "Revolving Credit Facility") bear interest, at our 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 our leverage ratio is less than or equal to 2.00 to 1.00. Our approximately $418.0 million of senior secured term loans under the Credit Agreement is based on LIBOR. As of March 31, 2020, the Revolving Credit Facility was undrawn. The one-month LIBOR rate as of April 6, 2020, which was the most recent date the interest rate on the term loan was fixed, was 1.00%, and as a result, the interest rate on our borrowings is currently 3.25% 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 $4.2 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. 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 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, 2020 and December 31, 2019, our top four customers accounted for approximately 88% and 84%, 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, 2020, the end of the period covered by this report.

Changes in Internal Control Over Financial Reporting. During the quarter ended March 31, 2020, 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

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, 2019, as filed with the SEC.

Risks Related to Our Business and Industry

*The COVID-19 global pandemic could 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, can be characterized as a pandemic. The President of the United States declared the COVID-19 pandemic a national emergency and many states and municipalities in the Unites States have announced 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 have implemented work-from-home policies for all employees and have moved to a "virtual" model with respect to our physician, patient and partner support activities. 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 may be adversely impacted by COVID-19 and actions taken to slow its spread. For example, patients may postpone 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 payors, distributors, logistics providers and other third parties that are necessary for our medicines to be prescribed, reimbursed and administered to patients. 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 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 drug products 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. At this time, we consider our inventories on hand to be sufficient to meet our commercial requirements.

In addition, our clinical trials may be affected by COVID-19. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital 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 to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Some clinical sites in the United States have started to slow or stop 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 recently 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 continue to 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, 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 key specialists;
- availability of 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 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 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 and to evaluate the use of KRYSTEXXA in kidney transplant patients. 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 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 encourage patients and physicians to continue 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 encourage patients and physicians to continue 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 and encourage patients and physicians to continue treatment once initiated. 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, studies indicate that physicians do not commonly co-prescribe gastrointestinal, or GI, protective agents to high-risk patients taking nonsteroidal anti-inflammatory drugs, or NSAIDs. We believe this is due in part to a lack of awareness among physicians prescribing NSAIDs regarding the risk of NSAID-induced upper GI ulcers, in addition to the inconvenience of prescribing two separate medications and patient compliance issues associated with multiple prescriptions. If physicians remain unaware of, or do not otherwise believe in, the benefits of combining GI protective agents with NSAIDs, our market opportunity for DUEXIS will be limited. Some physicians may also be reluctant to prescribe DUEXIS due to the inability to vary the dose of ibuprofen and naproxen, respectively, or if they believe treatment with NSAIDs or GI protective agents other than those contained in DUEXIS, including those of its competitors, would be more effective for their patients. 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 achieve or 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).

The COVID-19 pandemic and actions taken to slow its spread has had and will continue to have a negative impact on sales of our medicines. For example, in March 2020 we transitioned our sales force to a virtual model such that they no longer have in-person interactions with healthcare professionals. While we have attempted to maintain the effectiveness of our sales and marketing efforts in this 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 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 we expect this to negatively impact 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, we expect that sales of KRYSTEXXA will be negatively impacted in future quarters. 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.

*Our future prospects are highly dependent on our ability to successfully formulate 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, KRYSTEXXA, TEPEZZA, RAVICTI, PROCYSBI and ACTIMMUNE, 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 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 commercialization strategy for TEPEZZA has four components: (i) driving early uptake by continuing to define the role of TEPEZZA in the treatment of thyroid eye disease, or TED, and getting uptake from treating physicians; (ii) continuing to develop the TED market by driving awareness of the disease severity and benefits of treatment, educating the appropriate treating physicians on the urgency to diagnose and treat TED and continuing to drive patients' awareness of TED; (iii) supporting TEPEZZA with our comprehensive approach that includes a high-touch, patient-centric model; and (iv) facilitating patient and physician access to TEPEZZA.

