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HORIZON THERAPEUTICS PUBLIC LTD CO

FORM 10-Q

(Quarterly Report)

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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 June 30, 2023

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	**98-1195602**
(State or other jurisdiction of incorporation or organization)	**(I.R.S. Employer Identification No.)**
70 St. Stephen's Green Dublin 2, D02 E2X4, 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 August 2, 2023: 228,994,568.

HORIZON THERAPEUTICS PLC

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PART I. FINANCIAL INFORMATION

ITEM 1. FINANCIAL STATEMENTS

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

	As of June 30, 2023	As of December 31, 2022
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 2,464,623	$ 2,352,833
Restricted cash	4,791	4,755
Accounts receivable, net	717,417	676,347
Inventories, net	170,325	169,559
Prepaid expenses and other current assets	564,808	449,349
Total current assets	**3,921,964**	**3,652,843**
Property, plant and equipment, net	362,326	340,509
Developed technology and other intangible assets, net	2,486,565	2,664,777
In-process research and development	810,000	810,000
Goodwill	1,010,538	1,010,538
Deferred tax assets, net	444,306	431,814
Other long-term assets	263,042	204,135
Total assets	**$ 9,298,741**	**$ 9,114,616**
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 85,543	$ 155,800
Accrued expenses and other current liabilities	496,669	457,557
Accrued trade discounts and rebates	319,469	319,780
Long-term debt—current portion	16,000	16,000
Total current liabilities	**917,681**	**949,137**
LONG-TERM LIABILITIES:		
Long-term debt, net	2,541,458	2,546,837
Deferred tax liabilities, net	264,815	342,017
Other long-term liabilities	263,828	204,451
Total long-term liabilities	**3,070,101**	**3,093,305**
COMMITMENTS AND CONTINGENCIES		
SHAREHOLDERS' EQUITY:		
Ordinary shares, $0.0001 nominal value; 600,000,000 shares authorized at June 30, 2023 and December 31, 2022; 229,323,393 and 227,625,913 shares issued at June 30, 2023 and December 31, 2022, respectively; and 228,939,027 and 227,241,547 shares outstanding at June 30, 2023 and December 31, 2022, respectively	23	23
Treasury stock, 384,366 ordinary shares at June 30, 2023 and December 31, 2022	(4,585)	(4,585)
Additional paid-in capital	4,522,145	4,474,199
Accumulated other comprehensive income	21,612	12,528
Retained earnings	771,764	590,009
Total shareholders' equity	**5,310,959**	**5,072,174**
Total liabilities and shareholders' equity	**$ 9,298,741**	**$ 9,114,616**

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

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

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	**2022**	**2023**	**2022**
Net sales	$ 944,959	$ 876,411	$ 1,777,018	$ 1,761,656
Cost of goods sold	219,958	230,216	428,521	445,278
Gross profit	**725,001**	**646,195**	**1,348,497**	**1,316,378**
OPERATING EXPENSES:				
Research and development	150,035	103,246	284,183	206,378
Selling, general and administrative	434,125	398,221	887,479	770,955
Impairment of goodwill	—	56,171	—	56,171
Gain on sale of asset	(2,000)	—	(2,000)	—
Total operating expenses	**582,160**	**557,638**	**1,169,662**	**1,033,504**
Operating income	**142,841**	**88,557**	**178,835**	**282,874**
OTHER EXPENSE, NET:				
Interest expense, net	(12,098)	(21,409)	(27,638)	(42,665)
Foreign exchange gain	326	28	417	448
Other income (expense), net	4,183	(2,389)	2,840	(3,131)
Total other expense, net	**(7,589)**	**(23,770)**	**(24,381)**	**(45,348)**
Income before expense (benefit) for income taxes	**135,252**	**64,787**	**154,454**	**237,526**
Expense (benefit) for income taxes	8,181	3,813	(27,301)	(27,709)
Net income	**$ 127,071**	**$ 60,974**	**$ 181,755**	**$ 265,235**
Net income per ordinary share—basic	$ 0.56	$ 0.27	$ 0.80	$ 1.16
Weighted average ordinary shares outstanding—basic	228,743,143	230,020,004	228,571,356	229,559,715
Net income per ordinary share—diluted	$ 0.54	$ 0.26	$ 0.78	$ 1.12
Weighted average ordinary shares outstanding—diluted	233,935,591	236,166,384	233,938,149	236,077,147
OTHER COMPREHENSIVE INCOME (LOSS), NET OF TAX				
Foreign currency translation adjustments	$ 1,409	$ (1,433)	$ 794	$ (1,893)
Pension and other post-employment benefit plan remeasurements	179	(547)	2,003	(222)
Interest rate swap contracts designated as cash flow hedges	13,339	2,011	6,287	2,011
Other comprehensive income (loss)	**14,927**	**31**	**9,084**	**(104)**
Comprehensive income	**$ 141,998**	**$ 61,005**	**$ 190,839**	**$ 265,131**

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 Capital	Accumulated Other Comprehensive Income	Retained Earnings	Total Shareholders' Equity
	Shares	Amount	Shares	Amount				
Balances at December 31, 2022	**227,625,913**	**$ 23**	**384,366**	**$ (4,585)**	**$ 4,474,199**	**$ 12,528**	**$ 590,009**	**$ 5,072,174**
Issuance of ordinary shares in conjunction with the exercise of stock options and the vesting of restricted stock units and performance stock units	1,334,792	—	—	—	3,421	—	—	3,421
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(87,549)	—	—	(87,549)
Share-based compensation	—	—	—	—	58,673	—	—	58,673
Interest rate swap contracts designated as cash flow hedges	—	—	—	—	—	(7,052)	—	(7,052)
Pension and other post-employment benefit plan remeasurements	—	—	—	—	—	1,824	—	1,824
Foreign currency translation adjustments	—	—	—	—	—	(615)	—	(615)
Net income	—	—	—	—	—	—	54,684	54,684
Balances at March 31, 2023	**228,960,705**	**$ 23**	**384,366**	**$ (4,585)**	**$ 4,448,744**	**$ 6,685**	**$ 644,693**	**$ 5,095,560**
Issuance of ordinary shares in conjunction with the exercise of stock options and the vesting of restricted stock units and performance stock units	168,967	—	—	—	2,628	—	—	2,628
Issuance of ordinary shares in conjunction with the Employee Share Purchase Plan	193,721	—	—	—	14,912	—	—	14,912
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(4,506)	—	—	(4,506)
Share-based compensation	—	—	—	—	60,367	—	—	60,367
Interest rate swap contracts designated as cash flow hedges	—	—	—	—	—	13,339	—	13,339
Pension and other post-employment benefit plan remeasurements	—	—	—	—	—	179	—	179
Foreign currency translation adjustments	—	—	—	—	—	1,409	—	1,409
Net income	—	—	—	—	—	—	127,071	127,071
Balances at June 30, 2023	**229,323,393**	**$ 23**	**384,366**	**$ (4,585)**	**$ 4,522,145**	**$ 21,612**	**$ 771,764**	**$ 5,310,959**

	Ordinary Shares		Treasury Stock		Additional Paid-in Capital	Accumulated Other Comprehensive Loss	Retained Earnings	Total Shareholders' Equity
	Shares	Amount	Shares	Amount				
Balances at December 31, 2021	**227,760,936**	**$ 23**	**384,366**	**$ (4,585)**	**$ 4,373,337**	**$ (14,987)**	**$ 318,605**	**$ 4,672,393**
Issuance of ordinary shares in conjunction with the exercise of stock options and the vesting of restricted stock units and performance stock units	2,112,964	—	—	—	9,071	—	—	9,071
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(115,108)	—	—	(115,108)
Share-based compensation	—	—	—	—	47,347	—	—	47,347
Pension and other post-employment benefit plan remeasurements	—	—	—	—	—	325	—	325
Foreign currency translation adjustments	—	—	—	—	—	(460)	—	(460)
Net income	—	—	—	—	—	—	204,261	204,261
Balances at March 31, 2022	**229,873,900**	**$ 23**	**384,366**	**$ (4,585)**	**$ 4,314,647**	**$ (15,122)**	**$ 522,866**	**$ 4,817,829**
Issuance of ordinary shares in conjunction with the exercise of stock options and the vesting of restricted stock units and performance stock units	660,784	—	—	—	12,951	—	—	12,951
Issuance of ordinary shares in conjunction with the Employee Share Purchase Plan	182,109	—	—	—	13,884	—	—	13,884
Ordinary shares withheld for payment of employees' withholding tax liability	—	—	—	—	(5,419)	—	—	(5,419)
Share-based compensation	—	—	—	—	45,281	—	—	45,281
Pension and other post-employment benefit plan remeasurements	—	—	—	—	—	(547)	—	(547)
Foreign currency translation adjustments	—	—	—	—	—	(1,433)	—	(1,433)
Interest rate swap contracts designated as cash flow hedges	—	—	—	—	—	2,011	—	2,011
Net income	—	—	—	—	—	—	60,974	60,974
Balances at June 30, 2022	**230,716,793**	**$ 23**	**384,366**	**$ (4,585)**	**$ 4,381,344**	**$ (15,091)**	**$ 583,840**	**$ 4,945,531**

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 Six Months Ended June 30,	
	2023	**2022**
CASH FLOWS FROM OPERATING ACTIVITIES:		
Net income	$ 181,755	$ 265,235
Adjustments to reconcile net income to net cash provided by operating activities:		
Depreciation and amortization expense	191,145	192,538
Equity-settled share-based compensation	118,391	92,449
Amortization of debt discount and deferred financing costs	2,779	3,904
Impairment of goodwill	—	56,171
Gain on sale of asset	(2,000)	—
Deferred income taxes	(91,952)	(3,032)
Foreign exchange and other adjustments	(6,143)	10,566
Changes in operating assets and liabilities:		
Accounts receivable	(41,140)	(40,513)
Inventories	(766)	22,033
Prepaid expenses and other current assets	(108,816)	(71,578)
Accounts payable	(70,233)	(11,980)
Accrued trade discounts and rebates	(552)	20,232
Accrued expenses and other current liabilities	63,390	(76,901)
Other non-current assets and liabilities	11,931	5,863
Net cash provided by operating activities	**247,789**	**464,987**
CASH FLOWS FROM INVESTING ACTIVITIES:		
Purchases of property, plant and equipment	(42,594)	(24,352)
Payments related to license and collaboration agreements	(15,000)	(25,000)
Payments for long-term investments	(4,183)	(4,847)
Receipts from long-term investments	—	4,416
Payments for acquisitions, net of cash acquired	—	(3,122)
Net cash used in investing activities	**(61,777)**	**(52,905)**
CASH FLOWS FROM FINANCING ACTIVITIES:		
Repayment of term loans	(8,000)	(8,000)
Proceeds from the issuance of ordinary shares in connection with stock option exercises	6,049	22,022
Proceeds from the issuance of ordinary shares in connection with the Employee Share Purchase Plan	14,912	13,884
Payment of employee withholding taxes relating to share-based awards	(92,055)	(120,527)
Net cash used in financing activities	**(79,094)**	**(92,621)**
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	4,908	(6,317)
Net increase in cash, cash equivalents and restricted cash	**111,826**	**313,144**
Cash, cash equivalents and restricted cash, beginning of the period	2,357,588	1,584,156
Cash, cash equivalents and restricted cash, end of the period	**$ 2,469,414**	**$ 1,897,300**
SUPPLEMENTAL CASH FLOW INFORMATION:		
Cash paid for interest, net of interest swap payments	$ 74,619	$ 41,778
Cash paid for income taxes, net of refunds received	19,731	13,216
Cash paid for amounts included in the measurement of operating lease liabilities	6,545	4,312
SUPPLEMENTAL NON-CASH FLOW INFORMATION:		
Purchases of property, plant and equipment included in accounts payable and accrued expenses and other current liabilities	$ 8,955	$ 6,579
Lease liabilities arising from obtaining right-of-use assets	47,844	22,521

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

NOTE 1 – BASIS OF PRESENTATION AND BUSINESS OVERVIEW

Basis of Presentation

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

Transaction Agreement with Amgen Inc.

On December 12, 2022, the Company announced that it had entered into a transaction agreement with Amgen Inc. (“Amgen”) and Pillartree Limited (“Pillartree”), a wholly owned subsidiary of Amgen. Subject to the terms of the transaction agreement, Pillartree will acquire the Company (the “Transaction”), pursuant to a scheme of arrangement under Chapter 1 of Part 9 of the Companies Act 2014 of Ireland (the “Scheme”), or under certain circumstances, subject to the terms of the transaction agreement, a takeover offer (as such term is defined under the Irish Takeover Rules). As a result of the Scheme, the Company would become a wholly owned subsidiary of Amgen.

At the effective time of the Scheme (the “Effective Time”), holders of the Company’s ordinary shares will be entitled to receive $116.50 in cash per ordinary share (the “Consideration”). The Company’s equity awards will be treated as set forth in the transaction agreement, such that:

- each option to purchase the Company’s ordinary shares that is outstanding as of immediately prior to the Effective Time (whether or not vested) will, contingent upon and effective as of the Effective Time, be canceled and converted into the right to receive cash, without interest, in an amount equal to (a) the total number of the Company’s ordinary shares subject to such option immediately prior to the Effective Time, multiplied by (b) the excess of (i) the Consideration over (ii) the exercise price payable per share under such option;

- each of the Company’s restricted stock unit (“RSU”) awards, excluding PSUs (as defined below), that is outstanding as of immediately prior to the Effective Time (whether or not vested) will, contingent upon and effective as of the Effective Time, (a) if granted to a non-employee member of the Company’s board of directors or held by a person who, as of the date of the completion of the Transaction, is a former service-provider of the Company, be canceled and converted into the right to receive a cash amount equal to (i) the total number of the Company’s ordinary shares subject to such RSU immediately prior to the Effective Time multiplied by (ii) the Consideration, and (b) if not granted to an individual described in clause (a) above, be canceled and converted into a restricted stock unit (an “Amgen RSU”), denominated in shares of Amgen’s common stock. The number of shares of Amgen common stock subject to each such Amgen RSU will be equal to the product (rounded down to the nearest whole number) of (a) the total number of the Company’s ordinary shares subject to such RSU immediately prior to the Effective Time multiplied by (b) the quotient of (i) the Consideration divided by (ii) the volume weighted average of the per share closing price of Amgen’s common stock on the Nasdaq Global Select Market for five trading days ending on the second business day prior to the completion of the Transaction. Following the Effective Time, each Amgen RSU will continue to be governed by the same terms and conditions (including vesting terms) as were applicable to the applicable RSU immediately prior to the Effective Time; and

- each of the Company’s RSU awards with performance-based vesting or delivery requirements (“PSU”) that is outstanding as of immediately prior to the Effective Time (whether or not vested) will, contingent upon and effective as of the Effective Time, be canceled and converted into the right to receive cash, without interest, in an amount equal to (i) the total number of the Company’s ordinary shares issuable in settlement of such PSU as determined, in accordance with the terms of such PSU, by the compensation committee of the Company’s board of directors (the “Compensation Committee”) prior to the Effective Time multiplied by (ii) the Consideration.

On February 24, 2023, the Company’s shareholders approved the Scheme and certain scheme approval resolutions and amendments to the memorandum and articles of association of Horizon to enable the Scheme to be effected. The closing of the Transaction remains subject to customary closing conditions, including, among other things, (a) the sanction by the Irish High Court of the Scheme and delivery of the court order to the Irish Registrar of Companies, (b) the absence of an order or law that prevents consummation of the Transaction or imposes a burdensome condition (as defined in the transaction agreement), (c) absence of any Material Adverse Effect (as defined in the transaction agreement) from December 12, 2022 to the Sanction Date (as defined in the transaction agreement) that is continuing as of the Sanction Date, (d) the accuracy of the other party’s representations and warranties subject to certain materiality and material adverse effect exceptions and (e) the performance by each party of all of its covenants and agreements under the transaction agreement in all material respects. In connection with the Transaction, the Company and Amgen have received clearances or confirmation of non-applicability related to foreign direct investment in Denmark, Italy, Germany and France and clearances related to antitrust in Germany and Austria.

On May 16, 2023, the Federal Trade Commission ("FTC") filed a complaint in the United States District Court for the Northern District of Illinois seeking a temporary restraining order and preliminary injunction enjoining the Transaction. On May 23, 2023, the district court scheduled an evidentiary hearing on the FTC's request for a preliminary injunction beginning on September 11, 2023. Based on the district court's schedule, the Company, Amgen and the FTC then submitted a stipulated proposed temporary restraining order to the district court providing that the Company and Amgen would not close the Transaction until the earlier of October 31, 2023 or the second business day after the district court rules on the FTC's request for a preliminary injunction (the "Stipulated TRO"). On May 31, 2023, the district court entered a case management order, and on June 2, 2023, the district court issued an order granting the Stipulated TRO. On June 22, 2023, the FTC filed a parallel complaint in its administrative court and an amended complaint was filed in the district court adding several states as additional plaintiffs. On June 29, 2023, the Company and Amgen filed an answer to the amended complaint and counterclaims against the FTC. The Company cannot predict with certainty the outcome of the FTC litigation or whether or when the Company will be able to successfully consummate the pending Transaction.

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 and six months ended June 30, 2023 are not necessarily indicative of the results that may be expected for the year ending December 31, 2023. The December 31, 2022 condensed consolidated balance sheet was derived from audited financial statements, but does not include all disclosures required by GAAP.

Business Overview

Horizon is a global biotechnology company focused on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. The Company's pipeline is purposeful: it applies scientific expertise and courage to bring clinically meaningful therapies to patients. Horizon believes science and compassion must work together to transform lives. The Company's commercial portfolio is currently composed of 12 medicines in the areas of rare diseases, gout, ophthalmology and inflammation.

As of June 30, 2023, the Company's commercial portfolio consisted of the following medicines:

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

NOTE 2 – SUMMARY OF SIGNIFICANT ACCOUNTING POLICIES

Recent Accounting Pronouncements

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

In March 2020, the FASB issued a new accounting standard to ease the financial reporting burdens caused by the expected market transition from the London Inter Bank Offered Rate ("LIBOR") and other interbank offered rates to alternative reference rates, commonly referred to as reference rate reform. The new standard provides temporary optional expedients and exceptions to current GAAP guidance on contract modifications and hedge accounting. Specifically, a modification to transition to an alternative reference rate is treated as an event that does not require contract remeasurement or reassessment of a previous accounting treatment. Moreover, for all types of hedging relationships, an entity is permitted to change the reference rate without having to dedesignate the hedging relationship. In January 2021, the FASB issued a new accounting standard to expand the scope of the original March 2020 standard to include derivative instruments on discounting transactions. In the second quarter of 2022, the Company elected to apply the optional expedients for qualifying modifications to debt agreements under ASC 470 and for the assessment of hedge effectiveness for cash flow hedges affected by reference rate reform. LIBOR was discontinued as of June 30, 2023, and the discontinuation of LIBOR did not have a material impact on interest payments incurred under the Credit Agreement (as defined below). Refer to Note 12 for further details.

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 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, 2022.

NOTE 3 – NET INCOME PER SHARE

The following table presents basic and diluted net income per share for the three and six months ended June 30, 2023 and 2022 (in thousands, except share and per share data):

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	2022	2023	2022
Basic net income per share calculation:				
Numerator - net income	$ 127,071	$ 60,974	$ 181,755	$ 265,235
Denominator - weighted average of ordinary shares outstanding	228,743,143	230,020,004	228,571,356	229,559,715
Basic net income per share	**$ 0.56**	**$ 0.27**	**$ 0.80**	**$ 1.16**

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	2022	2023	2022
Diluted net income per share calculation:				
Numerator - net income	$ 127,071	$ 60,974	$ 181,755	$ 265,235
Denominator - weighted average of ordinary shares outstanding	233,935,591	236,166,384	233,938,149	236,077,147
Diluted net income per share	**$ 0.54**	**$ 0.26**	**$ 0.78**	**$ 1.12**

Basic net income per share is computed by dividing net income by the weighted-average number of ordinary shares outstanding during the period. Diluted net income 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 net income.

During the three and six months ended June 30, 2023 and 2022, the difference between the basic and diluted weighted average ordinary shares outstanding primarily represents the effect of incremental shares from the Company's share-based compensation programs.

The computation of diluted net income per share for the three and six months ended June 30, 2023 excluded 0.4 million and 1.2 million shares subject to equity awards, respectively, because their inclusion would have had an anti-dilutive effect on diluted net income per share. The computation of diluted net income per share for the three and six months ended June 30, 2022 excluded 1.2 million and 3.6 million shares subject to equity awards, respectively, because their inclusion would have had an anti-dilutive effect on diluted net income per share.

NOTE 4 – 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, drug product 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 June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023	December 31, 2022
Raw materials	$ 84,728	$ 44,230
Work-in-process	24,291	25,232
Finished goods	61,306	100,097
Inventories, net	**$ 170,325**	**$ 169,559**

As part of the Viela Bio Inc. ("Viela") acquisition, a step-up in the value of inventory of $151.6 million was recorded, which was composed of $10.1 million for raw materials, $120.9 million for work-in-process and $20.6 million for finished goods during the year ended December 31, 2021. Inventory step-up expense recorded in cost of goods sold relating to UPLIZNA was $1.6 million and $17.4 million for the three months ended June 30, 2023 and 2022, respectively, and was $31.3 million and $44.6 million for the six months ended June 30, 2023 and 2022, respectively. As of June 30, 2023, the total remaining balance of inventory step-up was $1.0 million.