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 the launch and 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. We also do not know 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. Further, the status of reimbursement codes for TEPEZZA could also affect reimbursement. J codes, Q codes and C codes are reimbursement codes maintained by the Centers for Medicare & Medicaid Services, or CMS, that are typically used to report injectable drugs that ordinarily cannot be self-administered. Initially, TEPEZZA will be reimbursed through a non-specific miscellaneous J code. The non-specific miscellaneous J code is used for a wide variety of products and health plans may have more difficulty determining the actual product used and billed for the patient. As a result, these claims must often be submitted with additional information and manually processed, which can create delays in claims processing times as well as increasing the likelihood for claim errors. These delays and claims errors may in turn slow adoption of TEPEZZA until a product-specific reimbursement code is issued by the CMS. Thus, significant uncertainty remains regarding the commercial potential of TEPEZZA. If the launch or commercialization of TEPEZZA is 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 achieve and 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 2019, 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 biopharma 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, 2020, we had approximately 455 sales representatives in the field, consisting of approximately 200 orphan disease sales representatives (including approximately 50 TEPEZZA sales representatives) and 255 inflammation 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, 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. We are required to expend significant time and resources to train our sales force to be credible and persuasive in convincing physicians to prescribe and pharmacists to dispense 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 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 and RAYOS 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 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 Centers for Medicare & Medicaid Services 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” scheme 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 (approximately 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 Centers for Medicare & Medicaid Services 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. That policy is currently undergoing litigation.

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 been considering proposals that would 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. 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. 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 Europe, 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.

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 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 outside of North America and Japan to Medical Need Europe AB, part of the Immedica Group, or Immedica, in December 2018, 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. Nuvo Pharmaceuticals Inc. (formerly known as Nuvo Research Inc.), or Nuvo, has retained its rights to PENNSAID 2% in territories outside of the United States. In March 2017, Nuvo 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 Nuvo 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 and Japan, over Chiesi's activities with respect to PROCYSBI in the EMEA, or over Nuvo'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 Nuvo 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 and Nuvo, 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 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 failed 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 Nuvo, 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 Nuvo 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. 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. If AGC Biologics failed to supply such drug substance, it may lead to TEPEZZA supply constraints.

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. For example, BASF Corporation, or BASF, our manufacturer of one of the APIs in DUEXIS, ibuprofen in a direct compression blend called DC85, previously notified us that it was not able to supply DC85 due to a technical issue at its manufacturing facility in Bishop, Texas during 2018. During 2019, BASF has supplied us with a limited amount of DC85 and informed us of their intention to return to full supply. We consider our DUEXIS inventory on hand to be sufficient to meet current and future commercial requirements. However, we cannot guarantee that BASF's manufacturing facility will return to full operations or that we will be able to enter into a new supply agreement with BASF for DC85. 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 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 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.

While KRYSTEXXA faces limited direct competition, a number of competitors have medicines in Phase 1 or Phase 2 trials, including Selecta Biosciences Inc. which has presented Phase 2 clinical data and is conducting a six-month trial comparing their candidate that uses an immunomodulator to KRYSTEXXA alone. 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., and an enzyme replacement for a specific UCD subtype (ARG) by Aeglea Bio Therapeutics Inc. PROCYSBI faces competition from Cystagon (immediate-release cysteamine bitartrate capsules) for the treatment of cystinosis 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. 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. is also conducting Phase 2 clinical studies of a medicine candidate for the treatment of active TED, also referred to as Graves' ophthalmopathy. 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.

Patent litigation is currently pending in the United States District Court for the District of New Jersey against Actavis Laboratories UT, Inc., formerly known as Watson Laboratories, Inc., Actavis, Inc. and Actavis plc, or collectively Actavis, who intend to market a generic version of PENNSAID 2% prior to the expiration of certain of our patents listed in the FDA's Orange Book, or the Orange Book. These cases arise from Paragraph IV Patent Certification notice letters from Actavis advising it had filed an Abbreviated New Drug Application, or ANDA, with the FDA seeking approval to market a generic version of PENNSAID 2% before the expiration of the patents-in-suit.