Because inventory step-up expense is related to an acquisition, will not continue indefinitely and has a significant effect on the Company's gross profit, gross margin percentage and net income for all affected periods, the Company discloses balance sheet and income statement amounts related to inventory step-up within the Notes to Condensed Consolidated Financial Statements.

NOTE 5 – PREPAID EXPENSES AND OTHER CURRENT ASSETS

Prepaid expenses and other current assets as of June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023	December 31, 2022
Deferred charge for taxes on intercompany profit	$ 206,232	$ 164,771
Advance payments for inventory	187,002	156,824
Rabbi trust assets	31,890	28,227
Interest rate swap contracts	20,050	15,520
Other prepaid expenses and other current assets	119,634	84,007
Prepaid expenses and other current assets	**$ 564,808**	**$ 449,349**

Advance payments for inventory as of June 30, 2023 and December 31, 2022, primarily represented payments made to the contract manufacturer of TEPEZZA drug substance.

NOTE 6 – PROPERTY, PLANT AND EQUIPMENT

Property, plant and equipment as of June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023	December 31, 2022
Buildings	$ 178,712	$ 173,560
Construction in process	105,457	88,825
Land and land improvements	44,346	44,323
Machinery and equipment	30,728	22,865
Leasehold improvements	26,177	24,428
Furniture and fixtures	21,707	20,318
Software	13,186	13,332
Other	12,713	11,966
	433,026	**399,617**
Less accumulated depreciation	(70,700)	(59,108)
Property, plant and equipment, net	**$ 362,326**	**$ 340,509**

Depreciation expense was $6.7 million and $6.1 million for the three months ended June 30, 2023 and 2022, respectively, and was $12.9 million and $11.9 million for the six months ended June 30, 2023 and 2022, respectively.

NOTE 7 – GOODWILL AND INTANGIBLE ASSETS

Goodwill

The gross carrying amount of goodwill as of June 30, 2023 and December 31, 2022 was $1,010.5 million.

	Total
Balance at December 31, 2021	$1,066,709
Goodwill impairment during the year	(56,171)
Balance at December 31, 2022	**$1,010,538**
Goodwill impairment during the period	—
Balance at June 30, 2023	**$1,010,538**

During the three and six months ended June 30, 2023, there were no goodwill impairment losses.

In May 2022, Apotex Corp. and its affiliate, Apotex Inc. (collectively, “Apotex”), initiated an at-risk launch of a generic version of PENNSAID 2% in the United States. The at-risk launch was expected to have an on-going negative impact on PENNSAID 2% net sales. As a result, the Company determined the generic product launch and the expected impact on PENNSAID 2% to be a triggering event to conduct an interim impairment analysis and an indicator it was more likely than not that the carrying amount of its former inflammation reporting unit exceeded its fair value as of June 30, 2022.

The Company determined the fair value of the former inflammation reporting unit as of June 30, 2022 using the income approach. The cash flow projections were based on a financial forecast developed by management that included net sales projections, which are updated annually, or more frequently based on events that may significantly impact forecasts.

The Company’s interim goodwill impairment test in the second quarter of 2022 indicated an impairment, which represented the difference between the estimated fair value of the former inflammation reporting unit and its carrying value. As a result, the Company recognized an impairment charge of $56.2 million in June 2022 representing the full amount of goodwill for the former inflammation reporting unit.

Intangible Assets

As of June 30, 2023, the Company’s finite-lived intangible assets primarily consisted of developed technology related to ACTIMMUNE, KRYSTEXXA, PROCYSBI, RAVICTI, TEPEZZA and UPLIZNA.

Intangible assets as of June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023			December 31, 2022		
	Cost Basis	Accumulated Amortization	Net Book Value	Cost Basis	Accumulated Amortization	Net Book Value
Developed technology	$ 4,650,292	$ (2,182,864)	$ 2,467,428	$ 4,650,292	$ (2,005,327)	$ 2,644,965
In-process research and development [1]	810,000	—	810,000	810,000	—	810,000
Other intangibles	29,894	(10,757)	19,137	29,894	(10,082)	19,812
Total intangible assets	**$5,490,186**	**$ (2,193,621)**	**$ 3,296,565**	**$ 5,490,186**	**$ (2,015,409)**	**$3,474,777**

(1)In July 2023, the Company received 48-week data for the Phase 2 clinical trial evaluating daxdilimab for the treatment of systemic lupus erythematous (“SLE”). The trial did not meet its primary endpoint and as a result, the Company will continue to work with investigators to assess the data to determine the next steps for the SLE clinical program, if any. The Company’s total in-process R&D assets of $810.0 million as of June 30, 2023 and December 31, 2022, included $20.0 million in relation to the SLE clinical program.

Amortization expense for the three months ended June 30, 2023 and 2022 was $89.6 million and $91.3 million, respectively, and was $178.2 million and $180.6 million for the six months ended June 30, 2023 and 2022, respectively. In-process research and development is not amortized until successful regulatory approval of a project. As of June 30, 2023, estimated future amortization expense was as follows (in thousands):

2023 (July to December)	$ 181,164
2024	359,426
2025	359,426
2026	304,164
2027	253,507
Thereafter	1,028,878
Total	**$ 2,486,565**

NOTE 8 – ACCRUED EXPENSES AND OTHER CURRENT LIABILITIES

Accrued expenses and other current liabilities as of June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023	December 31, 2022
Payroll-related expenses	$ 98,531	$ 121,066
Accrued royalties	88,147	106,126
Income taxes payable	82,790	2,829
R&D and manufacturing programs	82,213	66,725
Allowances for returns	25,367	28,347
Consulting and professional services	23,222	28,915
Advertising and marketing	22,682	12,030
Accrued interest	15,679	15,130
Refund liability [(1)]	14,900	12,218
Accrued upfront and milestone payments	—	15,000
Accrued other	43,138	49,171
Accrued expenses and other current liabilities	**$ 496,669**	**$ 457,557**

(1)The refund liability represents the amount of consideration that the Company may need to refund to Mitsubishi Tanabe Pharma Corporation (“MTPC”) if it does not sell the UPLIZNA drug product that was shipped to MTPC. The refund liability is remeasured at each reporting date to reflect changes in the estimate of variable consideration, with a corresponding adjustment to revenue. Amounts expected to be settled within the 12 months following the balance sheet date are classified as current liabilities in the accompanying balance sheets. Amounts not expected to be settled within the 12 months following the condensed consolidated balance sheet date are classified as long-term liabilities. The following represents the changes to the refund liability for the six months ended June 30, 2023 (in thousands):

Refund liability at December 31, 2022	$ 20,409
Shipments during the six months ended June 30, 2023	16,356
Remeasurement of refund liability recognized as revenue	(5,509)
Refund liability at June 30, 2023	**$ 31,256**
Less: current portion	14,900
Refund liability, net of current portion	**$ 16,356**

NOTE 9 – ACCRUED TRADE DISCOUNTS AND REBATES

Accrued trade discounts and rebates as of June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023	December 31, 2022
Accrued government rebates and chargebacks	$ 272,144	$ 235,216
Accrued commercial rebates and wholesaler fees	30,835	39,965
Accrued co-pay and other patient assistance	16,490	44,599
Accrued trade discounts and rebates	**$ 319,469**	**$ 319,780**
Invoiced commercial rebates and wholesaler fees, co-pay and other patient assistance, and government rebates and chargebacks in accounts payable	3,678	77,350
Total customer-related accruals and allowances	**$ 323,147**	**$ 397,130**

The following table summarizes changes in the Company’s customer-related accruals and allowances from December 31, 2022 to June 30, 2023 (in thousands):

	Government Rebates and Chargebacks	Commercial Rebates and Wholesaler Fees	Co-Pay and Other Patient Assistance	Total
Balance at December 31, 2022	$ 295,558	$ 46,159	$ 55,413	$ 397,130
Current provisions relating to sales during the six months ended June 30, 2023	439,339	80,535	51,588	571,462
Adjustments relating to prior-year sales	(20,279)	(1,400)	(7,420)	(29,099)
Payments relating to sales during the six months ended June 30, 2023	(183,439)	(47,291)	(36,312)	(267,042)
Payments relating to prior-year sales	(259,035)	(43,490)	(46,779)	(349,304)
Balance at June 30, 2023	**$ 272,144**	**$ 34,513**	**$ 16,490**	**$ 323,147**

NOTE 10 – SEGMENT AND OTHER INFORMATION

The Company substantially completed the wind down of its former inflammation business in the fourth quarter of 2022. Effective in the fourth quarter of 2022, management realigned the Company's reportable segments to reflect changes in the manner in which the chief operating decision maker ("CODM") assesses financial information for decision-making purposes. The Company transitioned its two reportable segments, the inflammation segment and the orphan segment, to one reportable segment for the year ended December 31, 2022. All prior year amounts have been reclassified to conform to the Company's current reporting structure.

The Company operates in one reportable segment, which focuses on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. The Company's operating segment is reported in a manner consistent with the internal reporting provided to the CODM. The Company's chief executive officer has been identified as its CODM.

The following table reflects net sales by medicine for the Company's reportable segment for the three and six months ended June 30, 2023 and 2022 (in thousands):

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	**2022**	**2023**	**2022**
TEPEZZA	$ 445,528	$ 479,814	$ 850,845	$ 981,265
KRYSTEXXA	244,296	167,755	431,277	308,459
RAVICTI	88,351	75,722	178,672	153,979
UPLIZNA [(1)]	68,084	38,598	121,913	69,075
PROCYSBI	53,145	47,706	103,608	97,277
ACTIMMUNE	29,039	29,989	58,160	61,424
PENNSAID 2%	6,913	23,586	16,107	58,954
RAYOS	8,012	11,150	12,989	24,637
BUPHENYL	1,246	1,387	2,659	3,548
QUINSAIR	345	335	641	631
DUEXIS	—	70	139	1,193
VIMOVO	—	299	8	1,214
Total net sales	**$ 944,959**	**$ 876,411**	**$ 1,777,018**	**$ 1,761,656**

(1)UPLIZNA revenue is affected each reporting period by the changes in the estimate of variable consideration included in the remeasurement of the refund liability for shipments to MTPC. During the three months ended June 30, 2023 and 2022, the Company recognized $1.6 million and $8.6 million, respectively, and $5.5 million and $10.1 million for the six months ended June 30, 2023 and 2022, respectively, of revenue as a result of the change in this estimate. The amount of variable consideration recognized is dependent on MTPC's sales over which the Company has no direct control.

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 reportable segment and all other customers as a group for the three and six months ended June 30, 2023 and 2022 (in thousands, except percentages):

	For the Three Months Ended June 30,			
	2023		2022	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Customer A	$ 339,179	27%	$ 315,484	25%
Customer B	242,564	20%	275,528	22%
Customer C	280,640	23%	305,531	25%
Customer D	282,486	23%	226,459	18%
Other customers	95,873	7%	118,272	10%
Gross sales	**$ 1,240,742**	**100%**	**$ 1,241,274**	**100%**

	For the Six Months Ended June 30,			
	2023		2022	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Customer A	$ 654,877	28%	$ 648,857	26%
Customer B	520,387	22%	576,738	23%
Customer C	500,369	21%	553,150	22%
Customer D	482,536	21%	460,585	19%
Other customers	189,575	8%	233,429	10%
Gross sales	**$ 2,347,744**	**100%**	**$ 2,472,759**	**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 and six months ended June 30, 2023 and 2022 (in thousands, except percentages):

	For the Three Months Ended June 30, 2023		For the Three Months Ended June 30, 2022	
	Amount	% of Total Net Sales	Amount	% of Total Net Sales
United States	$ 922,833	98%	$ 863,371	99%
Rest of world	22,126	2%	13,040	1%
Net sales	**$ 944,959**		**$ 876,411**	

	For the Six Months Ended June 30, 2023		For the Six Months Ended June 30, 2022	
	Amount	% of Total Net Sales	Amount	% of Total Net Sales
United States	$ 1,743,763	98%	$ 1,741,661	99%
Rest of world	33,255	2%	19,995	1%
Net sales	**$ 1,777,018**		**$ 1,761,656**	

NOTE 11 – 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.

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 June 30, 2023 and December 31, 2022 (in thousands):

	June 30, 2023			
	Level 1	**Level 2**	**Level 3**	**Total**
Assets:				
Money market funds	$ 2,268,900	$ —	$ —	$ 2,268,900
Bank time deposits	—	109,050	—	109,050
Interest rate swap contracts	—	38,419	—	38,419
Equity securities [(1)]	9,786	—	—	9,786
Foreign currency contracts	—	226	—	226
Other current assets	31,872	—	—	31,872
Total assets at fair value	**$ 2,310,558**	**$ 147,695**	**$ —**	**$ 2,458,253**
Liabilities:				
Other long-term liabilities	(31,872)	—	—	(31,872)
Total liabilities at fair value	**$ (31,872)**	**$ —**	**$ —**	**$ (31,872)**

	December 31, 2022			
	Level 1	**Level 2**	**Level 3**	**Total**
Assets:				
Money market funds	$ 2,151,500	$ —	$ —	$ 2,151,500
Interest rate swap contracts	—	30,348	—	30,348
Equity securities [(1)]	6,997	—	—	6,997
Foreign currency contracts	—	181	—	181
Other current assets	28,227	—	—	28,227
Total assets at fair value	**$ 2,186,724**	**$ 30,529**	**$ —**	**$ 2,217,253**
Liabilities:				
Other long-term liabilities	(28,227)	—	—	(28,227)
Total liabilities at fair value	**$ (28,227)**	**$ —**	**$ —**	**$ (28,227)**

(1)The Company held investments in equity securities with readily determinable fair values of $9.8 million and $7.0 million as of June 30, 2023 and December 31, 2022, respectively, which are included in other long-term assets in the condensed consolidated balance sheets. During the three and six months ended June 30, 2023, the Company recognized net unrealized gains of $2.4 million and $2.8 million, respectively, in the other income (expense), net line item of the Company's condensed consolidated statement of comprehensive income, due to the change in fair value of these securities. There were no sales of equity securities for the three and six months ended June 30, 2023.

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.

As of June 30, 2023, the Company's cash and cash equivalents included bank time deposits which were measured at fair value using Level 2 inputs and their carrying values were approximately equal to their fair values. Level 2 inputs, obtained from various third-party data providers, represent quoted prices for similar assets in active markets, or these inputs were derived from observable market data, or if not directly observable, were derived from or corroborated by other observable market data.

The Company's derivative assets and liabilities include interest rate swaps, which are carried at fair value. Interest rate swaps entered into by the Company are executed over-the-counter and are valued using discounted cash flows along with fair value models that primarily use observable market inputs. These models take into account a variety of factors including, where applicable, maturity, interest rate yield curves, and counterparty credit risks. Refer to Note 13 for further details.

The Company's derivative assets and liabilities also include foreign currency forward contracts, which all have maturities of one month or less. The Company estimates the fair values of these contracts by using observable market inputs including the forward and spot prices for foreign currencies. Refer to Note 13 for further details.

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.

NOTE 12 – DEBT AGREEMENTS

The Company's outstanding debt balances as of June 30, 2023 and December 31, 2022 consisted of the following (in thousands):

	June 30, 2023	December 31, 2022
Term Loan Facility due 2028	$ 1,564,000	$ 1,572,000
Term Loan Facility due 2026	418,026	418,026
Senior Notes due 2027	600,000	600,000
Total face value	**2,582,026**	**2,590,026**
Debt discount	(8,640)	(9,627)
Deferred financing fees	(15,928)	(17,562)
Total long-term debt	**2,557,458**	**2,562,837**
Less: current maturities	16,000	16,000
Long-term debt, net of current maturities	**$ 2,541,458**	**$ 2,546,837**

Term Loan Facility and Revolving Credit Facility

On March 15, 2021, Horizon Therapeutics USA, Inc. (the "Borrower" or "HTUSA"), a wholly-owned subsidiary of the Company, borrowed approximately $1.6 billion aggregate principal amount of loans (the "2028 Term Loans") pursuant to an amendment (the "March 2021 Amendment") to the credit agreement, dated as of May 7, 2015, by and among the Borrower, the Company and certain of its subsidiaries as guarantors, the lenders party thereto from time to time and Citibank, N.A., as administrative agent and collateral agent, as amended by Amendment No. 1, dated as of October 25, 2016, Amendment No. 2, dated March 29, 2017, Amendment No. 3, dated October 23, 2017, Amendment No. 4, dated October 19, 2018, Amendment No. 5, dated March 11, 2019, Amendment No. 6, dated May 22, 2019, Amendment No. 7, dated December 18, 2019, the Incremental Amendment and Joinder Agreement, dated August 17, 2020, the March 2021 Amendment and Amendment No. 10, dated June 16, 2023 (the "Term Loan Facility"). Pursuant to Amendment No. 7, the Borrower borrowed approximately $418.0 million aggregate principal amount of loans (the "2026 Term Loans"). Pursuant to Amendment No. 5, the Borrower received $200.0 million aggregate principal amount of revolving commitments, which was increased to $275.0 million aggregate amount of revolving commitments (the "Incremental Revolving Commitments") pursuant to the Incremental Amendment and Joinder Agreement. The Incremental Revolving Commitments were established pursuant to an incremental facility (the "Revolving Credit Facility") and include 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 June 30, 2023, 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 Amendment No. 10.

The 2028 Term Loans were incurred as a separate class of term loans under the Credit Agreement with substantially the same terms of the 2026 Term Loans. The Borrower used the proceeds of the 2028 Term Loans to fund a portion of the consideration payable in the acquisition of Viela. Pursuant to Amendment No. 10, the benchmark rate was amended to replace LIBOR with Secured Overnight Financing Rate ("SOFR"). The 2028 Term Loans bear interest at a rate, at Borrower's option, equal to SOFR (subject to a 0.00% SOFR floor), plus the SOFR adjustment, plus 2.00% per annum or the adjusted base rate plus 1.00% per annum, with a step-down to SOFR, plus the SOFR adjustment, plus 1.75% per annum or the adjusted base rate plus 0.75% per annum at the time the Company's leverage ratio is less than or equal to 2.00 to 1.00. The SOFR adjustment is an additional interest amount for either one-month, three-month or six-month interest periods, at our election: (a) 0.11% using a one-month interest period, (b) 0.26% using a three-month interest period, and (c) 0.43% using a six-month interest period. The adjusted base rate is defined as the greatest of (a) SOFR (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 2026 Term 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 2026 Term Loans to repay the Refinanced Loans, which totaled approximately $418.0 million. The 2026 Term Loans bear interest at a rate, at the Borrower's option, equal to SOFR (subject to a 0.00% SOFR floor), plus the SOFR adjustment, plus 2.25% per annum or the adjusted base rate plus 1.25% per annum, with a step-down to SOFR, plus the SOFR adjustment, plus 2.00% per annum or the adjusted base rate plus 1.00% per annum at the time the Company's leverage ratio is less than or equal to 2.00 to 1.00.

The loans under the Revolving Credit Facility bear interest, at the Borrower's option, at a rate equal to either SOFR (subject to a SOFR floor of 0.00%), plus the SOFR adjustment, plus an applicable margin of 2.25% per annum, or the adjusted base rate plus 1.25% per annum, with a step-down to SOFR, plus the SOFR adjustment, 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 2028 Term Loans, (ii) the 2026 Term Loans, (iii) the Revolving Credit Facility, (iv) one or more uncommitted additional incremental loan facilities subject to the satisfaction of certain financial and other conditions, and (v) one or more uncommitted refinancing loan facilities with respect to loans thereunder. The Credit Agreement allows for the Company and certain of its subsidiaries to become additional borrowers under incremental or refinancing facilities.

The obligations under the Credit Agreement (including obligations in respect of the 2028 Term Loans, 2026 Term 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 2028 Term Loans, 2026 Term Loans and the Revolving Credit Facility) and any related swap and cash management obligations are secured, subject to customary permitted liens and other agreed upon exceptions, by a perfected security interest in (i) all tangible and intangible assets of the Borrower and the guarantors, except for certain customary excluded assets, and (ii) all of the capital stock owned by the Borrower and guarantors thereunder (limited, in the case of the stock of certain non-U.S. subsidiaries of the Borrower, to 65% of the capital stock of such subsidiaries). The Borrower and the guarantors under the Credit Agreement are individually and collectively referred to herein as a "Loan Party" and the "Loan Parties," as applicable.

The Borrower is permitted to make voluntary prepayments of the loans under the Credit Agreement at any time without payment of a premium. 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 a 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 2028 Term Loans will amortize in equal quarterly installments in an aggregate annual amount equal to 1% of the original principal amount thereof, with any remaining balance payable on March 15, 2028, the final maturity date of the 2028 Term Loans. The principal amount of the 2026 Term Loans is due and payable on May 22, 2026, the final maturity date of the 2026 Term 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 2028 Term Loans is variable and, as of June 30, 2023, the interest rate on the 2028 Term Loans was 6.95% and the effective interest rate was 7.19%.

The interest on the 2026 Term Loans is variable and, as of June 30, 2023, the interest rate on the 2026 Term Loans was 7.20% and the effective interest rate was 7.49%.

As of June 30, 2023, the fair value of the amounts outstanding under the 2028 Term Loans and the 2026 Term Loans was approximately $1,560.1 million and $417.5 million, respectively, categorized as a Level 2 instrument, as defined in Note 11.

On April 25, 2022, the Company entered into two interest rate swap agreements with notional amounts totaling $800.0 million, effective June 24, 2022, to hedge or otherwise protect against interest rate fluctuations on a portion of its variable rate debt. Refer to Note 13 for further details.

2027 Senior Notes

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

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

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

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

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

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. 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 June 30, 2023, the interest rate on the 2027 Senior Notes was 5.50% and the effective interest rate was 5.76%.

As of June 30, 2023, the fair value of the 2027 Senior Notes was approximately $600.8 million, categorized as a Level 2 instrument, as defined in Note 11.

On April 18, 2023, in connection with the potential closing of the Transaction, HTUSA directed U.S. Bank Trust Company, National Association (as successor to U.S. Bank National Association), as trustee (the "Notes Trustee"), to give a notice (the "First Redemption Notice") of HTUSA's intent, in accordance with the indenture governing the 2027 Senior Notes (the "2027 Notes Indenture"), to redeem in full the aggregate principal amount of the outstanding 2027 Senior Notes. The redemption as set forth in the First Redemption Notice was conditioned on, among other things, the consummation of the Transaction by not later than June 26, 2023. On May 26, 2023, HTUSA revoked the First Redemption Notice and directed the Notes Trustee to give a notice (the "Second Redemption Notice") of HTUSA's intent, in accordance with the 2027 Notes Indenture, to redeem in full the aggregate principal amount of the outstanding 2027 Senior Notes. The redemption as set forth in the Second Redemption Notice was conditioned on, among other things, the consummation of the Transaction by not later than July 25, 2023. On July 21, 2023, HTUSA revoked the Second Redemption Notice and directed the Notes Trustee to give a notice (the "Third Redemption Notice") of HTUSA's intent, in accordance with the 2027 Notes Indenture, to redeem in full the aggregate principal amount of the outstanding 2027 Senior Notes. The redemption as set forth in the Third Redemption Notice is conditioned on, among other things, the consummation of the Transaction by not later than September 19, 2023.

NOTE 13 – DERIVATIVE INSTRUMENTS AND HEDGING ACTIVITIES

Interest rate risk

The Company is a party to interest rate swap agreements designated as cash flow hedges with notional amounts totaling $800.0 million as of June 30, 2023, which effectively fix SOFR at approximately 2.8% through December 24, 2026. These agreements were designated as cash flow hedges on the exposure of the variability of future cash flows subject to the variable monthly interest rates on $800.0 million of the Company's 2028 Term Loans and the 2026 Term Loans. The change in fair value is recorded as part of other comprehensive income (loss). Interest expense, net is adjusted to include the payments made or received under the swap agreements.

Foreign currency risk

The Company also enters into foreign currency forward contracts with durations of one month or less to mitigate the foreign currency risk related to certain balance sheet positions. The Company has not elected hedge accounting for these transactions and they are recorded at fair value. As of June 30, 2023, the Company had outstanding foreign currency forward contracts to sell $10.9 million and purchase €5.0 million and CHF5.0 million, and to purchase $1.8 million and sell JPY250 million, all of which had settlement dates of less than one month.

No amounts are excluded from the assessment of effectiveness for cash flow hedges. Refer to Note 11 for further details on the valuation methodologies for the Company's derivative instruments.

The following tables summarize the amounts and locations of the Company's derivative instruments on the condensed consolidated balance sheet as of June 30, 2023 and December 31, 2022 (in thousands):

	Fair value - Derivatives in asset position		**Fair value - Derivatives in liability position**	
	Balance sheet location	**June 30, 2023**	**Balance sheet location**	**June 30, 2023**
Interest rate swap contracts				
Designated as cash flow hedges	Prepaid expenses and other current assets	$ 20,050	Accrued expenses and other current liabilities	$ —
Designated as cash flow hedges	Other long-term assets	18,369	Other long-term liabilities	—
Foreign currency forward contracts				
Not designated as hedges	Prepaid expenses and other current assets	226	Accrued expenses and other current liabilities	—
Total derivatives		**$ 38,645**		**$ —**

	Fair value - Derivatives in asset position		Fair value - Derivatives in liability position	
	Balance sheet location	December 31, 2022	Balance sheet location	December 31, 2022
Interest rate swap contracts				
Designated as cash flow hedges	Prepaid expenses and other current assets	$ 15,520	Accrued expenses and other current liabilities	$ —
Designated as cash flow hedges	Other long-term assets	14,828	Other long-term liabilities	—
Foreign currency forward contracts				
Not designated as hedges	Prepaid expenses and other current assets	181	Accrued expenses and other current liabilities	—
Total derivatives		**$ 30,529**		**$ —**

While foreign currency forward contracts are subject to a master netting arrangement, the Company does not offset derivative assets and liabilities within the condensed consolidated balance sheet.

The following table summarizes the pre-tax amount and locations of derivative instrument net gains (losses) recognized in the condensed consolidated statement of comprehensive income (in thousands):

		For the Three Months Ended June 30,	
	Location	2023	2022
Interest rate swap contracts designated as cash flow hedges	Interest expense, net	$ 4,430	$ 157
Foreign currency forward contracts not designated as cash flow hedges	Foreign exchange gain	523	(3,248)

		For the Six Months Ended June 30,	
	Location	2023	2022
Interest rate swap contracts designated as cash flow hedges	Interest expense, net	$ 7,868	$ 157
Foreign currency forward contracts not designated as cash flow hedges	Foreign exchange gain	471	(3,248)

The following table presents the pre-tax amount of gains from derivative instruments recognized in other comprehensive income (loss) (in thousands):

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	2022	2023	2022
Interest rate swap contracts designated as cash flow hedges	$ 17,125	$ 2,615	$ 8,071	$ 2,615

Assuming market rates remain constant through contract maturities, the Company expects to reclassify pre-tax net gains of $20.1 million into interest expense, net for interest rate swap cash flow hedges within the next 12 months.

The cash flow effects of the Company’s derivative contracts in the condensed consolidated statement of cash flows are included in operating activities.

NOTE 14 – LEASE OBLIGATIONS

As of June 30, 2023, the Company had the following office space lease agreements in place for real properties:

Location	Approximate Square Feet	Lease Expiry Date
Dublin, Ireland	80,000	July 1, 2032 to May 4, 2041
Rockville, Maryland [(1)]	242,000	August 31, 2024 to April 30, 2040
Lake Forest, Illinois	160,000	March 31, 2031
South San Francisco, California	40,000	December 31, 2031
Chicago, Illinois	9,200	December 31, 2028
Washington, D.C.	6,000	September 30, 2024
Mannheim, Germany	4,800	December 31, 2023

(1)In November 2021, the Company entered into a lease agreement relating to approximately 192,000 square feet of office and laboratory space under construction in Rockville, Maryland. During the second quarter of 2023, the construction of the office was completed by the lessor and the lease became effective. As a result, the Company recognized an initial $46.0 million as a right-of-use asset and a $46.9 million lease liability on the condensed consolidated balance sheet. The lease is due to expire in April 2040. The Company expects to incur leasehold improvement costs through 2024 and 2025 in order to prepare the building for occupancy.

As of June 30, 2023 and December 31, 2022, the Company had right-of-use lease assets included in other long-term assets of $141.9 million and $99.5 million, respectively; current lease liabilities included in accrued expenses and other current liabilities of $9.2 million and $7.8 million, respectively; and non-current lease liabilities included in other long-term liabilities of $159.1 million and $114.3 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 $5.3 million and $3.1 million for the three months ended June 30, 2023 and 2022, respectively, and was $8.9 million and $6.1 million for six months ended June 30, 2023 and 2022, respectively.

The table below reconciles the undiscounted cash flows for each of the first five years and total of the remaining years to the lease liabilities recorded on the Company’s condensed consolidated balance sheet as of June 30, 2023 (in thousands):

2023 (July to December)	$	6,652
2024		14,566
2025		19,958
2026		21,482
2027		21,745
Thereafter		213,155
Total lease payments		297,558
Imputed interest		(129,172)
Total lease liabilities	**$**	**168,386**

The weighted-average discount rate and remaining lease term for leases as of June 30, 2023 was 5.75% and 13.44 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. As of June 30, 2023, the Company had binding purchase commitments with AGC Biologics for TEPEZZA drug substance of €89.3 million ($97.4 million converted at a Euro-to-Dollar exchange rate as of June 30, 2023 of 1.0905), to be delivered through June 2025. 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. As of June 30, 2023, the Company had binding purchase commitments with Catalent for TEPEZZA drug product of $6.2 million, to be delivered through December 2024. Under the Company's supply agreement with Patheon Pharmaceuticals Inc. ("Patheon") (the contract development and manufacturing services organization of Thermo Fisher Scientific), the Company must provide Patheon with rolling forecasts of TEPEZZA drug product requirements, with a portion of the forecast being a firm and binding order. As of June 30, 2023, the Company had binding purchase commitments with Patheon for TEPEZZA drug product of €6.8 million ($7.4 million converted at a Euro-to-Dollar exchange rate as of June 30, 2023 of 1.0905), to be delivered through December 2024.

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% of its annual worldwide bulk product requirements for KRYSTEXXA from BTG Israel. 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 each forecast is considered a binding firm order. As of June 30, 2023, the Company had a total purchase commitment, including the minimum annual order quantities and binding firm orders, with BTG Israel for KRYSTEXXA of $22.8 million, to be delivered through December 2026.

Under an agreement with Boehringer Ingelheim Biopharmaceuticals GmbH ("Boehringer Ingelheim Biopharmaceuticals"), Boehringer Ingelheim Biopharmaceuticals is required to manufacture and supply ACTIMMUNE to the Company. The Company is required to purchase minimum quantities of finished medicine during the term of the agreement, which term extends to at least September 30, 2024. As of June 30, 2023, the minimum purchase commitment to Boehringer Ingelheim Biopharmaceuticals was €5.9 million ($6.5 million converted using a Euro-to-Dollar exchange rate of 1.0905 as of June 30, 2023) through September 2024.

Excluding the above, additional purchase orders and other commitments relating to the manufacture of RAVICTI, PROCYSBI, KRYSTEXXA, BUPHENYL, UPLIZNA, RAYOS and QUINSAIR of $15.6 million were outstanding as of June 30, 2023.

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.

Disclosure of ongoing matters is considered at the time of each filing and matters may be removed if the statute of limitations has lapsed or circumstances have changed that reduce the risk of exposure.

On August 3, 2022, the Company received a civil investigative demand from the United States Department of Justice ("DOJ") pursuant to the Federal False Claims Act regarding an investigation concerning potentially false information in prior authorization forms. A prior authorization form is a managed care practice whereby the payer (either a commercial insurer or a government health program) requires that the prescribing physician provide additional justification or information supporting the physician's decision to prescribe a particular medicine. The civil investigative demand requests certain documents and information related to DUEXIS, PENNSAID 2%, VIMOVO and RAYOS. The Company is cooperating with the investigation and the DOJ has not indicated to the Company whether it believes the Company engaged in any wrongdoing or if the Company is the subject of the investigation. While the Company is not aware of any fraudulent scheme to provide false information in prior authorization forms for its medicines that resulted in improper payments from government healthcare programs, 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.

Beginning in the third quarter of 2022, the Company has been served with multiple complaints from plaintiffs alleging to have taken TEPEZZA and suffered hearing impairment. Although hearing impairment, including deafness, was identified as a potential adverse event in the pivotal clinical trials for TEPEZZA, addressed at the U.S. Food and Drug Administration ("FDA") advisory committee meeting that considered the safety and efficacy of TEPEZZA, and listed as a potential adverse event in the initial FDA-approved TEPEZZA product label, the plaintiffs allege that the Company failed to adequately inform them about the risk of hearing impairment before taking the medicine. In March 2023, one of the plaintiffs filed a motion with the United States Judicial Panel on Multidistrict Litigation ("MDL Panel") to transfer current and future product liability cases involving TEPEZZA and hearing impairment to the United States District Court for the Northern District of California. On June 2, 2023, the MDL Panel ordered the centralization of current and future federal cases to the United States District Court for the Northern District of Illinois, Eastern Division. On June 28, 2023, the court vacated the prior deadlines in the individual cases and instructed the parties to confer on a consolidated procedure to resolve the Company's motions to dismiss the cases on federal preemption grounds. The Company intends to vigorously defend itself in the lawsuits and maintains insurance coverage for product liability claims. Nevertheless, no assurance can be given as to the outcome of the litigation, whether additional similar lawsuits will be initiated or whether the Company's insurance coverage will be adequate to cover the costs of the litigation or any resulting settlements or judgments.

Other Agreements

Arrowhead Pharmaceuticals, Inc.

On June 18, 2021, the Company entered into a global agreement with Arrowhead Pharmaceuticals, Inc. ("Arrowhead") for HZN 457, a discovery-stage investigational RNAi therapeutic being developed by Arrowhead as a potential treatment for uncontrolled gout. Arrowhead granted the Company a worldwide exclusive license to develop, manufacture and commercialize medicines based on the RNAi therapeutic. Arrowhead is required to use commercially reasonable efforts to conduct research and preclinical development activities for the RNAi therapeutic products. The Company must use commercially reasonable efforts in, and will be responsible for, clinical development and commercialization of the RNAi therapeutic products. Under the terms of the agreement, the Company paid Arrowhead an upfront cash payment of $40.0 million in July 2021 and agreed to pay additional potential future milestone payments of up to $660.0 million contingent on the achievement of certain development, regulatory and commercial milestones, and low to mid-teens royalties on worldwide calendar year net sales of licensed medicines. In addition, a $15.0 million development milestone was recognized in the fourth quarter of 2022. The $15.0 million development milestone was subsequently paid in the first quarter of 2023.

Venture capital funds

The Company is committed to invest as a strategic limited partner in four venture capital funds: Forbion Growth Opportunities Fund I C.V., Forbion Capital Fund V C.V., Aisling Capital V, L.P. and RiverVest Venture Fund V, L.P. As of June 30, 2023, the total carrying amount of the Company's investments in these funds was $31.9 million, which is included in other long-term assets in the condensed consolidated balance sheet and includes $4.2 million in net cash payments for investments made during the first half of 2023. As of June 30, 2023, the Company's total future commitments to these funds were $35.4 million. During the six months ended June 30, 2023 and 2022, the Company recorded a loss under the equity method of $0.6 million and investment income under the equity method of $2.4 million, respectively, in the other income (expense), net line item of the Company's condensed consolidated statement of comprehensive income related to these funds.

Non-cancellable advertising commitments

As of June 30, 2023, the Company had $28.4 million of non-cancellable advertising commitments due within one year, primarily related to its U.S. commercial business.

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.

The Company also has indemnification obligations to the former officers and directors of Viela for certain events or occurrences related to their former roles at Viela, subject to certain limits. Several individual directors and officers of Viela were named as defendants in a lawsuit, *Sciannella v. Astrazeneca UK Limited et.al.*, Case No. 2023-0125, filed in the Court of Chancery of the State of Delaware, which alleges various breaches of fiduciary duties in connection with Viela's decision to be acquired by the Company. The Company has a director and officer insurance policy that enables it to recover a portion of certain amounts that may be paid by (and for which the Company may be obligated to indemnity) the former Viela officers and directors as a result of the lawsuit.

NOTE 16 - LEGAL PROCEEDINGS

Transaction Agreement with Amgen

On May 16, 2023, the FTC filed a complaint in the United States District Court for the Northern District of Illinois seeking a temporary restraining order and preliminary injunction enjoining the Transaction. Refer to Note 1 for further details.

TEPEZZA

Beginning in the third quarter of 2022, the Company has been served with multiple complaints from plaintiffs alleging to have taken TEPEZZA and suffered hearing impairment. Although hearing impairment, including deafness, was identified as a potential adverse event in the pivotal clinical trials for TEPEZZA, addressed at the FDA advisory committee meeting that considered the safety and efficacy of TEPEZZA, and listed as a potential adverse event in the initial FDA-approved TEPEZZA product label, the plaintiffs allege that the Company failed to adequately inform them about the risk of hearing impairment before taking the medicine. In these lawsuits, the plaintiffs are seeking unspecified monetary damages. In March 2023, one of the plaintiffs filed a motion with the MDL Panel to transfer current and future product liability cases involving TEPEZZA and hearing impairment to the United States District Court for the Northern District of California. On June 2, 2023, the MDL Panel ordered the centralization of current and future federal cases to the United States District Court for the Northern District of Illinois, Eastern Division. On June 28, 2023, the court vacated the prior deadlines in the individual cases and instructed the parties to confer on a consolidated procedure to resolve the Company's motions to dismiss the cases on federal preemption grounds.

PROCYSBI

On February 2, 2022 and February 16, 2022, the Company received notice from Teva Pharmaceuticals, Inc. ("Teva") that it had filed Abbreviated New Drug Applications ("ANDA") with the FDA seeking approval of generic versions of PROCYSBI granules and capsules, respectively. The ANDAs contained Paragraph IV Patent Certifications alleging that the patents covering PROCYSBI granules and capsules are invalid and/or will not be infringed by Teva's manufacture, use or sale of the medicines for which the ANDAs were submitted. On March 15, 2022, the Company filed suit against Teva in the United States District Court for the District of New Jersey for patent infringement, seeking to prevent Teva from selling its generic versions of PROCYSBI granules and capsules. On March 24, 2023, the parties stipulated to a stay of all proceedings.

PENNSAID 2%

On May 6, 2022, Apotex received FDA approval to market a generic diclofenac sodium topical solution 2% ("Apotex ANDA Product"), following the apparent forfeiture by Actavis Laboratories UT, Inc. ("Actavis") of its first-filer exclusivity. On May 13, 2022, the Company filed a complaint against Apotex asserting that the manufacture, use, offer for sale, or sale of the Apotex ANDA Product would infringe U.S. Patent No. 9,066,913 (the "'913 patent") in the United States District Court for the District of Delaware. The Company previously successfully enforced the '913 patent against Actavis in the District of New Jersey and the Federal Circuit subsequently affirmed the district court's ruling.

The Company purchased PENNSAID 2% from Nuvo Pharmaceuticals Inc. ("Nuvo") in 2014. Apotex alleged that a settlement agreement entered into in January 2013 with Nuvo ("Nuvo Settlement") provides it with a license to the '913 patent. The Company disputed the scope of Apotex's settlement and license with Nuvo, contending that it does not provide Apotex with a license to the '913 patent, which was issued to the Company after the Company's purchase of PENNSAID 2% from Nuvo.

On May 17, 2022, the Company moved for a preliminary injunction enjoining Apotex from engaging in the commercial manufacture, use, offer to sell, or sale of the Apotex ANDA Product. On May 27, 2022, the parties filed a stipulated preliminary injunction and a proposed expedited briefing schedule to present the underlying license dispute to the district court by way of a motion for summary judgment, which the district court entered on May 31, 2022. On August 23, 2022, the district court held a hearing on the motion for summary judgment and the parties subsequently provided supplemental briefing on certain legal matters requested by the district court. On November 7, 2022, the district court ruled in Apotex's favor, finding that the Nuvo Settlement provided Apotex a license to the '913 patent and that Apotex's ANDA Product consequently does not infringe the '913 patent. Apotex subsequently alleged that the preliminary injunction was wrongfully entered and caused Apotex to suffer monetary losses. Apotex also sought an award of its attorney fees. The Company disputed Apotex's allegations that it incurred monetary losses or that it was entitled to an award of attorney fees. On April 25, 2023, the parties entered into a confidential settlement of all claims. On April 28, 2023, the district court litigation was dismissed with prejudice.

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

The Company's equity incentive plans at June 30, 2023 included its 2011 Equity Incentive Plan, as amended, Amended and Restated 2014 Equity Incentive Plan ("2014 EIP"), 2014 Non-Employee Equity Plan, as amended ("2014 Non-Employee Plan"), 2020 Employee Share Purchase Plan ("2020 ESPP"), Amended and Restated 2020 Equity Incentive Plan, as amended ("2020 EIP"), and Amended and Restated 2018 Equity Incentive Plan ("2018 EIP").

As of June 30, 2023, an aggregate of 1,852,854 ordinary shares were authorized and available for future issuance under the 2020 ESPP, an aggregate of 15,303,445 ordinary shares were authorized and available for future grants under the 2020 EIP, an aggregate of 483,069 ordinary shares were authorized and available for future grants under the 2014 Non-Employee Plan and an aggregate of 1,547,592 ordinary shares were authorized and available for future grants under the 2018 EIP.

Stock Options

The following table summarizes stock option activity during the six months ended June 30, 2023:

	Options	Weighted Average Exercise Price	Weighted Average Contractual Term Remaining (in years)	Aggregate Intrinsic Value (in thousands)
Outstanding as of December 31, 2022	4,830,232	$ 24.04	2.91	$ 433,552
Exercised	(235,970)	25.67	—	—
Forfeited	(2,627)	53.46	—	—
Outstanding as of June 30, 2023	**4,591,635**	**$ 23.94**	**2.36**	**$ 362,319**
Exercisable as of June 30, 2023	**4,535,201**	**$ 23.53**	**2.31**	**$ 359,716**

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

Restricted Stock Units

The following table summarizes RSU activity for the six months ended June 30, 2023:

	Number of Units	Weighted Average Grant-Date Fair Value Per Unit
Outstanding as of December 31, 2022	3,466,272	$ 80.84
Granted	2,299,107	112.33
Vested	(1,496,049)	68.61
Forfeited	(151,375)	100.62
Outstanding as of June 30, 2023	**4,117,955**	**$ 102.14**

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

Performance Stock Unit Awards

The following table summarizes PSU activity for the six months ended June 30, 2023:

	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, 2022	1,233,584			
Granted	319,658	$ 159.52	5.54%	$ 150.68
Forfeited	(31,111)	112.02	52.13%	53.62
Vested	(587,075)	57.22	8.72%	52.23
Outstanding as of June 30, 2023	**935,056**			

On January 4, 2023, the Company awarded PSUs to key executive participants ("2023 PSUs"). The 2023 PSUs are subject to both performance-based and service-based vesting provisions. The 2023 PSUs utilize three long-term performance metrics, as follows:

- 50% of the 2023 PSUs that may vest (such portion of the PSU award, the "2023 Relative TSR PSUs") are determined by reference to the Company's total shareholder return ("TSR") over the three-year period ending December 31, 2025, as measured relative to the TSR of each company included in the Nasdaq Biotechnology Index ("NBI") during such three-year period (except with respect to the Company only, the period is measured from November 28, 2022, which is the last trading day prior to the public announcement that the Company was in preliminary discussions related to a possible acquisition transaction, through December 31, 2025). Generally, in order to vest in any portion of the 2023 Relative TSR PSUs, the participant must also remain in continuous service with the Company through the earlier of January 5, 2026 or the date immediately prior to a change in control.