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. As a result, we have repositioned our promotional efforts previously made on VIMOVO to the other inflammation segment medicines and expect that our VIMOVO net sales will decrease in future periods.

Patent litigation is currently pending in the United States District Court for the District of Delaware against Alkem Laboratories, Inc., or Alkem, who intends to market a generic version of DUEXIS prior to the expiration of certain of our patents listed in the Orange Book. This case arises from Paragraph IV Patent Certification notice letters from Alkem advising it had filed an ANDA with the FDA seeking approval to market a generic version of DUEXIS before the expiration of the patents-in-suit.

If we are unsuccessful in any of the PENNSAID 2% cases or DUEXIS case, we will likely face generic competition with respect to PENNSAID 2% and/or DUEXIS and sales of PENNSAID 2% and/or DUEXIS 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 research and development 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.

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.

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 has been granted orphan drug exclusivity by the FDA, which we expect will provide orphan drug marketing exclusivity in the United States until December 2020, with exclusivity for PROCYSBI extending to 2022 for patients ages one to six years. In addition, 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. 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.

*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 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 have limited ability to influence whether physicians 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 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, PENNSAID 2% and VIMOVO.

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. 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. 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, 2020, we employed approximately 1,185 full-time employees, including approximately 455 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, 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, 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, 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.

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 out research and development function over the last two 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.

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 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. For example, we assumed responsibility for the patent infringement litigation with respect to RAVICTI upon the closing of our acquisition of Hyperion Therapeutics, Inc., or Hyperion, and we have assumed responsibility for completing post-marketing clinical trials of RAVICTI that are required by the FDA, one of which is ongoing.

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, 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 intra-company 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.

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 intra-company 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. We do not expect these legislative changes to have a material impact on our effective tax rate. The timing of the introduction into Irish tax law of further ATAD measures, such as the interest limitation rules, is unclear. 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 4, 2019, the U.S. Treasury issued Proposed Regulations under Section 250 of the Code, which provide guidance on both the computation of the deductions for GILTI and "foreign-derived intangible income", or FDII, and the determination of FDII. We do not expect to be subject to the GILTI inclusion nor is it expected that the potential FDII deduction would have a material impact on our effective tax rate.

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.

On April 8, 2020, the U.S. Treasury published in the Federal Register the Final Regulations for Section 267A (commonly referred to as the "Anti-Hybrid Rules"). The Final Regulations for Section 267A provide several rules expanding the reach and scope of Section 267A of the Code particularly involving the payment of interest and royalties to certain branches, reverse hybrid entities, and other hybrid mismatch arrangements. We are in the process of assessing the impact, if any, of the provisions of the Final Regulations for Section 267A on our financial statements. If the Anti-Hybrid Rules under the Final Regulations for Section 267A are applicable to us, we will recognize a one-time tax provision of $15.2 million during the three months ended June 30, 2020. On April 8, 2020, the U.S. Treasury also published in the Federal Register further Proposed Regulations relating to Section 267A, conduit financing rules and the treatment of certain payments under the GILTI provisions. We are currently in the process of assessing these Proposed Regulations and the potential impact on us. We do not expect these Proposed Regulations to have a material impact on our effective tax rate.

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, with respect to our current medicines, and will be, with respect to any other medicine or medicine candidate for which we obtain FDA or EMA approval or which we acquire, subject to ongoing FDA or EMA obligations and continued regulatory review, which may result in significant additional expense. Additionally, any other medicine candidate, if approved by the FDA or EMA, could be subject to labeling and other restrictions and market withdrawal, and we may be subject to 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 achieve or 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 to regulate and to change the healthcare system in ways that could affect our ability to sell our medicines profitably. In the United States and elsewhere, there is significant interest in promoting changes in healthcare systems with the stated goals of containing healthcare costs (including a number of proposals pertaining to prescription drugs, specifically), improving quality and/or expanding access. In the United States, the pharmaceutical industry has been a particular focus of these efforts and has been significantly affected by major legislative initiatives.