- 25% of the 2023 PSUs that may vest (such portion of the PSU award, the "2023 Strategic PSUs") are determined by reference to the Company's achievement of certain performance objectives related to research and development and technical operations during the two-year period ending December 31, 2024. Generally, in order to vest in any portion of the 2023 Strategic PSUs, the participant must also remain in continuous service with the Company through the earlier of (i) January 5, 2025 (with respect to 2/3rds of the 2023 Strategic PSUs) and January 5, 2026 (with respect to 1/3rd of the 2023 Strategic PSUs) or (ii) the date immediately prior to a change in control.

- 25% of the 2023 PSUs that may vest (such portion of the PSU award, the "2023 Financial PSUs") are determined by reference to the Company's achievement of certain financial milestones. The 2023 Financial PSUs that may vest will be determined by reference to the Company's combined net sales of TEPEZZA and KRYSTEXXA during the two-year period ending December 31, 2024. Generally, in order to vest in any portion of the 2023 Financial PSUs, the participant must also remain in continuous service with the Company through the earlier of (i) January 5, 2025 (with respect to 2/3rds of the 2023 Financial PSUs) and January 5, 2026 (with respect to 1/3rd of the 2023 Financial PSUs) or (ii) the date immediately prior to a change in control.

If a change in control occurs prior to the completion of the defined performance period, a portion of any PSUs for which performance has not previously been determined will vest as measured through the date of the change in control (with respect to PSUs based on TSR) or based on an estimated level of performance through the end of the performance period as if the change in control had not occurred, which will be determined by the Compensation Committee.

All PSUs outstanding on June 30, 2023 may vest in a range of between 0% and 200%, with the exception of certain modified PSUs granted in 2020 and based on net sales which were capped at 150% and the 2023 PSUs, which will be capped at 100% to the extent the pending Transaction with Amgen closes prior to the defined performance period. The Company accounts for all PSUs as equity-settled awards in accordance with ASC 718, *Compensation-Stock Compensation*. Because the value of the 2023 Relative TSR PSUs is 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 on the grant date. As a result, the Monte Carlo model is applied and the most significant valuation assumptions used related to the 2023 Relative TSR PSUs during the six months ended June 30, 2023, included:

Valuation date stock price	$ 113.48
Expected volatility	47.55%
Risk free rate	4.07%

The value of outstanding PSUs based on strategic or financial goals that have not yet been determined are 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.

Share-Based Compensation Expense

The following table summarizes share-based compensation expense included in the Company's condensed consolidated statements of operations for the six months ended June 30, 2023 and 2022 (in thousands):

	For the Six Months Ended June 30,	
	2023	2022
Share-based compensation expense		
Cost of goods sold	$ 5,803	$ 4,471
Research and development	18,561	15,720
Selling, general and administrative	94,027	72,258
Total share-based compensation expense	**$ 118,391**	**$ 92,449**

During the six months ended June 30, 2023 and 2022, the Company recognized $24.5 million and $53.9 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 RSUs and PSUs. As of June 30, 2023, the Company estimated that pre-tax unrecognized compensation expense of $422.7 million for all unvested share-based awards, including stock options, RSUs and PSUs, will be recognized through the first quarter of 2026. The Company expects to satisfy the exercise of stock options and future distribution of shares for RSUs and PSUs by issuing new ordinary shares which have been reserved under the 2020 EIP, the 2018 EIP and 2014 Non-Employee Plan.

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 expense (benefit) for income taxes for the three months ended June 30, 2023 and 2022 (in thousands):

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	2022	2023	2022
Income before expense (benefit) for income taxes	$ 135,252	$ 64,787	$ 154,454	$ 237,526
Expense (benefit) for income taxes	8,181	3,813	(27,301)	(27,709)
Net income	**$ 127,071**	**$ 60,974**	**$ 181,755**	**$ 265,235**

During the three and six months ended June 30, 2023, the Company recorded an expense for income taxes of $8.2 million and a benefit for income taxes of $27.3 million, respectively. During the three and six months ended June 30, 2022, the Company recorded an expense for income taxes of $3.8 million and a benefit for income taxes of $27.7 million, respectively. The benefit for income taxes recorded during the six months ended June 30, 2023 is primarily attributable to tax benefits recognized on share-based compensation and the mix of pre-tax income and losses incurred in various tax jurisdictions.

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 the pending transaction with Amgen Inc., 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 a global biotechnology company focused on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. Our pipeline is purposeful: we apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives.

Effective in the fourth quarter of 2022, management realigned our reportable segments to reflect changes in the manner in which the chief operating decision maker, or CODM, assesses financial information for decision-making purposes. We transitioned our two reportable segments, the inflammation segment and the orphan segment, to one reportable segment for the year ended December 31, 2022. All prior year amounts have been reclassified to conform to our current reporting structure. Our commercial portfolio is currently composed of 12 medicines in the areas of rare diseases, gout, ophthalmology and inflammation.

On December 12, 2022, we announced we had entered into a transaction agreement with Amgen Inc., or Amgen, and Pillartree Limited, or Pillartree, a wholly owned subsidiary of Amgen. Subject to the terms of the transaction agreement, Pillartree will acquire our company, or the Transaction, pursuant to a scheme of arrangement under Chapter 1 of Part 9 of the Companies Act 2014 of Ireland, or the Scheme. As a result of the Scheme, we would become a wholly owned subsidiary of Amgen.

At the effective time of the Scheme, or the Effective Time, holders of our ordinary shares will be entitled to receive $116.50 in cash per ordinary share, or the Consideration. Our equity awards will be treated as set forth in the transaction agreement, such that:

- each option to purchase our ordinary shares that is outstanding as of immediately prior to the Effective Time (whether or not vested) will, contingent upon and effective as of the Effective Time, be canceled and converted into the right to receive cash, without interest, in an amount equal to (a) the total number of our ordinary shares subject to such option immediately prior to the Effective Time, multiplied by (b) the excess of (i) the Consideration over (ii) the exercise price payable per share under such option;

- each of our restricted stock unit, or RSU, awards, excluding PSUs (as defined below), that is outstanding as of immediately prior to the Effective Time (whether or not vested) will, contingent upon and effective as of the Effective Time, (a) if granted to a non-employee member of our board of directors, or held by a person who, as of the date of the completion of the Transaction, is a former service-provider of our company, be canceled and converted into the right to receive a cash amount equal to (i) the total number of our ordinary shares subject to such RSU immediately prior to the Effective Time multiplied by (ii) the Consideration, and (b) if not granted to an individual described in clause (a) above, be canceled and converted into a restricted stock unit, or an Amgen RSU, denominated in shares of Amgen's common stock. The number of shares of Amgen common stock subject to each such Amgen RSU will be equal to the product (rounded down to the nearest whole number) of (a) the total number of our ordinary shares subject to such RSU immediately prior to the Effective Time multiplied by (b) the quotient of (i) the Consideration divided by (ii) the volume weighted average of the per share closing price of Amgen's common stock on the Nasdaq Global Select Market for five trading days ending on the second business day prior to the completion of the Transaction. Following the Effective Time, each Amgen RSU will continue to be governed by the same terms and conditions (including vesting terms) as were applicable to the applicable RSU immediately prior to the Effective Time; and

•each of our RSU awards with performance-based vesting or delivery requirements, or a PSU, that is outstanding as of immediately prior to the Effective Time (whether or not vested) will, contingent upon and effective as of the Effective Time, be canceled and converted into the right to receive cash, without interest, in an amount equal to (i) the total number of our ordinary shares issuable in settlement of such PSU as determined, in accordance with the terms of such PSU, by the compensation committee of our board of directors prior to the Effective Time multiplied by (ii) the Consideration.

On February 24, 2023, our shareholders approved the Scheme and certain scheme approval resolutions and amendments to the memorandum and articles of association of Horizon to enable the Scheme to be effected. The closing of the Transaction remains subject to customary closing conditions, including, among other things, (a) the sanction by the Irish High Court of the Scheme and delivery of the court order to the Irish Registrar of Companies, (b) the absence of an order or law that prevents consummation of the Transaction or imposes a burdensome condition (as defined in the transaction agreement), (c) absence of any Material Adverse Effect (as defined in the transaction agreement) from December 12, 2022 to the Sanction Date (as defined in the transaction agreement) that is continuing as of the Sanction Date, (d) the accuracy of the other party's representations and warranties subject to certain materiality and material adverse effect exceptions and (e) the performance by each party of all of its covenants and agreements under the transaction agreement in all material respects. In connection with the Transaction, we and Amgen have received clearances or confirmation of non-applicability related to foreign direct investment in Denmark, Italy, Germany and France and clearances related to antitrust in Germany and Austria.

On May 16, 2023, the Federal Trade Commission, or FTC, filed a complaint in the United States District Court for the Northern District of Illinois seeking a temporary restraining order and preliminary injunction enjoining the Transaction. On May 23, 2023, the district court scheduled an evidentiary hearing on the FTC's request for a preliminary injunction beginning on September 11, 2023. Based on the district court's schedule, we, Amgen and the FTC then submitted a stipulated proposed temporary restraining order to the district court providing that we and Amgen would not close the Transaction until the earlier of October 31, 2023 or the second business day after the district court rules on the FTC's request for a preliminary injunction, or the Stipulated TRO. On May 31, 2023, the district court entered a case management order, and on June 2, 2023, the district court issued an order granting the Stipulated TRO. On June 22, 2023, the FTC filed a parallel complaint in its administrative court and an amended complaint was filed in the district court adding several states as additional plaintiffs. On June 29, 2023, we and Amgen filed an answer to the amended complaint and counterclaims against the FTC. We expect that the schedule set by the district court would allow the Transaction to close by mid-December 2023 if the district court denies the request for a preliminary injunction. We cannot predict with certainty whether and when any of the required closing conditions, including the termination of the Stipulated TRO and absence of any other order preventing consummation of the Transaction, will be satisfied or if additional uncertainties may arise and cannot guarantee that we will be able to successfully consummate the pending Transaction as currently contemplated under the transaction agreement or at all. In particular, there can be no guarantee that the district court will deny the FTC's request for a preliminary injunction or when, if ever, such a ruling would be issued. If the FTC's request for a preliminary injunction is granted, it is highly unlikely that the Transaction could close before the December 12, 2023 end date specified in the transaction agreement. In the event that the Transaction does not close before the December 12, 2023 end date specified in the transaction agreement, each party would then have the right, in its sole discretion, to terminate the transaction agreement and abandon the Transaction, which Amgen may determine to do, particularly if the FTC's request for a preliminary injunction is granted. If the transaction agreement is terminated and the Transaction is abandoned, whether due to the failure to satisfy applicable closing conditions related to obtaining antitrust clearance for the Transaction or otherwise, our business, results of operations, financial condition and our share price would be materially and adversely affected.

As of June 30, 2023, our commercial portfolio consisted of the following medicines:

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

Strategy

Horizon is a leading high-growth, innovation-driven, profitable global biotechnology company. We are focused on the discovery, development and commercialization of medicines that address critical needs for people impacted by rare, autoimmune and severe inflammatory diseases. Our three strategic goals are to: (i) maximize the value of our on-market rare disease medicines through commercial execution and clinical investment; (ii) expand our research and development, or R&D, pipeline through significant internal investment and external business development; and (iii) build a global presence in targeted international markets. Our vision is to build healthier communities, urgently and responsibly, supported by our philosophy to make a meaningful difference for patients and communities in need. We believe this generates value for our multiple stakeholders, including our shareholders.

Our commercialization strategy for our on-market rare disease medicines, including our key growth drivers TEPEZZA, KRYSTEXXA and UPLIZNA, includes initiatives to increase awareness of the conditions each medicine is designed to treat, enhancing efforts to identify target patients and in certain cases pursue opportunities for international commercialization and more effective uses through clinical trials. For TEPEZZA and KRYSTEXXA, initiatives include promoting earlier treatment by driving awareness of the benefits of the medicines, and for UPLIZNA, initiatives include increasing awareness of what differentiates our medicines from other available therapies. Additional strategies for our on-market rare disease medicines include optimizing timely access for patients to the medicines and maximizing the value of the medicines through investment in clinical trials. Specifically, with respect to TEPEZZA, we expanded our commercial team, continued to invest in our direct-to-consumer marketing activities, refined our marketing and physician education strategies, and conducted extensive market analysis to identify further opportunities to accelerate growth, which we are implementing. These growth opportunities involve our efforts to increase adoption by ocular specialists and driving an urgency among ophthalmologists and endocrinologists to diagnose and refer thyroid eye disease, or TED, patients. In April 2023, we announced positive topline results from the randomized, double-masked, placebo-controlled Phase 4 clinical trial evaluating TEPEZZA in patients with chronic/low clinical activity score, or CAS, TED. In addition, we received U.S. Food and Drug Administration, or FDA, approval to update the TEPEZZA label to specify its use for the treatment of TED “regardless of Thyroid Eye Disease activity or duration,” which we believe reinforces the importance of unrestricted access for all eligible patients across the full spectrum of TED and creates an opportunity to ease the access burden for patients and physicians with the goal of decreasing time to therapy for patients who may benefit from TEPEZZA. As part of our strategy to maximize the value of TEPEZZA, we are educating key stakeholders, including physicians, patients and payers on the trial results and updated label indication. As a result of this process, large national and regional payers are beginning the process of updating their access requirements. To date, we have obtained favorable policy changes for greater than 20% of U.S. covered lives, which are expected to take effect in the second half of 2023. With respect to KRYSTEXXA, after receiving FDA approval of our supplemental biologics license application, or sBLA, in July 2022 to expand the label to include co-treatment of KRYSTEXXA with the immunomodulator methotrexate, we launched a successful commercial campaign related to the use of KRYSTEXXA with methotrexate, expanded our commercial team and are focused on promoting the expanded label with physicians and patients. This campaign has helped drive an increase in the usage of an immunomodulator with KRYSTEXXA to more than 70 percent of new patient starts in the second quarter of 2023 from the initial low-single digits in 2018.

Our R&D strategy is to expand our pipeline of preclinical and clinical development programs to drive sustainable growth, as well as maximizing the benefit and value of our existing medicines through development programs. Subject to the terms of the transaction agreement with Amgen and Pillartree, we are (i) acquiring, licensing and developing medicines for indications that address unmet needs in rare, autoimmune and severe inflammatory diseases, particularly those in our therapeutic areas of focus; (ii) maximizing our pipeline candidates through internal R&D; (iii) expanding our early-stage pipeline through partnerships and collaborations; and (iv) continuing to build out our research capabilities to generate discovery-stage candidates internally. Our R&D pipeline includes more than 20 programs. We expect to initiate several clinical trials in the second half of 2023, including a planned Phase 3 program for dazodalibep in Sjögren’s syndrome. This follows the announcement of our Phase 2 results where we achieved the primary endpoint in Sjögren’s syndrome patients with both moderate-to-severe systemic disease activity and moderate-to-severe symptomatology. This Phase 2 trial was the first to meet the primary endpoint in both patient populations. In the first half of 2023, we announced the initiation of two daxdilimab Phase 2 trials in discoid lupus erythematosus and lupus nephritis. In May 2023, we announced initiation of our TEPEZZA chronic/low CAS TED Phase 3 trial in Japan, which follows impressive topline results in patients with high CAS announced in June 2023.

The aim of our global expansion strategy is to build a global presence in targeted international markets to support the (i) continued launch of UPLIZNA in certain European markets and Brazil this year; (ii) potential approvals and commercial launches of UPLIZNA in additional markets in the coming years; and (iii) the pending commercial launch of TEPEZZA in Brazil; and (iv) potential approvals and commercial launches of TEPEZZA in Japan, Europe and other international markets over the next several years. We plan to use a combination of direct marketing and partnerships for our global expansion efforts and are establishing the infrastructure needed to support these activities. In June 2023, we announced approval by the Brazilian Health Regulatory Agency for TEPEZZA for the treatment of TED, making Brazil the first country outside of the United States to approve TEPEZZA. In July 2023, we announced positive topline results from the randomized, double-masked, placebo-controlled Phase 3 clinical trial evaluating TEPEZZA for the treatment of TED in Japanese patients with high CAS. There are no other medicines approved for the treatment of TED in Brazil or Japan, representing a significant unmet need in both markets.

RESULTS OF OPERATIONS

Comparison of Three Months Ended June 30, 2023 and 2022

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 June 30, 2023, compared to the three months ended June 30, 2022.

	For the Three Months Ended June 30,		Change	Change
	2023	2022	$	%
	(in thousands, except percentages)			
Net sales	$ 944,959	$ 876,411	$ 68,548	8 %
Cost of goods sold	219,958	230,216	(10,258)	(4)%
Gross profit	**725,001**	**646,195**	**78,806**	**12 %**
Operating expenses:				
Research and development	150,035	103,246	46,789	45 %
Selling, general and administrative	434,125	398,221	35,904	9 %
Impairment of goodwill	—	56,171	(56,171)	(100)%
Gain on sale of asset	(2,000)	—	(2,000)	(100)%
Total operating expenses	**582,160**	**557,638**	**24,522**	**4 %**
Operating income	**142,841**	**88,557**	**54,284**	**61 %**
Other expense, net:				
Interest expense, net	(12,098)	(21,409)	9,311	43 %
Foreign exchange gain	326	28	298	NM
Other income (expense), net	4,183	(2,389)	6,572	275 %
Total other expense, net	**(7,589)**	**(23,770)**	**16,181**	**68 %**
Income before expense for income taxes	**135,252**	**64,787**	**70,465**	**109 %**
Expense for income taxes	8,181	3,813	4,368	(115)%
Net income	**$ 127,071**	**$ 60,974**	**$ 66,097**	**108 %**

Beginning with the third quarter of 2022, we separately present upfront, milestone, and similar payments pursuant to collaborations, licenses of third-party technologies, and asset acquisitions as “Acquired in-process research and development and milestones” expenses in the condensed consolidated statement of comprehensive income. Amounts recorded in this line item would have historically been recorded to R&D expenses. We believe the new classification assists users of the financial statements in better understanding the payments incurred to acquire in-process research and development, or IPR&D. Prior period consolidated statements of comprehensive income have been reclassified to conform with the new classification. There were no acquired IPR&D and milestones expenses during the three months ended June 30, 2023 and 2022.

Net sales. Net sales increased $68.5 million, or 8%, to $944.9 million during the three months ended June 30, 2023, from $876.4 million during the three months ended June 30, 2022. The increase during the three months ended June 30, 2023 was primarily due to an increase in KRYSTEXXA net sales of $76.5 million and an increase in UPLIZNA net sales of $29.5 million, partially offset by a decrease in TEPEZZA net sales of $34.3 million.

The following table reflects net sales by medicine for the three months ended June 30, 2023 and 2022 (in thousands, except percentages):

	For the Three Months Ended June 30,		Change	Change
	2023	2022	$	%
TEPEZZA	$ 445,528	$ 479,814	(34,286)	(7)%
KRYSTEXXA	244,296	167,755	76,541	46 %
RAVICTI	88,351	75,722	12,629	17 %
UPLIZNA	68,084	38,598	29,486	76 %
PROCYSBI	53,145	47,706	5,439	11 %
ACTIMMUNE	29,039	29,989	(950)	(3)%
RAYOS	8,012	11,150	(3,138)	(28)%
PENNSAID 2%	6,913	23,586	(16,673)	(71)%
BUPHENYL	1,246	1,387	(141)	(10)%
QUINSAIR	345	335	10	3 %
DUEXIS	—	70	(70)	(100)%
VIMOVO	—	299	(299)	(100)%
Total net sales	**$ 944,959**	**$ 876,411**	**$ 68,548**	**8 %**

TEPEZZA. Net sales decreased $34.3 million, or 7%, to $445.5 million during the three months ended June 30, 2023, from $479.8 million during the three months ended June 30, 2022. Net sales decreased by approximately $34.0 million due to lower sales volume and $0.3 million due to lower net pricing. In the second half of 2022, we were impacted by certain challenges, including the often-burdensome reimbursement process, that we believe contributed to the decline in TEPEZZA net sales in the first half of 2023, compared to the 2022 period. These challenges, as well as challenges related to a lower rate of adherence to the full course of TEPEZZA therapy, have continued to moderate TEPEZZA net sales. We continue to execute on several opportunities designed to address these challenges and resume growth, including significantly expanding the size of our TEPEZZA sales force in late 2022 to allow our representatives more time with core TEPEZZA prescribers while educating other key physicians, including ophthalmologists and endocrinologists, about TED and TEPEZZA. As a result of the field-force expansion, through the first half of 2023, there was a 50% year-over-year increase in the number of ophthalmologists and endocrinologists prescribing TEPEZZA. In line with our expansion strategy, prescriber growth has largely come from ophthalmologists, with continued strong referral volume from endocrinologists. We are also spending additional time and focus on the reimbursement process to more effectively support the patient access journey, which includes beginning to obtain favorable policy changes to improve patient access following the update to the indication language on the TEPEZZA label and Phase 4 data release. We also continue to invest significantly in direct-to-consumer advertising based on the returns we have seen to date. In April 2023, we announced positive topline results from our Phase 4 clinical trial in chronic/low CAS TED and received FDA approval of an update to TEPEZZA's label specifying the use of TEPEZZA regardless of TED disease activity or duration, which we believe reinforces the importance of unrestricted access for all eligible patients across the full spectrum of TED. As part of our strategy to maximize the value of TEPEZZA, we are educating key stakeholders, including physicians, patients and payers on the trial results and updated label indication. As a result of this process, large national and regional payers are beginning to update their access requirements. To date, we have obtained favorable policy changes for more than 20% of U.S. covered lives, which are expected to take effect in the second half of 2023. We have seen improving trends in patient enrollment forms and patient starts as a result of our strategies and our expansion; however, it is taking longer than initially anticipated for our strategies and our expansion to contribute meaningfully to TEPEZZA net sales growth.