If we are found to be in violation of any of these laws or any other federal or state regulations, we may be subject to significant civil and/or criminal penalties, damages, fines, exclusion, additional reporting requirements and/or oversight from federal health care programs and 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 remain judicial and Congressional challenges to certain aspects of the ACA, as well as recent efforts by the Trump administration to repeal or replace certain aspects of the ACA. Since January 2017, President Trump has signed two Executive Orders and other directives designed to delay the implementation of certain provisions of the ACA. Concurrently, Congress has considered legislation that would repeal or repeal and 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 such as removing penalties, starting January 1, 2019, for not complying with the ACA's individual mandate to carry health insurance, and eliminating the implementation of certain ACA-mandated fees, and increasing the point-of-sale discount that is owed by pharmaceutical manufacturers who participate in Medicare Part D. In particular, the Tax Act included a provision which repealed, effective January 1, 2019, the tax-based shared responsibility payment imposed by the ACA on certain individuals who fail to maintain qualifying health coverage for all or part of a year that is commonly referred to as the "individual mandate". 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 eliminates the health insurer tax. 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. On March 2, 2020, the United States Supreme Court granted the petitions for writs of certiorari to review this case, and has allotted one hour for oral arguments, which are expected to occur in the fall. It is unclear how such litigation and other efforts to repeal and replace the ACA will impact the ACA and our business.

Likewise, in the 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 products and any approved product 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.

In addition, drug pricing by pharmaceutical companies has come under increased scrutiny. Specifically, there have been several recent state and U.S. Congressional inquiries, proposed federal and state legislation and state laws enacted designed to, among other things, bring more transparency to drug pricing by requiring drug companies to notify insurers and government regulators of price increases and provide an explanation of the reasons for the increase, reduce the out-of-pocket cost of prescription drugs, review the relationship between pricing and manufacturer patient programs, reduce the cost of drugs under Medicare, and reform government program reimbursement methodologies. This scrutiny has resulted in several recent congressional inquiries and proposed and enacted federal and state legislation designed to, among other things, bring more transparency to product pricing, review the relationship between pricing and manufacturer patient programs, and reform government program reimbursement methodologies for products. For example, legislation signed into law in 2017 in California requires drug manufactures to provide advance notice and explanation to state regulators, health plans and insurers and PBMs for price increases of more than 16% over two years. At the federal level, the President's budget proposal for the fiscal year 2021 includes a $135 billion allowance to support legislative proposals seeking to reduce drug prices, increase competition, lower out-of-pocket drug costs for patients, and increase patient access to lower-cost generic and biosimilar drugs. On March 10, 2020, the Trump administration sent "principles" for drug pricing to Congress, calling for legislation that would, among other things, cap Medicare Part D beneficiary out-of-pocket pharmacy expenses, provide an option to cap Medicare Part D beneficiary monthly out-of-pocket expenses, and place limits on pharmaceutical price increases. These principles build upon the Trump administration's previously released "Blueprint to Lower Drug Prices and Reduce Out-of-Pocket Costs", or Blueprint. The Blueprint contained several potential regulatory actions and legislative recommendations aimed at lowering prescription drug prices including measures to promote innovation and competition for biologics, changes to Medicare Part D to give plan sponsors more leverage when negotiating prices with manufacturers and updating the Medicare drug-pricing dashboard to make price increases and generic competition more transparent. HHS has solicited feedback on some of these measures and, at the same, has implemented others under its existing authority. For example, in May 2019, CMS issued a final rule to allow Medicare Advantage plans the option to use step therapy for Part B drugs beginning January 1, 2020. This final rule codified CMS's policy change that was effective January 1, 2019. In addition, certain governmental initiatives, if enacted by Congress and HHS, could lead to changes to Medicare Parts B and D. Further, the Bipartisan Budget Act of 2018, among other things, amended the ACA, effective January 1, 2019, to close the coverage gap in most Medicare drug plans, commonly referred to as the "donut hole". The majority of our medicines are purchased by private payers, and much of the focus of pending legislation is on government program reimbursement. In December 2019, the Further Consolidated Appropriations Act was signed into law which included the Creating and Restoring Equal Access to Equivalent Samples Act, or CREATES Act. The CREATES Act allows generic drug manufacturers to bring suit against a brand name manufacturer to compel the provision of brand samples if the generic manufacturer has made a request for samples and the brand manufacturer fails to deliver sufficient quantities of the sample on commercially reasonable, market-based terms within 31 days of receipt of the request. Congress and the Trump administration have each indicated that it will continue to seek new legislative and/or administrative measures to control drug costs. Additionally, it is possible that additional governmental action is taken to address the COVID-19 pandemic. 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 or through our customers, 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 beneficiary inducements, and similar state and local laws, federal and state privacy and security laws, 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 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/European Economic Area, 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. If we are unsuccessful with our HorizonCares programs, any other 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.

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 and their immediate family members. In November 2019, HHS published a final 2020 Physician Fee Schedule rule which for calendar year 2021, expands the definition of “covered recipients” for which reporting of payments and transfers is required to be submitted beginning in 2022, to include physician assistants, nurse practitioners, clinical nurse specialists, 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 encourage or assist 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. 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 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. With respect to PROCYSBI, the most common side effects include vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue, rash and headache. 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 common side effects observed in pivotal trials for ACTIMMUNE were “flu-like” or constitutional symptoms such as fever, headache, chills, myalgia and fatigue. 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. 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.

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 enforces 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 may require us to perform additional clinical trials before approving our marketing applications. We cannot assure that, upon inspection, the FDA 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.

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.

In addition, our clinical trials may be affected by COVID-19. Clinical site initiation and patient enrollment may be delayed due to prioritization of hospital 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 to comply with clinical trial protocols if quarantines impede patient movement or interrupt healthcare services. Some clinical sites in the United States have started to slow or stop 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.

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. 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.

*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 Lake Forest, Illinois. If our Dublin or Lake Forest 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 are dependent upon our own or third-party information technology systems, infrastructure and data, including mobile technologies, to operate our business. The multitude and complexity of our computer systems may make them vulnerable to service interruption or destruction, disruption of data integrity, 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. Cyberattacks are increasing in their frequency, sophistication and intensity. Cyberattacks could include the deployment of harmful malware, denial-of-service, social engineering and other means to affect service reliability and threaten data confidentiality, integrity and availability. Our business partners 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. 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, a 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, our liability insurance may not be sufficient in type or amount to cover us against claims related to security breaches, cyberattacks and other related breaches.

*We are subject to extensive 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 provided to the individuals, 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, 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.

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 cause of action for data breaches. Despite amendments and multiple revisions of draft regulations, 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. As we expand our operations and trials (both preclinical or clinical), the CCPA may increase our compliance costs and potential liability. Some observers have noted that the CCPA could mark the beginning of a trend toward more stringent privacy legislation in the United States. Other states are beginning to pass similar laws.

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. If we fail to comply with any such laws or regulations, we may face significant fines and penalties that could adversely affect our business, financial condition and results of operations. 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.

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 Business 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.

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. We recorded an operating loss of $16.5 million for the three months ended March 31, 2020, and an operating income of $126.6 million and $37.9 million for the years ended December 31, 2019 and 2018, respectively. We recorded a net loss of $13.6 million for the three months ended March 31, 2020, a net income of $573.0 million for the year ended December 31, 2019, and a net loss of $38.4 million for the year ended December 31, 2018. As of March 31, 2020, we had an accumulated deficit of $619.3 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, costs associated with our acquisition transactions and costs associated with derivative liability accounting. 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 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 have limited sources of revenues and significant expenses. We cannot be certain that we will achieve or 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 achieve and 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 achieve or 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 will be sufficient to fund our operations based on our current expectations of continued revenue growth, 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 recently 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 continue to 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 research and development 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, 2020, we had $1,358.4 million book value, or $1,418.0 million aggregate principal amount of indebtedness, including $418.0 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.