KRYSTEXXA. Net sales increased $76.5 million, or 46%, to $244.3 million during the three months ended June 30, 2023, from $167.8 million during the three months ended June 30, 2022. Net sales increased by approximately $54.6 million due to volume growth and $21.9 million due to higher net pricing. We expect net sales for KRYSTEXXA to continue to increase in future periods primarily due to the use of KRYSTEXXA with an immunomodulator following the approval of our sBLA in July 2022, which expanded KRYSTEXXA's labeling to include co-administration with methotrexate.

RAVICTI. Net sales increased $12.6 million, or 17%, to $88.4 million during the three months ended June 30, 2023, from $75.7 million during the three months ended June 30, 2022. Net sales increased by approximately $8.4 million due to higher net pricing and $4.2 million due to volume growth.

UPLIZNA. Net sales increased $29.5 million, or 76%, to $68.1 million during the three months ended June 30, 2023, from $38.6 million during the three months ended June 30, 2022. Net sales in the United States increased by $22.7 million, which was composed of an increase of $22.9 million due to higher sales volume, partially offset by a decrease of $0.2 million due to lower net pricing. The remaining $6.8 million increase in net sales related to higher international net sales recognized during the three months ended June 30, 2023.

PENNSAID 2%. Net sales decreased $16.7 million, or 71%, to $6.9 million during the three months ended June 30, 2023, from $23.6 million during the three months ended June 30, 2022. Net sales decreased by approximately $15.3 million due to lower sales volume and by approximately $1.4 million resulting from lower net pricing, as a result of generic competition.

Due to the impact of the at-risk launch of generic PENNSAID 2% during the year ended December 31, 2022, we redeployed a portion of our inflammation commercial team to support our TEPEZZA and KRYSTEXXA expansions. In the fourth quarter of 2022, we substantially completed a wind down of our former inflammation business, including active promotion efforts and associated HorizonCares support, for our inflammation medicines. As a result, sales volumes for PENNSAID 2%, RAYOS and DUEXIS declined significantly since the second quarter of 2022 and we expect net sales of our inflammation medicines to be immaterial going forward.

The table below reconciles our gross to net sales for the three months ended June 30, 2023 and 2022 (in millions, except percentages):

	Three Months Ended June 30, 2023		Three Months Ended June 30, 2022	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Gross sales	$ 1,240.7	100.0%	$ 1,241.3	100.0%
Adjustments to gross sales:				
Prompt pay discounts	(6.4)	(0.5)%	(10.0)	(0.8)%
Medicine returns	(9.0)	(0.7)%	(7.8)	(0.6)%
Co-pay and other patient assistance	(11.6)	(0.9)%	(98.8)	(8.0)%
Commercial rebates and wholesaler fees	(41.0)	(3.3)%	(51.2)	(4.1)%
Government rebates and chargebacks	(227.7)	(18.4)%	(197.1)	(15.9)%
Total adjustments	**(295.7)**	**(23.8)%**	**(364.9)**	**(29.4)%**
Net sales	**$ 945.0**	**76.2%**	**$ 876.4**	**70.6%**

During the three months ended June 30, 2023, co-pay and other patient assistance costs, as a percentage of gross sales, decreased to 0.9% from 8.0% during the three months ended June 30, 2022, primarily due to a decreased proportion of PENNSAID 2% sold. We expect co-pay and other patient assistance costs to continue to decrease as a percentage of total gross sales.

Cost of Goods Sold. Cost of goods sold decreased $10.3 million, or 4%, to $219.9 million during the three months ended June 30, 2023, from $230.2 million during the three months ended June 30, 2022. The decrease during the three months ended June 30, 2023 was primarily due to a decrease in inventory step-up expense. Inventory step-up expense decreased by $15.8 million related to acquired units of UPLIZNA inventory sold during the three months ended June 30, 2023 compared to the three months ended June 30, 2022. As of June 30, 2023, the total remaining balance of inventory step-up was $1.0 million. As a percentage of net sales, cost of goods sold (excluding intangible amortization expense of $89.3 million during the three months ended June 30, 2023 and $90.4 million during the three months ended June 30, 2022) was 16% during each of the three months ended June 30, 2023 and 2022.

Research and Development Expenses. R&D expenses increased $46.8 million, or 45%, to $150.0 million during the three months ended June 30, 2023, from $103.2 million during the three months ended June 30, 2022. The increase during the three months ended June 30, 2023 was primarily due to a $29.7 million increase in clinical trial and manufacturing development costs and an increase of $14.9 million in employee-related expenses during the three months ended June 30, 2023 compared to the three months ended June 30, 2022, reflecting increased activity in our R&D pipeline.

We expect our R&D expenses to continue increasing significantly in future periods as a result of our on-going and planned clinical trials for our pipeline.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased $35.9 million, or 9%, to $434.1 million during the three months ended June 30, 2023, from $398.2 million during the three months ended June 30, 2022. The increase during the three months ended June 30, 2023 was primarily due to costs associated with the commercialization of our medicines and global expansion initiatives, including an increase of $34.3 million in employee-related expenses. In addition, there was a $7.2 million increase in legal costs primarily relating to costs incurred in connection with the Transaction with Amgen, including responding to the FTC's second request and subsequent lawsuit seeking to enjoin the Transaction. This was partially offset by a decrease of $12.1 million in marketing program costs.

We expect our selling, general and administrative expenses to increase in future periods primarily due to continued support for our U.S. commercial and global expansion activities.

Impairment of goodwill. During the three months ended June 30, 2022, we recorded an impairment charge of $56.2 million in relation to our former inflammation reporting unit. Refer to Note 7, *Goodwill and Intangible Assets*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q for further details.

RESULTS OF OPERATIONS

Comparison of Six Months Ended June 30, 2023 and 2022

Consolidated Results

The table below should be referenced in connection with a review of the following discussion of our results of operations for the six months ended June 30, 2023, compared to the six months ended June 30, 2022.

	For the Six Months Ended June 30,		Change	Change
	2023	2022	$	%
	(in thousands, except percentages)			
Net sales	$ 1,777,018	$ 1,761,656	$ 15,362	1 %
Cost of goods sold	428,521	445,278	(16,757)	(4)%
Gross profit	**1,348,497**	**1,316,378**	**32,119**	**2 %**
Operating expenses:				
Research and development	284,183	206,378	77,805	38 %
Selling, general and administrative	887,479	770,955	116,524	15 %
Impairment of goodwill	—	56,171	(56,171)	(100)%
Gain on sale of asset	(2,000)	—	(2,000)	(100)%
Total operating expenses	**1,169,662**	**1,033,504**	**136,158**	**13 %**
Operating income	**178,835**	**282,874**	**(104,039)**	**(37)%**
Other expense, net:				
Interest expense, net	(27,638)	(42,665)	15,027	35 %
Foreign exchange gain	417	448	(31)	(7)%
Other income (expense), net	2,840	(3,131)	5,971	191 %
Total other expense, net	**(24,381)**	**(45,348)**	**20,967**	**46 %**
Income before benefit for income taxes	**154,454**	**237,526**	**(83,072)**	**(35)%**
Benefit for income taxes	(27,301)	(27,709)	408	1 %
Net income	**$ 181,755**	**$ 265,235**	**$ (83,480)**	**(31)%**

Beginning with the third quarter of 2022, we separately present upfront, milestone, and similar payments pursuant to collaborations, licenses of third-party technologies, and asset acquisitions as “Acquired in-process research and development and milestones” expenses in the condensed consolidated statement of comprehensive income. Amounts recorded in this line item would have historically been recorded to R&D expenses. We believe the new classification assists users of the financial statements in better understanding the payments incurred to acquire IPR&D. Prior period consolidated statements of comprehensive income have been reclassified to conform with the new classification. There were no acquired IPR&D and milestones expenses during the six months ended June 30, 2023 and 2022.

Net sales. Net sales increased $15.4 million, or 1%, to $1,777.0 million during the six months ended June 30, 2023, from $1,761.6 million during the six months ended June 30, 2022. The increase during the six months ended June 30, 2023 was primarily due to an increase in KRYSTEXXA net sales of $122.8 million and an increase in UPLIZNA net sales of $52.8 million, partially offset by a decrease in TEPEZZA net sales of $130.4 million and a decrease in PENNSAID 2% net sales of $42.8 million.

The following table reflects net sales by medicine for the six months ended June 30, 2023 and 2022 (in thousands, except percentages):

	For the Six Months Ended June 30,		Change	Change
	2023	2022	$	%
TEPEZZA	$ 850,845	$ 981,265	(130,420)	(13)%
KRYSTEXXA	431,277	308,459	122,818	40 %
RAVICTI	178,672	153,979	24,693	16 %
UPLIZNA	121,913	69,075	52,838	76 %
PROCYSBI	103,608	97,277	6,331	7 %
ACTIMMUNE	58,160	61,424	(3,264)	(5)%
PENNSAID 2%	16,107	58,954	(42,847)	(73)%
RAYOS	12,989	24,637	(11,648)	(47)%
BUPHENYL	2,659	3,548	(889)	(25)%
QUINSAIR	641	631	10	2 %
DUEXIS	139	1,193	(1,054)	(88)%
VIMOVO	8	1,214	(1,206)	(99)%
Total net sales	**$ 1,777,018**	**$ 1,761,656**	**$ 15,362**	**1 %**

TEPEZZA. Net sales decreased $130.4 million, or 13%, to $850.8 million during the six months ended June 30, 2023, from $981.2 million during the six months ended June 30, 2022. Net sales decreased by approximately $135.4 million due to lower sales volume, partially offset by an increase of $5.0 million due to higher net pricing. In the second half of 2022, we were impacted by certain challenges, including the often-burdensome reimbursement process, that we believe contributed to the decline in TEPEZZA net sales in the first half of 2023, compared to the 2022 period. These challenges, as well as challenges related to a lower rate of adherence to the full course of TEPEZZA therapy, have continued to moderate TEPEZZA net sales. We continue to execute on several opportunities designed to address these challenges and resume growth, including significantly expanding the size of our TEPEZZA sales force in late 2022 to allow our representatives more time with core TEPEZZA prescribers while educating other key physicians, including ophthalmologists and endocrinologists, about TED and TEPEZZA. As a result of the field-force expansion, through the first half of 2023, there was a 50% year-over-year increase in the number of ophthalmologists and endocrinologists prescribing TEPEZZA. In line with our expansion strategy, prescriber growth has largely come from ophthalmologists, with continued strong referral volume from endocrinologists. We are also spending additional time and focus on the reimbursement process to more effectively support the patient access journey, which includes beginning to obtain favorable policy changes to improve patient access following the update to the indication language on the TEPEZZA label and Phase 4 data release. We also continue to invest significantly in direct-to-consumer advertising based on the returns we have seen to date. In April 2023, we announced positive topline results from our Phase 4 clinical trial in chronic/low CAS TED and received FDA approval of an update to TEPEZZA's label specifying the use of TEPEZZA regardless of TED disease activity or duration, which we believe reinforces the importance of unrestricted access for all eligible patients across the full spectrum of TED. As part of our strategy to maximize the value of TEPEZZA, we are educating key stakeholders, including physicians, patients and payers on the trial results and updated label indication. As a result of this process, large national and regional payers are beginning to update their access requirements. To date, we have obtained favorable policy changes for more than 20% of U.S. covered lives, which are expected to take effect in the second half of 2023. We have seen improving trends in patient enrollment forms and patient starts as a result of our strategies and our expansion; however, it is taking longer than initially anticipated for our strategies and our expansion to contribute meaningfully to TEPEZZA net sales growth.

KRYSTEXXA. Net sales increased $122.8 million, or 40%, to $431.3 million during the six months ended June 30, 2023, from $308.5 million during the six months ended June 30, 2022. Net sales increased by approximately $85.9 million due to volume growth and $36.9 million due to higher net pricing. We expect net sales for KRYSTEXXA to continue to increase in future periods primarily due to the use of KRYSTEXXA with an immunomodulator following the approval of our sBLA in July 2022, which expanded KRYSTEXXA's labeling to include co-administration with methotrexate.

RAVICTI. Net sales increased $24.7 million, or 16%, to $178.7 million during the six months ended June 30, 2023, from $154.0 million during the six months ended June 30, 2022. Net sales increased by approximately $17.1 million due to higher net pricing and $7.6 million due to volume growth.

UPLIZNA. Net sales increased $52.8 million, or 76%, to $121.9 million during the six months ended June 30, 2023, from $69.1 million during the six months ended June 30, 2022. Net sales in the United States increased by $44.6 million, which was composed of an increase of $42.1 million due to higher sales volume and $2.5 million due to higher net pricing. The remaining $8.2 million increase in net sales related to higher international net sales recognized during the six months ended June 30, 2023.

PENNSAID 2%. Net sales decreased $42.8 million, or 73%, to $16.1 million during the six months ended June 30, 2023, from $58.9 million during the six months ended June 30, 2022. Net sales decreased by approximately $37.1 million due to lower sales volume and by approximately $5.7 million resulting from lower net pricing, as a result of generic competition.

RAYOS. Net sales decreased $11.6 million, or 47%, to $13.0 million during the six months ended June 30, 2023, from $24.6 million during the six months ended June 30, 2022. Net sales decreased by approximately $12.2 million due to lower sales volume, partially offset by an increase of approximately $0.6 million due to higher net pricing.

Under our settlement agreement with Teva Pharmaceuticals Industries Limited (formerly known as Actavis Laboratories FL, Inc., which itself was formerly known as Watson Laboratories, Inc. – Florida), or Teva, we expect Teva to enter the market with a generic version of RAYOS in second half of 2023. As a result, we expect our net sales for RAYOS to continue declining in future periods.

Due to the impact of the at-risk launch of generic PENNSAID 2% during the year ended December 31, 2022, we redeployed a portion of our inflammation commercial team to support our TEPEZZA and KRYSTEXXA expansions. In the fourth quarter of 2022, we substantially completed a wind down of our former inflammation business, including active promotion efforts and associated HorizonCares support, for our inflammation medicines. As a result, sales volumes for PENNSAID 2%, RAYOS and DUEXIS declined significantly since the second quarter of 2022 and we expect net sales of our inflammation medicines to be immaterial going forward.

The table below reconciles our gross to net sales for the six months ended June 30, 2023 and 2022 (in millions, except percentages):

	Six Months Ended June 30, 2023		Six Months Ended June 30, 2022	
	Amount	% of Gross Sales	Amount	% of Gross Sales
Gross sales	$ 2,347.7	100.0%	$ 2,472.8	100.0%
Adjustments to gross sales:				
Prompt pay discounts	(13.1)	(0.6)%	(20.2)	(0.8)%
Medicine returns	(15.9)	(0.7)%	(12.2)	(0.5)%
Co-pay and other patient assistance	(44.2)	(1.9)%	(183.6)	(7.4)%
Commercial rebates and wholesaler fees	(79.1)	(3.4)%	(102.4)	(4.2)%
Government rebates and chargebacks	(418.4)	(17.8)%	(392.7)	(15.9)%
Total adjustments	**(570.7)**	**(24.4)%**	**(711.1)**	**(28.8)%**
Net sales	**$ 1,777.0**	**75.6%**	**$ 1,761.7**	**71.2%**

During the six months ended June 30, 2023, co-pay and other patient assistance costs, as a percentage of gross sales, decreased to 1.9% from 7.4% during the six months ended June 30, 2022, primarily due to a decreased proportion of PENNSAID 2% sold. We expect co-pay and other patient assistance costs to continue to decrease as a percentage of total gross sales.

Cost of Goods Sold. Cost of goods sold decreased $16.8 million, or 4%, to $428.5 million during the six months ended June 30, 2023, from $445.3 million during the six months ended June 30, 2022. The decrease during the six months ended June 30, 2023 was primarily due to a decrease in inventory step-up expense. Inventory step-up expense decreased by $13.2 million related to acquired units of UPLIZNA inventory sold during the six months ended June 30, 2023 compared to the six months ended June 30, 2022. As of June 30, 2023, the total remaining balance of inventory step-up was $1.0 million. As a percentage of net sales, cost of goods sold (excluding amortization expense of $177.5 million during the first half of 2023 and $179.2 million during first half of 2022) was 14% during the six months ended June 30, 2023, compared to 15% during the six months ended June 30, 2022. The decrease in cost of goods sold as a percentage of net sales was primarily due to a decrease in inventory step-up expense related to UPLIZNA as noted above.

Research and Development Expenses. R&D expenses increased $77.8 million, or 38%, to $284.2 million during the six months ended June 30, 2023, from $206.4 million during the six months ended June 30, 2022. The increase during the six months ended June 30, 2023 was primarily due to a $54.0 million increase in clinical trial and manufacturing development costs and an increase of $21.9 million in employee-related expenses during the six months ended June 30, 2023 compared to the six months ended June 30, 2022, reflecting increased activity in our R&D pipeline.

We expect our R&D expenses to continue increasing significantly in future periods as a result of our on-going and planned clinical trials for our pipeline.

Selling, General and Administrative Expenses. Selling, general and administrative expenses increased $116.5 million, or 15%, to $887.5 million during the six months ended June 30, 2023, from $771.0 million during the six months ended June 30, 2022. The increase during the six months ended June 30, 2023 was primarily due to costs associated with the commercialization of our medicines and global expansion initiatives, including increases of $64.3 million in employee-related expenses and $12.5 million in marketing program costs. In addition, there was a $16.5 million increase in legal costs primarily relating to costs incurred in connection with the Transaction with Amgen, including responding to the FTC’s second request and subsequent lawsuit seeking to enjoin the Transaction.

We expect our selling, general and administrative expenses to increase in future periods primarily due to continued support for our U.S. commercial and global expansion activities.

Impairment of goodwill. During the six months ended June 30, 2022, we recorded an impairment charge of $56.2 million in relation to our former inflammation reporting unit. Refer to Note 7, *Goodwill and Intangible Assets*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q for further details.

NON-GAAP FINANCIAL MEASURES

We provide certain non-GAAP financial measures, including EBITDA, or earnings before interest, taxes, depreciation and amortization, adjusted EBITDA, non-GAAP net income and non-GAAP earnings per share. 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, transaction-related costs, manufacturing facility start-up costs, restructuring and realignment costs and gain on sale of asset, as well as non-cash items such as share-based compensation, inventory step-up expense, depreciation and amortization, non-cash interest expense, (gain) loss on equity security investments 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. 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 income 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 June 30,		For the Six Months Ended June 30,	
	2023	2022	2023	2022
GAAP net income	**$ 127,071**	**$ 60,974**	**$ 181,755**	**$ 265,235**
Depreciation [1]	6,687	6,091	12,933	11,943
Amortization and step-up:				
Intangible amortization expense [2]	89,598	91,335	178,212	180,595
Inventory step-up expense [3]	1,572	17,362	31,315	44,563
Interest expense, net (including amortization of debt discount and deferred financing costs)	12,098	21,409	27,638	42,665
Expense (benefit) for income taxes	8,181	3,813	(27,301)	(27,709)
EBITDA	**245,207**	**200,984**	**404,552**	**517,292**
Other non-GAAP adjustments:				
Share-based compensation [4]	60,271	45,149	118,391	92,449
Transaction-related costs [5]	16,539	—	26,323	—
Manufacturing facility start-up costs [6]	1,896	1,582	5,372	2,389
Restructuring and realignment costs [7]	854	1,253	2,676	1,790
Acquisition/divestiture-related costs [8]	52	1,023	733	2,612
Impairment of goodwill [9]	—	56,171	—	56,171
Gain on sale of asset [10]	(2,000)	—	(2,000)	—
(Gain) loss on equity security investments [11]	(2,437)	438	(2,789)	5,084
Total of other non-GAAP adjustments	**75,175**	**105,616**	**148,706**	**160,495**
Adjusted EBITDA	**$ 320,382**	**$ 306,600**	**$ 553,258**	**$ 677,787**

	For the Three Months Ended June 30,		For the Six Months Ended June 30,	
	2023	2022	2023	2022
GAAP net income	**$ 127,071**	**$ 60,974**	**$ 181,755**	**$ 265,235**
Non-GAAP adjustments:				
Depreciation [1]	6,687	6,091	12,933	11,943
Amortization and step-up:				
Intangible amortization expense [2]	89,598	91,335	178,212	180,595
Amortization of debt discount and deferred financing costs [12]	1,308	2,327	2,779	3,904
Inventory step-up expense [3]	1,572	17,362	31,315	44,563
Share-based compensation [4]	60,271	45,149	118,391	92,449
Transaction-related costs [5]	16,539	—	26,323	—
Manufacturing facility start-up costs [6]	1,896	1,582	5,372	2,389
Restructuring and realignment costs [7]	854	1,253	2,676	1,790
Acquisition/divestiture-related costs [8]	52	1,023	733	2,612
Impairment of goodwill [9]	—	56,171	—	56,171
Gain on sale of asset [10]	(2,000)	—	(2,000)	—
(Gain) loss on equity security investments [11]	(2,437)	438	(2,789)	5,084
Total of pre-tax non-GAAP adjustments	**174,340**	**222,731**	**373,945**	**401,500**
Income tax effect of pre-tax non-GAAP adjustments [13]	(21,354)	(29,919)	(81,297)	(97,131)
Total non-GAAP adjustments	**152,986**	**192,812**	**292,648**	**304,369**
Non-GAAP net income	**$ 280,057**	**$ 253,786**	**$ 474,403**	**$ 569,604**
Non-GAAP Earnings Per Share:				
Weighted average ordinary shares – Basic	**228,743,143**	**230,020,004**	**228,571,356**	**229,559,715**
Non-GAAP Earnings Per Share – Basic				
GAAP earnings per share – Basic	**$ 0.56**	**$ 0.27**	**$ 0.80**	**$ 1.16**
Non-GAAP adjustments	0.66	0.83	1.28	1.32
Non-GAAP earnings per share – Basic	**$ 1.22**	**$ 1.10**	**$ 2.08**	**$ 2.48**
Weighted average ordinary shares – Diluted				
Weighted average ordinary shares – Basic	228,743,143	230,020,004	228,571,356	229,559,715
Ordinary share equivalents	5,192,448	6,146,380	5,366,793	6,517,432
Weighted average ordinary shares – Diluted	**233,935,591**	**236,166,384**	**233,938,149**	**236,077,147**
Non-GAAP Earnings Per Share – Diluted				
GAAP earning per share – Diluted	**$ 0.54**	**$ 0.26**	**$ 0.78**	**$ 1.12**
Non-GAAP adjustments	0.66	0.81	1.25	1.29
Non-GAAP earnings per share – Diluted	**$ 1.20**	**$ 1.07**	**$ 2.03**	**$ 2.41**

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

(2)Intangible amortization expenses are primarily associated with our developed technology related to TEPEZZA, KRYSTEXXA, RAVICTI, UPLIZNA, PROCYSBI, ACTIMMUNE, RAYOS and BUPHENYL.

(3)During the three and six months ended June 30, 2023, we recognized in cost of goods sold $1.6 million and $31.3 million, respectively, for inventory step-up expense related to UPLIZNA inventory revalued in connection with the Viela Bio, Inc. acquisition. We recorded $17.4 million and $44.6 million of UPLIZNA inventory step-up expense in cost of goods sold during the three and six months ended June 30, 2022, respectively. Refer to Note 4, *Inventories*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q for further details.

(4)Represents share-based compensation expense associated with RSU and PSU grants to our employees and non-employee directors, and our employee share purchase plan.

(5)Primarily represents transaction-related costs, including, advisory, legal, consulting and field-based employee retention costs, incurred in connection with the Transaction with Amgen. The legal costs include costs incurred in responding to the FTC’s second request and subsequent lawsuit seeking to enjoin the Transaction.

(6)During the three months ended June 30, 2023 and 2022, we recorded $1.9 million and $1.6 million, respectively, and $5.4 million and $2.4 million for the six months ended June 30, 2023 and 2022, respectively, of manufacturing facility start-up costs related to our drug product biologics manufacturing facility in Waterford, Ireland.

(7)Primarily represents severance and consulting costs related to the wind down of our former inflammation business during 2022 and rent and maintenance charges as a result of vacating the leased Lake Forest office in the first quarter of 2021.

(8)Primarily represents transaction and integration costs, including, advisory, legal, consulting and certain employee-related costs, incurred in connection with our acquisitions and divestitures.

(9)Our interim goodwill impairment test in the second quarter of 2022 indicated an impairment which represented the difference between the estimated fair value of the former inflammation reporting unit and its carrying value. As a result, we recognized an impairment charge of $56.2 million in June 2022 representing the full amount of goodwill for the former inflammation reporting unit. Refer to Note 7, *Goodwill and Intangible Assets*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q, for further details.

(10)During the six months ended June 30, 2023, gain on sale of asset represents a $2.0 million contingent consideration payment related to the sale of MIGERGOT in 2019. The contingent consideration payment was triggered during the second quarter of 2023 and it was received in July 2023.

(11)We held investments in equity securities with readily determinable fair values of $9.8 million and $8.1 million as of June 30, 2023 and 2022, respectively, which are included in other long-term assets in the condensed consolidated balance sheet. For the three and six months ended June 30, 2023, we recognized net unrealized gains of $2.4 million and $2.8 million, respectively, due to the change in fair value of these securities.

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

(13)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

On December 12, 2022, we announced that we had entered into a transaction agreement with Amgen and Pillartree. We have agreed to various covenants and agreements, including, among others, agreements to conduct our business in the ordinary course during the period between the execution of the transaction agreement and the Effective Time. Outside of certain limited exceptions, we may not take, authorize, commit, resolve, or agree to do certain actions without Amgen's consent, including: (i) acquiring businesses and disposing of significant assets; (ii) incurring capital expenditures above specified thresholds; (iii) issuing equity; (iv) incurring indebtedness; and (v) repurchasing outstanding ordinary shares. We do not believe these restrictions will prevent us from being able to fund our operations, working capital needs or capital expenditure requirements. The following discussion assumes that the Transaction is not consummated and we continue to operate as an independent entity.

As of June 30, 2023, we had retained earnings of $771.8 million. We expect that our sales and marketing expenses will continue to increase as a result of the commercialization of our medicines and global expansion initiatives, but we believe these cost increases will be offset by higher net sales and gross profits in future periods. Additionally, we expect that our R&D and IPR&D and milestones expenses will continue to increase as we advance our candidates through the clinical development and regulatory approval processes. In particular, we expect to incur substantial costs in connection with advancing our pipeline of medicine candidates and development programs in on-going and planned clinical trials.

We are in the process of expanding our production capacity to meet anticipated future demand for TEPEZZA, primarily for 2023 and beyond. As of June 30, 2023, we had total purchase commitments, including the minimum annual order quantities and binding firm orders, with AGC Biologics A/S (formerly known as CMC Biologics A/S) for TEPEZZA drug substance of €89.3 million ($97.4 million converted at a Euro-to-Dollar exchange rate as of June 30, 2023 of 1.0905).

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

Under our license agreement with F. Hoffmann-La Roche Ltd and Hoffmann-La Roche Inc., or together referred to as Roche, our remaining obligation to Roche relating to the attainment of various TEPEZZA development and regulatory milestones is CHF43.0 million ($47.9 million when converted using a CHF-to-Dollar exchange rate at June 30, 2023 of 1.1150).

In July 2021, we completed the purchase of a drug product biologics manufacturing facility from EirGen Pharma Limited for $67.9 million. We expect to incur approximately $15.0 million in capital expenditures during the second half of 2023 in order to prepare the drug product facility to manufacture the first medicine for commercial use, which, assuming the timely receipt of regulatory approvals, we anticipate to occur in the fourth quarter of 2023. In August 2022, we submitted a planning application to build a drug substance biologics manufacturing facility adjacent to our existing drug product biologics manufacturing facility in Waterford, Ireland. Based on our current operating plan, we do not anticipate making significant investments in building a drug substance biologics manufacturing facility during 2023.

On June 18, 2021, we entered into a global agreement with Arrowhead Pharmaceuticals, Inc., or Arrowhead, for HZN-457, a discovery-stage investigational RNA interference therapeutic being developed by Arrowhead as a potential treatment for uncontrolled gout. Under the terms of the agreement, we paid Arrowhead an upfront cash payment of $40.0 million in July 2021 and agreed to pay additional potential future milestone payments of up to $660.0 million contingent on the achievement of certain development, regulatory and commercial milestones, and low to mid-teens royalties on worldwide calendar year net sales of licensed medicines. In addition, we recognized a $15.0 million development milestone in the fourth quarter of 2022. The $15.0 million development milestone was subsequently paid in the first quarter of 2023.

We are committed to invest as a strategic limited partner in four venture capital funds: Forbion Growth Opportunities Fund I C.V., Forbion Capital Fund V C.V., Aisling Capital V, L.P. and RiverVest Venture Fund V, L.P. As of June 30, 2023, the total carrying amount of our investments in these funds was $31.9 million, which is included in other long-term assets in the condensed consolidated balance sheet, and our total future commitments to these funds are $35.4 million.

We have financed our operations to date through equity financings, debt financings and the issuance of convertible notes, along with cash flows from operations during the last several years. As of June 30, 2023, we had $2.5 billion in cash and cash equivalents and total debt with a book value of $2.6 billion and face value of $2.6 billion. We believe our existing cash and cash equivalents and our expected cash flows from our operations will be sufficient to fund our business needs for at least the next 12 months from the issuance of the financial statements in this Quarterly Report on Form 10-Q. Because of the short-term maturities of our cash equivalents, we do not believe that a change in interest rates or the risk relating to recent bank failures would have any material negative impact on the fair value of our cash equivalents. We do not have any financial covenants or non-financial covenants that we expect to be affected by the economic disruptions and negative effects of recent bank failures, global macro-economic issues or inflationary pressures.

We have a significant amount of debt outstanding on a consolidated basis. For a description of our debt agreements, refer to Note 12, *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, R&D 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, including rising interest rates and recent bank failures; limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; and placing us at a disadvantage as compared to our competitors, to the extent that they are not as highly leveraged. We may not be able to generate sufficient cash to service all of our indebtedness and may be forced to take other actions to satisfy our obligations under our indebtedness.

In addition, the indenture governing our 5.5% Senior Notes due 2027, 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.

On April 18, 2023, in connection with the potential closing of the Transaction, Horizon Therapeutics USA, Inc., our wholly owned subsidiary, or the Issuer, directed U.S. Bank Trust Company, National Association (as successor to U.S. Bank National Association), as trustee, or Notes Trustee, to give a notice, or First Redemption Notice, of the Issuer's intent, in accordance with the indenture governing the 2027 Senior Notes, or 2027 Notes Indenture, to redeem in full the aggregate principal amount of our outstanding 2027 Senior Notes. The redemption as set forth in the First Redemption Notice was conditioned on, among other things, the consummation of the Transaction by not later than June 26, 2023. On May 26, 2023, HTUSA revoked the First Redemption Notice and directed the Notes Trustee to give a notice, or Second Redemption Notice, of HTUSA's intent, in accordance with the 2027 Notes Indenture, to redeem in full the aggregate principal amount of the outstanding 2027 Senior Notes. The redemption as set forth in the Second Redemption Notice was conditioned on, among other things, the consummation of the Transaction by not later than July 25, 2023. On July 21, 2023, HTUSA revoked the Second Redemption Notice and directed the Notes Trustee to give a notice, or the Third Redemption Notice, of HTUSA's intent, in accordance with the 2027 Notes Indenture, to redeem in full the aggregate principal amount of the outstanding 2027 Senior Notes. The redemption as set forth in the Third Redemption Notice is conditioned on, among other things, the consummation of the Transaction by not later than September 19, 2023.

On April 25, 2022, we entered into two interest rate swap agreements with notional amounts totaling $800.0 million, effective June 24, 2022, to hedge or otherwise protect against interest rate fluctuations on a portion of our variable rate debt. The agreements effectively fix the Secured Overnight Financing Rate, or SOFR, at approximately 2.8% through December 24, 2026. These agreements were designated as cash flow hedges of the variability of future cash flows subject to the variable monthly interest rates on $800.0 million of our senior secured term loans borrowed under our Credit Agreement in December 2019 and March 2021. Refer to Note 13, *Derivative Instruments and Hedging Activities*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q for further details.

During the six months ended June 30, 2023, we issued an aggregate of 1.7 million of our ordinary shares in connection with stock option exercises, the vesting of RSUs and PSUs, and employee share purchase plan purchases. We received a total of $21.0 million in net proceeds in connection with such issuances. During the six months ended June 30, 2023, we made payments of $92.1 million for employee withholding taxes relating to vesting of share-based awards.

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.

Sources and Uses of Cash

The following table provides a summary of our cash position and cash flows for the six months ended June 30, 2023 and 2022 (in thousands):

	For the Six Months Ended June 30,	
	2023	2022
Cash, cash equivalents and restricted cash	$ 2,469,414	$ 1,897,300
Cash provided by (used in):		
Operating activities	247,789	464,987
Investing activities	(61,777)	(52,905)
Financing activities	(79,094)	(92,621)

Operating Cash Flows

Net cash provided by operating activities during the six months ended June 30, 2023 of $247.8 million was primarily attributable to cash collections from gross sales, partially offset by payments made related to government rebates and patient assistance costs for our medicines, payments for inventory, payments related to selling, general and administrative expenses and payments related to R&D expenses.

During the six months ended June 30, 2022, net cash provided by operating activities of $465.0 million was primarily attributable to cash collections from gross sales, partially offset by payments made related to patient assistance costs for our former inflammation segment medicines and government rebates for our orphan segment medicines, payments related to selling, general and administrative expenses and payments related to R&D expenses.

Investing Cash Flows

Net cash used in investing activities during the six months ended June 30, 2023 of $61.8 million was primarily attributable to payments related to purchases of property, plant and equipment of $42.6 million and milestone-based development funding of $15.0 million paid to Arrowhead in the first quarter of 2023. Refer to 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.

During the six months ended June 30, 2022, net cash used in investing activities of $52.9 million was primarily attributable to an upfront payment of $25.0 million paid to Alpine Immune Sciences, Inc. in the first quarter of 2022 relating to an exclusive license agreement entered into in December 2021 and payments related to purchases of property, plant and equipment of $24.4 million.

Financing Cash Flows

Net cash used in financing activities during the six months ended June 30, 2023 of $79.1 million was primarily attributable to $92.1 million in payments of employee withholding taxes relating to share-based awards, partially offset by $21.0 million in proceeds from the issuance of ordinary shares in connection with stock option exercises and employee share purchase plan purchases.

During the six months ended June 30, 2022, net cash used in financing activities of $92.6 million was primarily attributable to $120.5 million in payments of employee withholding taxes relating to share-based awards, partially offset by $35.9 million in proceeds from the issuance of ordinary shares in connection with stock option exercises and employee share purchase plan purchases.

Financial Condition as of June 30, 2023 Compared to December 31, 2022

Prepaid expenses and other current assets. Prepaid expenses and other current assets increased $115.5 million, from $449.3 million as of December 31, 2022 to $564.8 million as of June 30, 2023. The increase was primarily due to an increase of $41.5 million in deferred charges for taxes on intercompany profits, an increase of $30.2 million in advance payments for inventory and an increase of $14.9 million in prepaid clinical study costs.

Developed technology and other intangible assets, net. Developed technology and other intangible assets, net decreased $178.2 million, from $2,664.8 million as of December 31, 2022 to $2,486.6 million as of June 30, 2023, primarily related to $178.2 million of amortization of developed technology recorded during the six months ended June 30, 2023.

Other long-term assets. Other long-term assets increased $58.9 million, from $204.1 million as of December 31, 2022 to $263.0 million as of June 30, 2023. The increase was primarily due to the recognition of a $46.0 million right-of-use asset relating to a new lease entered into in Rockville, Maryland. Refer to Note 14, *Lease Obligations*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q, for further details.

Accounts Payable. Accounts payable decreased $70.3 million, from $155.8 million as of December 31, 2022 to $85.5 million as of June 30, 2023. The decrease was primarily due to the timing of payments, including a decrease of $73.7 million in accounts payable related to government rebates, co-pay and patient assistance costs and commercial rebates and wholesaler fees.

Deferred tax liabilities, net. Deferred tax liabilities, net, decreased $77.2 million from $342.0 million as of December 31, 2022 to $264.8 million as of June 30, 2023, primarily due to a benefit for income taxes recognized during the six months ended June 30, 2023.

Other long-term liabilities. Other long-term liabilities increased $59.3 million, from $204.5 million as of December 31, 2022 to $263.8 million as of June 30, 2023. The increase was primarily due to the recognition of a $46.9 million lease liability relating to a new lease entered into in Rockville, Maryland. Refer to Note 14, *Lease Obligations*, of the Notes to Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q, for further details.

Contractual Obligations

As of June 30, 2023, there were no material changes 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, 2022, except as described 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.

CRITICAL ACCOUNTING POLICIES

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

During the six months ended June 30, 2023, there were no significant changes in our application of our critical accounting policies. A summary of our critical accounting policies is included in Item 7 to our Annual Report on Form 10-K for the year ended December 31, 2022.

ITEM 3. QUANTITATIVE AND QUALITATIVE DISCLOSURES ABOUT MARKET RISK

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

Interest Rate Risk. We are subject to interest rate fluctuation exposure through our borrowings under our Credit Agreement and our investment in money market accounts which bear a variable interest rate. Our approximately $418.0 million aggregate principal amount of senior secured term loans borrowed under our Credit Agreement in December 2019, or the 2026 Term Loans, and loans under our incremental revolving credit facility, or Revolving Credit Facility, bear interest, at our option, at a rate equal to SOFR (subject to a 0.00% SOFR floor), plus the SOFR adjustment, plus 2.25% per annum, or the adjusted base rate plus 1.25% per annum with a step-down to SOFR, plus the SOFR adjustment, 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 SOFR adjustment is an additional interest amount for either one-month, three-month or six-month interest periods, at our election: (a) 0.11% using a one-month interest period, (b) 0.26% using a three-month interest period, and (c) 0.43% using a six-month interest period. The adjusted base rate is defined as the greatest of (a) SOFR (using one-month interest period) plus 1.00%, (b) the prime rate, (c) the federal funds rate plus 0.50%, and (d) 1.00%. Our 2026 Term Loans are borrowed in SOFR. The one-month SOFR rate as of July 24, 2023, which was the most recent date the interest rate on the 2026 Term Loans was fixed, was 5.29%, and as a result, the interest rate on our 2026 Term Loans is currently 7.41% per annum. Our $1.6 billion aggregate principal amount of senior secured term loans borrowed under our Credit Agreement in March 2021, or the 2028 Term Loans, bear interest, at our option, at a rate equal to SOFR (subject to a 0.00% SOFR floor), plus the SOFR adjustment, plus 2.00% per annum, or the adjusted base rate plus 1.00% per annum with a step-down to SOFR, plus the SOFR adjustment, plus 1.75% per annum or the adjusted base rate plus 0.75% per annum at the time our leverage ratio is less than or equal to 2.00 to 1.00. Our 2028 Term Loans are based on SOFR. The one-month SOFR rate as of July 24, 2023, which was the most recent date the interest rate on the 2028 Term Loans was fixed, was 5.29%, and as a result, the interest rate on our 2028 Term Loans is currently 7.16% per annum. As of June 30, 2023, the Revolving Credit Facility was undrawn.

As of June 30, 2023, an increase in the SOFR of 100 basis points above the current SOFR rate, which includes the effect of the two interest rate swaps entered into in the second quarter of 2022, would increase our interest expense related to the Credit Agreement by $12.0 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, time deposits and U.S. federal government securities. Because of the short-term maturities of our cash equivalents, we do not believe that a change in interest rates or risk relating to recent bank failures would have any material negative impact on the fair value of our cash equivalents.

Foreign Currency Risk. Our purchase costs of TEPEZZA drug substance, TEPEZZA drug product with our second drug product manufacturer, Patheon Pharmaceuticals Inc. (the contract development and manufacturing services organization of Thermo Fisher Scientific), and ACTIMMUNE inventory are principally denominated in Euros and are subject to foreign currency risk. In addition, we are obligated to pay certain milestones and a royalty on sales of TEPEZZA to Roche in Swiss Francs, which obligations are subject to foreign currency risk. We also incur certain operating expenses and earn certain revenues 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 Swiss Franc. In addition, we enter into forward currency contracts to hedge our foreign currency risk exposure.

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 biopharmaceutical distributors who, in turn, sell the medicines to pharmacies, hospitals and other customers. As of June 30, 2023 and December 31, 2022, our top four customers accounted for approximately 89% and 94% of our total outstanding accounts receivable balances, respectively. Given the size and creditworthiness of the customers, we have not experienced and do not expect to experience material credit related losses with such customers.

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 June 30, 2023, the end of the period covered by this report.

Changes in Internal Control Over Financial Reporting. During the quarter ended June 30, 2023, there have been no 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 Condensed Consolidated Financial Statements, included in Item 1 of this Quarterly Report on Form 10-Q.