The credit agreement and the indenture governing our 5.500% 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 recently 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 continue to 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 the 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 the 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. 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 2020 through 2028. In addition, we recognized $32.2 million of federal net operating losses, $2.2 million of state net operating losses and $9.5 million of federal tax credits following our acquisition of River Vision Development Corp. These acquired federal net operating losses and tax credits are subject to an annual limitation of $2.6 million. 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. It remains uncertain if and to what extent various U.S. states will conform 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 the Vidara Merger with respect to certain intra-company 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 intra-company 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 continue to 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.

The United Kingdom's referendum to leave the EU and the United Kingdom'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 United Kingdom and the EU, the United Kingdom will be subject to a transition period, or Transition Period, until December 31, 2020, during which EU rules will continue to apply. Negotiations between the United Kingdom and the EU are expected to continue in relation to the customs and trading relationship between the United Kingdom and the EU following the expiry of the Transition Period. During this period of negotiation and afterwards, 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.

At March 31, 2020, we had $754.6 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, 2020, 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.

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 comprised 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 agreements and the indenture governing our 2.50% Exchangeable Senior Notes due 2022, or Exchangeable Senior Notes. 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 United States District Court for the District of New Jersey against Actavis, who intend to market a generic version of PENNSAID 2% 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 Actavis advising they had filed an ANDA with the FDA seeking approval to market a generic version of PENNSAID 2% before the expiration of the patents-in-suit. For a more detailed description of the PENNSAID 2% 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 for the District of New Jersey and the Court of Appeals for the Federal Circuit against Dr. Reddy's for marketing a generic version of VIMOVO before the expiration of certain of our patents listed in the Orange Book. The cases arise from Paragraph IV Patent Certification notice letters from Dr. Reddy's, advising that it had filed an ANDA with the FDA seeking approval to market generic versions of VIMOVO before the expiration of the patents-in-suit. On July 30, 2019, the Federal Circuit Court of Appeals denied our request for a rehearing of the Court's invalidity ruling against the 6,926,907 and 8,557,285 patents for VIMOVO coordinated-release tablets. As a result, the District Court entered judgment in September 2019 invalidating the '907 and '285 patents, which ended any restriction against the FDA from granting final approval to Dr. Reddy's generic version of VIMOVO. On February 18, 2020, the FDA granted final approval for Dr. Reddy's generic version of VIMOVO. On February 27, 2020, Dr. Reddy's launched its generic version of VIMOVO in the United States. Patent litigation against Dr. Reddy's for infringement continues with respect to certain patents in the New Jersey District Court. We have repositioned our promotional efforts previously made on VIMOVO to the other inflammation segment medicines and expect that our VIMOVO net sales will decrease in future periods. For a more detailed description of the VIMOVO 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 for the District of Delaware against Alkem, who intends to market a generic version of DUEXIS prior to the expiration of certain of our patents listed in the Orange Book. This case arises from Paragraph IV Patent Certification notice letters from Alkem advising it 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.

We intend to vigorously defend our intellectual property rights relating to our medicines, but we cannot predict the outcome of the DUEXIS case and the PENNSAID 2% cases. 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.

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.

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 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.

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 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 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.

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 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.

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.

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 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.

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.

In addition, any conversion or exchange of our Exchangeable Senior Notes, whether pursuant to their terms or pursuant to privately negotiated transactions between the issuer and/or us and a holder of such securities, could depress the market price for our ordinary shares.

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 2014 Equity Incentive Plan, 2014 Non-Employee Equity Plan, as amended, and 2014 Employee Share Purchase Plan, as amended, 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.

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.

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.

ITEM 6. EXHIBITS

Exhibit Number	Description of Document
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 March 13, 2015, by and among Horizon Therapeutics Public Limited Company, Horizon Therapeutics Investment Limited and U.S. Bank National Association (incorporated by reference to Exhibit 4.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on March 13, 2015).
4.2	Form of 2.50% Exchangeable Senior Note due 2022 (incorporated by reference to Exhibit 4.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on March 13, 2015).
4.3	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).
4.4	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).
4.5	First Supplemental Indenture, dated November 19, 2019, by and between HZNP Finance Limited and U.S. Bank National Association.
4.6	Second Supplemental Indenture, dated April 23, 2020, by and among Horizon Properties Holding LLC, Curzion Pharmaceuticals, Inc. and U.S. Bank National Association.
10.1+	Separation Agreement, dated January 23, 2020, by and between Horizon Therapeutics USA, Inc. and Shao-Lee Lin, M.D., Ph.D. (incorporated by reference to Exhibit 10.45 to Horizon Therapeutics Public Limited Company's Annual Report on Form 10-K, filed on February 26, 2020).
10.2+	Horizon Therapeutics Public Limited Company 2020 Equity Incentive Plan (incorporated by reference to Exhibit 99.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on May 1, 2020).
10.3+	Horizon Therapeutics Public Limited Company 2020 Employee Share Purchase Plan (incorporated by reference to Exhibit 99.2 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on May 1, 2020).
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)

+ Indicates management contract or compensatory plan.

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 6, 2020

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

Date: May 6, 2020

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

Exhibit 4.5

FIRST SUPPLEMENTAL INDENTURE

FIRST SUPPLEMENTAL INDENTURE (this "*Supplemental Indenture*"), dated as of November 19, 2019, between HZNP FINANCE LIMITED (the "*Guaranteeing Entity*"), a subsidiary of Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc.), a Delaware corporation (the "*Issuer*"), 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, 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 and in 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, as such, will have any liability for any obligations of the Issuer or the Guarantors under the Notes, this 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 ISSUER AND THE GUARANTORS 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 ISSUER AND THE GUARANTORS 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 ISSUER AND THE GUARANTORS, 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 ISSUER AND THE GUARANTORS 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 ISSUER AND THE GUARANTORS, 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 EACH OF THE GUARANTORS 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.

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.

HZNP FINANCE LIMITED

By: */s/ Kevin Insley*
Name: Kevin Insley
Title: Director

U.S. BANK NATIONAL ASSOCIATION,
as Trustee

By: */s/ Richard Prokosch*
Name: Richard Prokosch
Title: Vice President

Exhibit 4.6

SECOND SUPPLEMENTAL INDENTURE

SECOND SUPPLEMENTAL INDENTURE (this "*Supplemental Indenture*"), dated as of April 23, 2020, between HORIZON PROPERTIES HOLDING LLC and CURZION PHARMACEUTICALS, INC. (each, a "*Guaranteeing Entity*"), each a subsidiary of Horizon Therapeutics USA, Inc. (formerly known as Horizon Pharma USA, Inc.), a Delaware corporation (the "*Issuer*"), 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, 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 each Guaranteeing Entity shall execute and deliver to the Trustee a supplemental indenture pursuant to which such 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, each 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. Each Guaranteeing Entity hereby agrees to provide an unconditional Guarantee on the terms and subject to the conditions set forth in the Note Guarantee and in 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, as such, will have any liability for any obligations of the Issuer or the Guarantors under the Notes, this 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 ISSUER AND THE GUARANTORS 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 ISSUER AND THE GUARANTORS 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 ISSUER AND THE GUARANTORS, 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 ISSUER AND THE GUARANTORS 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 ISSUER AND THE GUARANTORS, 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 EACH OF THE GUARANTORS 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 each 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.

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.

HORIZON PROPERTIES HOLDING LLC

By: */s/ Paul Hoelscher*
Name: Paul Hoelscher
Title: Executive Vice President and Chief Financial Officer

CURZION PHARMACEUTICALS, INC.

By: */s/ Paul Hoelscher*
Name: Paul Hoelscher
Title: Executive Vice President and Chief Financial Officer

U.S. BANK NATIONAL ASSOCIATION,
as Trustee

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

Exhibit 31.1

Certification of Principal Executive Officer

I, Timothy 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 6, 2020

/s/ Timothy Walbert
Timothy 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 6, 2020

/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 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, 2020 (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 6, 2020

/s/ Timothy Walbert
Timothy 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, 2020 (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 6, 2020

/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.