ITEM 1A: RISK FACTORS

Risk Factors Summary

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

- Failure to complete, or further delays in completing, the pending transaction with Amgen Inc., or Amgen, announced on December 12, 2022 could materially and adversely affect our results of operations and our share price.
- Our ability to generate revenues from our medicines is subject to attaining significant market acceptance among physicians, patients and healthcare payers.
- Our future prospects are highly dependent on our ability to successfully develop and execute commercialization strategies for each of our medicines. Failure to do so would adversely impact our financial condition and prospects.
- In order to increase adoption and sales of our medicines, we will need to continue developing our commercial organization as well as recruit and retain qualified sales representatives.
- Coverage and reimbursement may not be available, or reimbursement may be available at only limited levels, for our medicines, which could make it difficult for us to sell our medicines profitably.
- Our medicines are subject to extensive regulation, and we may not obtain additional regulatory approvals for our medicines.
- We are subject to ongoing obligations and continued regulatory review by the U.S. Food and Drug Administration, or FDA, and comparable foreign regulatory authorities, and we may be subject to penalties and litigation and large incremental expenses if we fail to comply with regulatory requirements or experience problems with our medicines.
- We rely on third parties to manufacture commercial supplies of all of our medicines, and we currently intend to rely, in whole or in part, on third parties to manufacture commercial supplies of any other approved medicines. The commercialization of any of our medicines could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of medicine or fail to do so at acceptable quality levels or prices or fail to maintain or achieve satisfactory regulatory compliance.
- We face significant competition from other biopharmaceutical companies, including those marketing generic medicines and our operating results will suffer if we fail to compete effectively.
- Clinical development of drugs and biologics involves a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.
- If we fail to develop or acquire other medicine candidates or medicines, our business and prospects would be limited.
- We are subject to federal, state and foreign healthcare laws and regulations and implementation or changes to such healthcare laws and regulations, or other regulatory reforms, could adversely affect our business and results of operations.
- If we are unable to obtain or protect intellectual property rights related to our medicines and medicine candidates, we may not be able to compete effectively in our markets.

Risk Factors

You should consider carefully the risks described below, together with all of the other information included in this report, and in our other filings with the Securities and Exchange Commission, or SEC, before deciding whether to invest in or continue to hold our ordinary shares. The risks described below are all material risks currently known, expected or reasonably foreseeable by us. If any of these risks actually occurs, our business, financial condition, results of operations or cash flow could be seriously harmed. This could cause the trading price of our ordinary shares to decline, resulting in a loss of all or part of your investment. The risk factors set forth below with an asterisk (*) next to the title are new risk factors or risk factors containing changes, including any material changes, from the risk factors previously disclosed in Item 1A of our Annual Report on Form 10-K for the year ended December 31, 2022, as filed with the SEC.

Risks Relating to Our Pending Transaction with Amgen

*Failure to complete, or further delays in completing, the pending transaction with Amgen announced on December 12, 2022 could materially and adversely affect our results of operations and our share price.**

On December 12, 2022, we announced that we entered into a transaction agreement with Amgen and Pillartree Limited, or Pillartree, a wholly owned subsidiary of Amgen. Subject to the terms of the transaction agreement, Pillartree will acquire our company, or the Transaction, pursuant to a scheme of arrangement under Chapter 1 of Part 9 of the Companies Act 2014 of Ireland, or the Scheme, or under certain circumstances, subject to the terms of the transaction agreement, a takeover offer (as such term is defined in the Irish Takeover Rules) rather than the Scheme. As a result of the Scheme, we would become a wholly owned subsidiary of Amgen. Consummation of the Transaction is subject to certain closing conditions, some of which are not within our control, and may prevent, delay, or otherwise materially adversely affect the completion of the Transaction. On May 16, 2023, the Federal Trade Commission, or FTC, filed a complaint in the United States District Court for the Northern District of Illinois seeking a temporary restraining order and preliminary injunction enjoining the Transaction. On May 23, 2023, the court scheduled an evidentiary hearing on the FTC's request for a preliminary injunction beginning on September 11, 2023. Based on the court's schedule, we, Amgen and the FTC then submitted a stipulated proposed temporary restraining order to the court providing that we and Amgen would not close the Transaction until the earlier of October 31, 2023 or the second business day after the court rules on the FTC's request for a preliminary injunction, or Stipulated TRO. On May 31, 2023, the court entered a case management order, and on June 2, 2023, the court issued an order granting the Stipulated TRO. On June 22, 2023, the FTC filed a parallel complaint in its administrative court and an amended complaint was filed in the federal district court adding several states as additional plaintiffs. On June 29, 2023, we and Amgen filed an answer to the amended complaint and counterclaims against the FTC. We expect that the schedule set by the federal district court would allow the Transaction to close by mid-December 2023, but only if the court denies the request for a preliminary injunction. We cannot predict with certainty whether and when any of the required closing conditions, including the termination of the Stipulated TRO and absence of any other order preventing consummation of the Transaction, will be satisfied or if additional uncertainties may arise and cannot guarantee that we will be able to successfully consummate the pending Transaction as currently contemplated under the transaction agreement or at all. In particular, there can be no guarantee that the federal district court will deny the FTC's request for a preliminary injunction or when, if ever, such a ruling would be issued. If the FTC's request for a preliminary injunction is granted, it is highly unlikely that the Transaction could close before the December 12, 2023 end date specified in the transaction agreement. In the event that the Transaction does not close before the December 12, 2023 end date specified in the transaction agreement, each party would then have the right, in its sole discretion, to terminate the transaction agreement and abandon the Transaction, which Amgen may determine to do, particularly if the FTC's request for a preliminary injunction is granted. If the transaction agreement is terminated and the Transaction is abandoned, whether due to the failure to satisfy applicable closing conditions related to obtaining antitrust clearance for the Transaction or otherwise, our business, results of operations, financial condition, and our share price would be materially and adversely affected. Risks related to the failure of the pending Transaction to be consummated include, but are not limited to, the following:

- the current market price for our ordinary shares reflects a market assumption that the Transaction will be completed but the trading price of our ordinary shares may decline;
- potential adverse effects on our relationships with current collaboration partners, suppliers, healthcare providers and other business partners, or those with which we are seeking to establish business relationships, due to uncertainties about the Transaction;
- the loss of potential business opportunities that we did not pursue during the pendency of the Transaction and may not be available to us in the future;
- potential adverse effects resulting from open employee positions resulting from the pendency of the Transaction;
- we will remain liable for significant transaction costs, including legal, financial advisory, accounting, and other costs relating to the Transaction regardless of whether the Transaction is consummated;
- the attention of our management will have been diverted to the Transaction; and
- we could be subject to litigation related to any failure to complete the Transaction.

Additionally, the retention of our employees, hiring of new qualified employees and the performance of our employees have been negatively affected during the pendency of the Transaction as employees or prospective employees face uncertainty about their future roles following completion of the Transaction.

Further, under the transaction agreement, we are generally required to conduct our business in the ordinary course, consistent with past practice and are restricted from taking certain specified actions absent Amgen's prior written consent.

The occurrence of any of these events individually or in combination could materially and adversely affect our business, results of operations, financial condition, and our share price.

*The ability to complete the Transaction is subject to the receipt of consents and clearances from government entities, which may impose conditions that could have an adverse effect or could cause either party to abandon the Transaction.**

The Transaction remains subject to customary closing conditions, including, among other things, (a) the sanction by the Irish High Court of the Scheme and delivery of the court order to the Irish Registrar of Companies, (b) the absence of an order or law that prevents consummation of the Transaction or imposes a burdensome condition (as defined in the transaction agreement), (c) absence of any Material Adverse Effect (as defined in the transaction agreement) from December 12, 2022 to the Sanction Date (as defined in the transaction agreement) that is continuing as of the Sanction Date, (d) the accuracy of each party's representations and warranties subject to certain materiality and material adverse effect exceptions and (e) the performance by each party of all of its covenants and agreements under the transaction agreement in all material respects. As a result of the FTC's lawsuit and the Stipulated TRO, we expect that the closing of the Transaction will continue to be delayed. In addition, if the FTC's request for a preliminary injunction is granted, it is highly unlikely that the Transaction could close before the December 12, 2023 end date specified in the transaction agreement. In the event that the Transaction does not close before the December 12, 2023 end date specified in the transaction agreement, each party would then have the right, in its sole discretion, to terminate the transaction agreement and abandon the Transaction, which Amgen may determine to do, particularly if the FTC's request for a preliminary injunction is granted. If the transaction agreement is terminated and the Transaction is abandoned, whether due to the failure to satisfy applicable closing conditions related to obtaining antitrust clearance for the Transaction or otherwise, our business, results of operations, financial condition, and our share price would be materially and adversely affected.

The transaction agreement limits our ability to pursue alternative transactions which could deter a third party from proposing an alternative transaction.

The transaction agreement contains provisions that, subject to certain exceptions, limit our ability to solicit or knowingly encourage discussions or negotiations with any third party regarding alternative acquisition proposals. It is possible that these or other provisions in the transaction agreement might discourage a potential competing acquirer that might have an interest in acquiring all or a significant part of our outstanding ordinary shares from considering or proposing an acquisition or that the price at which Amgen has proposed to acquire Horizon might result in a potential competing acquirer proposing to pay a lower per share price to acquire our ordinary shares than it might otherwise have proposed to pay.

Risks Related to Our Business and Industry

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

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

- timing of market introduction of our medicines as well as competitive medicines;
- efficacy and safety of our medicines;
- continued projected growth of the markets in which our medicines compete;
- the extent to which physicians diagnose and treat the conditions that our medicines are approved to treat;
- prevalence and severity of any side effects;
- if and when we are able to obtain regulatory approvals for additional indications for our medicines;
- acceptance by patients, physicians and applicable specialists;
- availability of, and ability to maintain, coverage and adequate reimbursement and pricing from government and other third-party payers;
- potential or perceived advantages or disadvantages of our medicines over alternative treatments, including cost of treatment and relative convenience and ease of administration;
- strength of sales, marketing and distribution support;
- the price of our medicines, both in absolute terms and relative to alternative treatments;
- impact of past and limitation of future medicine price increases;
- our ability to maintain a continuous supply of our medicines for commercial sale;
- the effect of current and future healthcare laws;
- the extent and duration of public health epidemics or outbreaks, including the extent to which physicians and patients delay visits or writing or filling prescriptions for our medicines and the extent to which operations of healthcare facilities, including infusion centers, are reduced;
- the performance of third-party distribution partners, over which we have limited control; and
- medicine labeling or medicine insert requirements of the FDA, or other comparable foreign regulatory authorities.

With respect to TEPEZZA, sales will depend on market acceptance and adoption by physicians, healthcare payers and patients, 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 and of certain physicians to refer patients to ocular specialists familiar with thyroid eye disease, or TED, and the use of TEPEZZA. 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 further evaluate uses and ways of enhancing the patient experience of KRYSTEXXA. With respect to RAVICTI, which is approved to treat a very limited patient population, our ability to grow sales will depend in large part on our ability to transition urea cycle disorder, or UCD, patients from BUPHENYL or generic equivalents, which are comparatively much less expensive, to RAVICTI and to educate patients and physicians on the benefits of continuing RAVICTI therapy once initiated. With respect to PROCYSBI, which is also approved to treat a very limited patient population, our ability to grow sales will depend in large part on our ability to transition patients from the first-generation immediate-release cysteamine therapy to PROCYSBI, to identify additional patients with nephropathic cystinosis and to educate patients and physicians on the benefits of continuing therapy once initiated. With respect to UPLIZNA, sales will depend on market acceptance and adoption by physicians and healthcare payers, as well as the ability and willingness of physicians who do not have in-house infusion capability to refer patients to infusion sites of care. With respect to ACTIMMUNE, while it is the only FDA-approved treatment for chronic granulomatous disease, or CGD, and severe, malignant osteopetrosis, or SMO, which are very rare conditions and, as a result, our ability to grow ACTIMMUNE sales will depend on our ability to identify additional patients with such conditions and educate patients and physicians on the benefits of continuing treatment once initiated. If our current medicines or any other medicine that we may seek approval for, or acquire, fail to attain market acceptance, we may not be able to generate significant revenue to sustain profitability, which would have a material adverse effect on our business, results of operations, financial condition and prospects (including, possibly, the value of our ordinary shares).

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

A substantial majority of our resources are focused on the commercialization of our current medicines. Our ability to generate significant medicine revenues and to achieve commercial success in the near-term will initially depend almost entirely on our ability to successfully commercialize these medicines in the United States. 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 more effective use through clinical trials, as well as opportunities for commercialization outside of the United States. Our comprehensive commercial strategy for TEPEZZA aims to enable more TED patients to benefit from TEPEZZA. We are doing this by: (i) facilitating continued TEPEZZA uptake in the treatment of TED through continued promotion of TEPEZZA to treating physicians; (ii) continuing to develop the TED market by increasing physician awareness of the disease severity and the urgency to diagnose and treat it, as well as the benefits of treatment with TEPEZZA, including through the expansion of our TEPEZZA commercial team and targeting ophthalmologists and endocrinologists; (iii) driving accelerated disease identification and time to treatment through our digital and broadcast marketing campaigns; (iv) enhancing the patient journey with our high-touch, patient-centric model as well as support for the patient and site-of-care referral processes; (v) pursuing more timely access to TEPEZZA for TED patients; (vi) educating physicians and payers on the effectiveness of TEPEZZA in patients with chronic/low clinical activity score, or CAS, TED, including through the results of our recently-completed Phase 4 clinical trial in this patient population and FDA approval of an update to TEPEZZA's label specifying the use of TEPEZZA regardless of TED disease activity or duration; and (vii) pursuing a global expansion strategy, which includes bringing TEPEZZA to patients with TED outside of the United States. Our strategy with respect to KRYSTEXXA includes existing rheumatology account growth, new rheumatology account growth and accelerating nephrology growth, the use of KRYSTEXXA with methotrexate following the approval of our supplemental biologics license application, in July 2022, as well as development efforts to further evaluate uses and ways of enhancing the patient experience of KRYSTEXXA.

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. With respect to our strategy for UPLIZNA, which leverages the successful strategies we have employed with TEPEZZA and KRYSTEXXA, our aim is to (i) increase physician awareness of the benefits of UPLIZNA for the treatment of neuromyelitis optica spectrum disorder, or NMOSD, and what differentiates UPLIZNA from other medicines by generating additional trial data analyses and clinical evidence; (ii) drive patient initiation and adherence, and cultivate a positive patient experience; and (iii) maximize the potential of UPLIZNA through additional indications and global expansion. Our strategy with respect to ACTIMMUNE, includes increasing awareness and diagnosis of CGD, driving utilization of ACTIMMUNE prophylaxis in newly diagnosed CGD patients as recommended in current treatment guidelines, encouraging use of ACTIMMUNE in CGD patients prior to bone marrow transplant and in symptomatic carriers of x-linked CGD and increasing compliance rates overall.

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 medicine launched for a disease that had no previously approved treatments, successful commercialization of TEPEZZA is subject to many risks. While we believe the launch of TEPEZZA was one of the most successful launches to date for a rare disease treatment, there are numerous examples of failures to meet high expectations of market potential, including by biopharmaceutical companies with more experience and resources than us. We will need to continue training and developing our U.S. commercial team in order to successfully commercialize TEPEZZA. There are many factors that could cause commercialization of TEPEZZA to be unsuccessful, including a number of factors that are outside our control. Because no medicine has previously been approved by the FDA for the treatment of TED, it is especially difficult to estimate TEPEZZA's market potential or the time it will take to increase patient and physician awareness of TED and change current treatment paradigms. In addition, some physicians that are potential prescribers of TEPEZZA do not have the necessary infusion capabilities to administer the medicine or may not have significant experience managing patients on medications like TEPEZZA and may not otherwise be able or willing to refer their patients to third-party infusion centers or other healthcare providers, which may discourage them from treating their patients with TEPEZZA. In the second half of 2022, we were impacted by certain challenges, including the often-burdensome reimbursement process, that we believe contributed to the decline in TEPEZZA net sales in the first half of 2023, compared to the 2022 period. These challenges, as well as challenges related to a lower rate of adherence to the full course of TEPEZZA therapy, have continued to moderate TEPEZZA net sales. We continue to execute on several opportunities designed to address these challenges and resume growth, including significantly expanding the size of our TEPEZZA sales force in late 2022 to allow our representatives more time with core TEPEZZA prescribers while educating other key physicians, including ophthalmologists and endocrinologists, about TED and TEPEZZA. We are also spending additional time and focus on the reimbursement process to more effectively support the patient access journey, which includes beginning to obtain favorable policy changes to improve patient access following the update to the indication language on the TEPEZZA label and Phase 4 data release. We also continue to invest significantly in direct-to-consumer advertising based on the returns we have seen to date. In April 2023, we announced positive topline results from our Phase 4 clinical trial in chronic/low CAS TED and received FDA approval of an update to TEPEZZA's label specifying the use of TEPEZZA regardless of TED disease activity or duration, which we believe reinforces the importance of unrestricted access for all eligible patients across the full spectrum of TED. We have seen improving trends in patient enrollment forms and patient starts as a result of our strategies and our expansion; however, it is taking longer than initially anticipated for our strategies and our expansion to contribute meaningfully to TEPEZZA net sales growth and we cannot otherwise be certain that our strategies will be successful in overcoming these challenges or that new challenges to TEPEZZA adoption will not arise. In addition, if the patient population suffering from TED or that is appropriate for treatment with TEPEZZA 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 for the full course of therapy, the commercial potential of TEPEZZA will be limited. Our ability to continue TEPEZZA supply could be impacted by additional government-mandated vaccine production orders and other risks associated with our reliance on our third-party manufacturers discussed below. We also have limited information regarding how physicians, patients and payers will respond to the pricing of TEPEZZA. Physicians may not prescribe TEPEZZA and patients may be unwilling to use TEPEZZA if coverage is not provided or reimbursement is inadequate to cover a significant portion of the cost. Thus, significant uncertainty remains regarding the commercial potential of TEPEZZA. If the continued commercialization of TEPEZZA becomes unsuccessful or perceived as disappointing, the price of our ordinary shares could decline significantly and long-term success of the medicine and our company could be harmed.

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

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

During the six months ended June 30, 2023, 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 addition, net sales of our medicines may be affected by end customer buying patterns and fluctuations in wholesaler inventory levels.

*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 global biotechnology 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 June 30, 2023, we had approximately 370 sales representatives and sales management in the field. Due to the impact of the at-risk launch of generic PENNSAID 2% and wind down of our former inflammation business during 2022, we redeployed a portion of our inflammation commercial team to support our TEPEZZA and KRYSTEXXA expansions. We may encounter difficulties transitioning sales representatives from promoting our inflammation medicines to promoting TEPEZZA and KRYSTEXXA, or in hiring additional qualified sales representatives. The pending Transaction with Amgen has also made it more difficult to attract and retain qualified employees due to the uncertainty about whether or when the Transaction will close and impact of the Transaction on our employees. 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 if the Transaction is not completed will be expensive and time-consuming. We also cannot be certain that we will be able to continue to successfully expand this capability.

As we continue to add medicines through development efforts and acquisition transactions (assuming the Transaction is not completed) and execute on our international expansion initiatives, the members of our sales force may have limited experience promoting certain of our medicines. To the extent we employ an acquired entity's sales forces to promote acquired medicines, we may not be successful in continuing to retain these employees and we otherwise will have limited experience marketing these medicines under our commercial organization. We are required to expend significant time and resources to train our sales force to be credible and able to educate physicians on the benefits of prescribing and pharmacists dispensing our medicines. In addition, we must train our sales force to ensure that a consistent and appropriate message about our medicines is being delivered to our potential customers. Our sales representatives may also experience challenges promoting multiple medicines when we call on physicians and their office staff. We have experienced, and may continue to experience, turnover of the sales representatives that we hired or will hire, requiring us to train new sales representatives. If we are unable to recruit and retain qualified personnel outside of the United States, we may not be able to execute our global expansion strategy successfully. If we are unable to effectively train our sales force and equip them with effective materials, including medical and sales literature to help them inform and educate physicians about the benefits of our medicines and their proper administration and label indication, as well as our patient assistance programs, our efforts to successfully commercialize our medicines could be put in jeopardy, which could have a material adverse effect on our financial condition, share price and operations.

We will also have to compete with other biopharmaceutical 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.**

Market acceptance and sales of our medicines will depend in large part on global coverage and reimbursement policies and may be affected by future healthcare reform measures, both in the United States and other key international markets. Successful commercialization of our medicines will depend in part on the availability of governmental and third-party payer reimbursement for the cost of our medicines. Government health administration authorities, private health insurers and other organizations generally provide reimbursement for healthcare. In particular, in the United States, private health insurers and other third-party payers often provide reimbursement for medicines and services based on the level at which the government (through the Medicare or Medicaid programs) provides reimbursement for such treatments. In the United States, the European Union, or EU, and other significant or potentially significant markets for our medicines and medicine candidates, government authorities and third-party payers are increasingly attempting to limit or regulate the price of medicines and services, particularly for new and innovative medicines and therapies, which has resulted in lower average selling prices. Further, the increased scrutiny of prescription drug pricing practices and emphasis on managed healthcare in the United States and on country and regional pricing and reimbursement controls in the EU and other significant or potentially significant markets will put additional pressure on medicine pricing, reimbursement and usage, which may adversely affect our medicine sales and results of operations. These pressures can arise from rules and practices of managed care groups, judicial decisions and governmental laws and regulations related to Medicare, Medicaid and healthcare reform, biopharmaceutical 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, or CMS, issued a final rule in 2018 that implemented civil monetary penalties for manufacturers who exceeded the ceiling price methodology for a covered outpatient drug when selling to a 340B covered entity. Pursuant to the final rule, after January 1, 2019, manufacturers must calculate 340B program ceiling prices on a quarterly basis. Moreover, manufacturers could be subject to a $5,000 penalty for each instance where they knowingly and intentionally overcharge a covered entity under the 340B program. With respect to KRYSTEXXA, the “additional rebate” methodology of the 340B pricing rules, as applied to the historical pricing of KRYSTEXXA both before and after we acquired the medicine, have resulted in a 340B ceiling price of one penny. A material portion of KRYSTEXXA prescriptions (currently in the range of high-single digits to low-teens 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. CMS previously revised 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. However, on June 15, 2022, the Supreme Court ruled that CMS was not authorized to set the rates in the previous final rules because it did not conduct the requisite survey of acquisition data. Therefore, it was required to utilize the average price for the drug in the given year and not vary rates by hospital group. It is unclear whether CMS will attempt to implement the same rate changes by other means.

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 pharmacy benefit managers, or PBMs, in the United States for some of our non-infused medicines, 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 our patient assistance programs or other programs whereby we assist qualified patients with certain out-of-pocket expenditures for our medicines, 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.

Many EU Member States periodically review their reimbursement procedures for medicinal products, which could have an adverse impact on reimbursement status. We expect that legislators, policymakers and healthcare insurance funds in the EU Member States will continue to propose and implement cost-containing measures, such as lower maximum prices, lower or lack of reimbursement coverage and incentives to use cheaper, usually generic, products as an alternative to branded products, and/or branded products available through parallel import to keep healthcare costs down. Moreover, in order to obtain reimbursement for our products in some European countries, including some EU Member States, we may be required to compile additional data comparing the cost-effectiveness of our products to other available therapies. Health Technology Assessment, or HTA, of medicinal products is becoming an increasingly common part of the pricing and reimbursement procedures in some EU Member States, including those representing the larger markets. The HTA process is the procedure to assess therapeutic, economic and societal impact of a given medicinal product in the national healthcare systems of the individual country. The outcome of an HTA will often influence the pricing and reimbursement status granted to these medicinal products by the competent authorities of individual EU Member States. The extent to which pricing and reimbursement decisions are influenced by the HTA of the specific medicinal product currently varies between EU Member States.

In December 2021, Regulation No 2021/2282 on HTA, amending Directive 2011/24/EU, was adopted in the EU. This Regulation, which entered into force in January 2022 and will apply as of January 2025, is intended to boost cooperation among EU Member States in assessing health technologies, including new medicinal products, and providing the basis for cooperation at EU level for joint clinical assessments in these areas. The Regulation foresees a three-year transitional period and will permit EU Member States to use common HTA tools, methodologies, and procedures across the EU, working together in four main areas, including joint clinical assessment of the innovative health technologies with the most potential impact for patients, joint scientific consultations whereby developers can seek advice from HTA authorities, identification of emerging health technologies to identify promising technologies early, and continuing voluntary cooperation in other areas. Individual EU Member States will continue to be responsible for assessing non-clinical (e.g., economic, social, ethical) aspects of health technologies, and making decisions on pricing and reimbursement. If we are unable to maintain favorable pricing and reimbursement status in EU Member States for medicine candidates that we may successfully develop and for which we may obtain regulatory approval, any anticipated revenue from and growth prospects for those products in the EU could be negatively affected.

Legislators, policymakers and healthcare insurance funds in the EU may continue to propose and implement cost-containing measures to keep healthcare costs down. These measures could include limitations on the prices we would be able to charge for medicine candidates that we may successfully develop and for which we may obtain regulatory approval or the level of reimbursement available for these products from governmental authorities or third-party payers. Further, an increasing number of EU and other foreign countries use prices for medicinal products established in other countries as “reference prices” to help determine the price of the product in their own territory. Consequently, a downward trend in prices of medicinal products in some countries could contribute to similar downward trends elsewhere.

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 or foreign 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 patient assistance programs or any other co-pay programs. Certain state and federal enforcement authorities and members of Congress have initiated inquiries about co-pay assistance programs. Some state legislatures have implemented or have been considering implementing laws to restrict or ban co-pay coupons for branded drugs. For example, legislation was signed into law in California that limits the use of co-pay coupons in cases where a lower cost generic drug is available and if individual ingredients in combination therapies are available over the counter at a lower cost. It is possible that similar legislation could be proposed and enacted in additional states. Additionally, numerous organizations, including biopharmaceutical manufacturers, have been subject to ongoing litigation, enforcement actions and settlements related to their patient assistance programs and support.

*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 comparable foreign regulatory authorities. Failure to comply with FDA and other comparable foreign regulatory requirements may, either before or after medicine approval, subject us to administrative or judicially imposed sanctions. In addition, the label inclusion criteria may differ by geography.

We are pursuing a global expansion strategy, which includes bringing TEPEZZA to patients with TED and UPLIZNA to adult patients with NMOSD outside of the United States. 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 the European Economic Area (which consists of the 27 Member States of the EU, Iceland, Liechtenstein and Norway), or EEA, must be supported by extensive clinical and pre-clinical data, as well as extensive information regarding chemistry, manufacturing and controls, or CMC, to demonstrate the safety and effectiveness of the applicable medicine candidate. The number and types of pre-clinical studies and clinical trials that will be required for regulatory approval varies depending on the medicine candidate, the disease or the condition that the medicine candidate is designed to target and the regulations applicable to any particular medicine candidate. Despite the time and expense associated with pre-clinical and clinical studies, failure can occur at any stage, and we could encounter problems that cause us to repeat or perform additional pre-clinical studies, CMC studies or clinical trials. Regulatory authorities could delay, limit or deny approval of a medicine candidate for many reasons, including because they:

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

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

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

*The United Kingdom's withdrawal from the EU may have a negative effect on global economic conditions, financial markets and our business, which could reduce the price of our ordinary shares.**

Following the result of a referendum in 2016, the United Kingdom, or UK, left the EU on January 31, 2020, commonly referred to as Brexit. Pursuant to the formal withdrawal arrangements agreed between the UK and the EU, the UK was subject to a transition period until December 31, 2020 during which EU rules continued to apply. The UK and the EU have signed a EU-UK Trade and Cooperation Agreement, or TCA, which became provisionally applicable on January 1, 2021 and entered into force on May 1, 2021. This agreement provides details on how some aspects of the UK and EU's relationship will operate going forwards however there are still many uncertainties. The TCA primarily focuses on ensuring free trade between the EU and the UK in relation to goods, including medicinal products. Although the body of the TCA includes general terms which apply to medicinal products, greater detail on sector-specific issues is provided in an Annex to the TCA. The Annex provides a framework for the recognition of Good Manufacturing Practice, or GMP, inspections and for the exchange and acceptance of official GMP documents. The regime does not, however, extended to procedures such as batch release certification. Among the changes that have occurred are that Great Britain (England, Scotland and Wales) is treated as a "third country", a country that is not a member of the EU and whose citizens do not enjoy the EU right to free movement. Northern Ireland has continued to follow many aspects of the EU regulatory rules, particularly in relation to trade in goods. As part of the TCA, the EU and the UK recognize GMP inspections carried out by the other party and the acceptance of official GMP documents issued by the other party. The TCA also encourages, although it does not oblige, the parties to consult one another on proposals to introduce significant changes to technical regulations or inspection procedures. Among the areas of absence of mutual recognition are batch testing and batch release. The UK has unilaterally agreed to accept EU batch testing and batch release. However, the EU continues to apply EU laws that require batch testing and batch release to take place in the EU territory. This means that medicinal products that are tested and released in the UK must be retested and re-released when entering the EU market for commercial use. As it relates to marketing authorizations, Great Britain has a separate regulatory submission process, approval process and a separate national marketing authorization. Northern Ireland has continued, however, to be covered by the marketing authorizations granted by the European Commission. For example, the scope of a marketing authorization for a medicinal product granted by the European Commission no longer encompasses Great Britain (England, Scotland and Wales). In these circumstances, a separate marketing authorization granted by the UK competent authorities is required to place medicinal products on the market in Great Britain. On February 27, 2023, the European Commission and the UK government reached a political agreement in principle, commonly referred to as the "Windsor Framework". The purpose of the agreement is to establish a set of joint solutions that would allow goods to be traded between Great Britain and Northern Ireland and between Northern Ireland and Ireland while ensuring the integrity of the EU Single Market. New legislation must be passed by the UK and the EU in order to implement the provisions of the Windsor Framework, including those that relate to medicinal products. The implementation of the proposed framework would take place in stages with measures relating to medicinal products scheduled to take effect in January 2025. The Windsor Framework provides, however, that medicinal products to be placed on the market in Northern Ireland will be authorized solely in accordance with UK laws.

Since a significant proportion of the regulatory framework in the UK applicable to our business and our medicines is derived from EU directives and regulations, Brexit has materially impacted the regulatory regime with respect to the development, manufacture, importation, approval and commercialization of our medicines and medicine candidates in the UK and the EU, now that UK legislation has the potential to diverge from EU legislation. All of these changes could increase our costs and otherwise adversely affect our business. In addition, we may be required to pay taxes or duties or be subjected to other hurdles in connection with the importation of our medicine candidates into the EU. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK or the EU for our medicine candidates, or incur significant additional expenses to operate our business, which could significantly and materially harm or delay our ability to generate revenues or achieve profitability of our business. Any further changes in international trade, tariff and import/export regulations as a result of Brexit or otherwise may impose unexpected duty costs or other non-tariff barriers on us. These developments, or the perception that any of them could occur, may significantly reduce global trade and, in particular, trade between the impacted nations and the UK. It is also possible that Brexit may negatively affect our ability to attract and retain employees, particularly those from the EU. The regulatory changes that are a result of Brexit may also materially impact upon the development, manufacture, importation, approval and commercialization of our medicines in the EEA, should any development or manufacture of these medicines take place in the UK.

Since Great Britain is no longer covered by the EU's procedures for the grant of marketing authorizations and Northern Ireland may not, as a result of the Windsor Framework, be in the future our medicine candidates require a separate marketing authorization for Great Britain (or, once Northern Ireland is no longer covered by the EU procedures, the UK), which involves additional administrative burden. Any delay in obtaining, or an inability to obtain, any marketing approvals, as a result of Brexit or otherwise, could prevent us from or delay us commercializing our medicine candidates in the UK and/or the EEA and restrict our ability to generate revenue and achieve and sustain profitability. If any of these outcomes occur, we may be forced to restrict or delay efforts to seek regulatory approval in the UK and/or EEA for our medicine candidates, which could significantly and materially harm our business.

We are subject to ongoing obligations and continued regulatory review by the FDA and comparable foreign regulatory authorities, and 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.

Our current approved medicines (and our medicine candidates, if approved) are subject to extensive ongoing obligations and continued regulatory review with respect to many operational aspects including our manufacturing processes, labeling, packaging, distribution, storage, import, export, safety surveillance, 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, International Council for Harmonisation, or ICH, guidelines, good pharmacovigilance practice, good distribution practices and good laboratory practices, or GLPs, which are regulations and guidelines enforced by the FDA and comparable foreign regulatory authorities for all of our medicines in clinical development and for any clinical trials that we conduct post-approval.

Later discovery of previously unknown problems with a medicine or medicine candidate, 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:

- injunctions or restrictions on the marketing, manufacturing or distribution of the medicine, suspension, variation or withdrawal of medicine approvals, withdrawal of the medicine from the market, revocation of necessary licenses or suspension of medicine reimbursement;
- issuance of warning letters, show cause notices or untitled letters describing alleged violations, which may be publicly available;
- suspension of any ongoing clinical trials or delay or prevention of the initiation of clinical trials;
- delay or refusal to approve pending applications or supplements to approved applications we have filed;
- refusal to permit drugs or precursor or intermediary chemicals to be imported or exported to or from the United States or foreign countries;
- medicine seizure or detention, refusal to permit the import or export of medicines, or voluntary or mandatory medicine recalls;
- suspension, restrictions or additional requirements on operations, including costly new manufacturing quality or pharmacovigilance requirements; and/or
- criminal investigations and prosecutions, injunctions, the imposition of civil or criminal penalties, or exclusion, debarment or suspension from government healthcare programs.

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, including Phase 4 clinical trials, 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 biopharmaceutical forms of the same active biopharmaceutical ingredients, or APIs, may be used off-label in those indications. A significant number of biopharmaceutical companies have been the target of inquiries and investigations by various U.S. federal and state regulatory, investigative, prosecutorial and administrative entities or comparable foreign regulatory authorities 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, or FDCA, anti-kickback laws, and other alleged violations in connection with the promotion of medicines for unapproved uses, pricing and Medicare and/or Medicaid reimbursement and comparable foreign regulatory requirements. 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 biopharmaceutical 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 biopharmaceutical 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 authorities 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, there remains a substantial amount of uncertainty regarding internet and social media promotion of regulated medical products. We cannot predict the likelihood, nature or extent of adverse government regulation that may arise from pending or future legislation or administrative action, either in the United States or abroad. If we are unable to achieve and maintain regulatory compliance, we will not be permitted to market our drugs, which would materially adversely affect our business, results of operations and financial condition.

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

Following our sale of the rights to RAVICTI outside of North America to Medical Need Europe AB, part of the Immedica Group, or Immedica, Immedica has marketing and distribution rights to RAVICTI in those regions. Following our sale of the rights to PROCYSBI in Europe, the 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. Mitsubishi Tanabe Pharma Corporation, or MTPC, has rights to develop and commercialize UPLIZNA for NMOSD as well as other potential future indications in Japan and certain other countries in Asia. Hansoh has rights to develop and commercialize UPLIZNA for NMOSD as well as other potential future indications in China. We have little or no control over Immedica's activities with respect to RAVICTI outside of North America, over Chiesi's activities with respect to PROCYSBI in the EMEA, or over MTPC's or Hansoh's activities with respect to UPLIZNA in the certain countries in Asia, even though those activities could impact our ability to successfully commercialize these medicines. For example, Immedica or its assignees, Chiesi or its assignees, MTPC or Hansoh or their respective assignees can make statements or use promotional materials with respect to RAVICTI, PROCYSBI or UPLIZNA, 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 UPLIZNA, respectively, in foreign countries at prices that are dramatically lower than the prices we charge in the United States. These activities and decisions, while occurring outside of the United States, could harm our commercialization strategy in the United States. In addition, medicine recalls or safety issues with these medicines outside the United States, even if not related to the commercial medicine we sell in the United States, could result in serious damage to the brand in the United States and impair our ability to successfully market them. We also rely on Immedica, Chiesi, MTPC and Hansoh, 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, in whole or in part, on third parties to manufacture commercial supplies of any other approved medicines. The commercialization of any of our medicines could be stopped, delayed or made less profitable if those third parties fail to provide us with sufficient quantities of medicine or fail to do so at acceptable quality levels or prices or fail to maintain or achieve satisfactory regulatory compliance.**

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

We rely on AGC Biologics A/S (formerly known as CMC Biologics A/S), or AGC Biologics, as our exclusive manufacturer of TEPEZZA drug substance and Catalent Indiana, LLC, or Catalent, and Patheon Pharmaceuticals Inc., or Patheon (the contract development and manufacturing services organization of Thermo Fisher Scientific), as our manufacturers for TEPEZZA drug product. If AGC Biologics fails to supply TEPEZZA drug substance or if Catalent and Patheon fail to supply TEPEZZA drug product for a period beyond our current expectation or any manufacturer is otherwise unable to meet our volume requirements due to unexpected market demand for TEPEZZA, it may lead to further TEPEZZA supply constraints.

We rely on NOF Corporation, or NOF, as our exclusive supplier of the PEGylation agent that is a critical raw material in the manufacture of KRYSTEXXA. If NOF fails to supply such PEGylation agent, it may lead to KRYSTEXXA supply constraints. We rely on AstraZeneca UK Limited for the manufacture of clinical and commercial supplies of UPLIZNA, and for clinical and nonclinical supplies of the other medicine candidates acquired in the acquisition of Viela Bio, Inc., or Viela. In addition, we rely on an exclusive supply agreement with Boehringer Ingelheim Biopharmaceuticals GmbH, or Boehringer Ingelheim Biopharmaceuticals, for manufacturing and supply of ACTIMMUNE. ACTIMMUNE is manufactured by starting with cells from working cell bank samples which are derived from a master cell bank. We and Boehringer Ingelheim Biopharmaceuticals separately store multiple vials of the master cell bank. In the event of catastrophic loss at our or Boehringer Ingelheim Biopharmaceuticals' storage facility, it is possible that we could lose multiple cell banks and have the manufacturing capacity of ACTIMMUNE severely impacted by the need to substitute or replace the cell banks.

In July 2021, we purchased a drug product biologics manufacturing facility in Waterford, Ireland, which is intended to be an additional source of manufacturing to supplement the capabilities of our third-party drug product manufacturers. We are in the process of completing the build-out and validation of this facility and assuming timely receipt of regulatory approvals, we expect the first medicine manufactured for commercial use at the facility to be approved for release in the fourth quarter of 2023. In August 2022, we submitted a planning application to build a drug substance biologics manufacturing facility adjacent to our existing drug product biologics manufacturing facility in Waterford, Ireland. Based on our current operating plan, we do not anticipate making significant investments in building a drug substance biologics manufacturing facility during 2023. To the extent that we proceed with building a drug substance biologics manufacturing facility in the future, we have minimal experience in building, developing, validating, obtaining regulatory approval for or running manufacturing facilities and we therefore may not be successful in these activities. In particular, we may experience delays and unforeseen expenses in connection with building a drug substance biologics manufacturing facility or hiring qualified personnel to operate such a facility. Even if we are successful in producing medicines at the Waterford facilities for commercial sale once we receive the required regulatory approvals, we expect to remain dependent on our third-party drug product filling and drug substance manufacturing partners in the near-term and to a lesser extent in the medium/longer term, but we plan to always dual source our strategic medicines.

If we or 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, we or our third-party manufacturers will not be able to secure or maintain regulatory approval for the manufacturing facilities. In addition, we have no direct 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 our manufacturing facility or that of 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 such facilities 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, we or our third-party manufacturers may experience manufacturing difficulties due to resource constraints or as a result of labor disputes or unstable political environments. If we or our third-party manufacturers were to encounter any of these difficulties, or our third-party manufacturers 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 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 biopharmaceutical companies, including those marketing generic medicines and our operating results will suffer if we fail to compete effectively.**

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

Although TEPEZZA does not face direct competition, other therapies, such as corticosteroids, have been used on an off-label basis to alleviate some of the symptoms of TED. While these therapies have not proved effective in treating the underlying disease, and carry with them potential significant side effects, their off-label use could reduce or delay treatment with TEPEZZA among the addressable patient population. Viridian Therapeutics, Inc., or Viridian, is pursuing development of both an intravenous (VRDN-001) and subcutaneous (VRDN-001, VRDN-002 or VRDN-003) formulations of anti-IGF-1R monoclonal antibodies for TED. In August 2022, Viridian announced positive initial clinical data from the first cohort, 10mg/kg, of the ongoing Phase 1/2 clinical trial for an IGF-1R monoclonal antibody VRDN-001 (intravenous), in patients with TED. On November 14, 2022 and January 8, 2023, Viridian announced positive data for their second and third cohorts, 20mg/kg and 3mg/kg, respectively, of the ongoing Phase 1/2 trial showing improvements in signs and symptoms of TED after two infusions. In addition, in the fourth quarter of 2022, Viridian enrolled the first patient in its THRIVE Phase 3 trial of VRDN-001 (intravenous) with active TED. Additionally, on July 10, 2023, Viridian announced positive results from a cohort of 12 chronic TED patients in the Phase 1/2 trial. Viridian expects to initiate a Phase 3 trial in the third quarter of 2023, with top-line results expected by the end of 2024. Viridian has initiated a Phase 2 trial with a subcutaneous version of VRDN-002 in the fourth quarter of 2022. Viridian filed an investigational new drug, or IND, application for VRDN-003 in June of 2023 and upon approval plans to subsequently begin a Phase 1 trial in healthy volunteers with topline results expected by the end of 2023. In March 2023, Viridian announced it is conducting a Phase 1 trial of a subcutaneous formulation of VRDN-001 in healthy volunteers, with topline results expected by the end of 2023. Viridian has stated that it intends to select one of the three subcutaneous formulations to move into pivotal trials by the end of 2023, with a subsequent Phase 2/3 trial to be initiated in early 2024. In addition, Sling Therapeutics, Inc. is conducting a Phase 2b study of an oral IGF-1R for the treatment of moderate-to-severe TED. Immunovant Inc., or Immunovant, initiated two Phase 3 clinical trials of a fully human anti-FcRn monoclonal antibody candidate for the treatment of active TED, also referred to as Graves' ophthalmopathy, in the fourth quarter of 2022. Immunovant has indicated that it expects data from the Phase 3 trials in the first half of 2025. On January 5, 2023, Acelyrin, Inc., or Acelyrin, announced the acquisition of ValenzaBio Inc., or ValenzaBio. Previously, ValenzaBio received IND clearance and subsequently had begun a Phase 1 trial in the first half of 2022 with VB421 or lonigutamab, an anti-IGF-1R monoclonal antibody designed for subcutaneous use. In January 2023, Acelyrin modified the trial design into a Phase 1/2 adaptive trial in active TED. Lassen Therapeutics, Inc. has included a TED cohort into their ongoing Phase 1 trial of LASN01, an IL-11 monoclonal antibody, also in development for pulmonary fibrosis. Argenx SE announced a registrational trial of efgartigimod for the treatment of TED due to begin in the fourth quarter of 2023.

While KRYSTEXXA faces limited direct competition, a number of competitors have medicines in clinical trials, including Selecta Biosciences Inc., or Selecta, which has initiated a Phase 3 clinical program of a candidate for the treatment of chronic refractory gout. In September 2020, Selecta announced topline clinical data that did not meet the primary endpoint or demonstrate statistical superiority for its Phase 2 trial that compared its candidate, which includes an immunomodulator, to KRYSTEXXA alone. In July 2020, Selecta and Swedish Orphan Biovitrum AB, or Sobi, entered into a strategic licensing agreement under which Sobi will assume responsibility for certain development, regulatory, and commercial activities for this candidate. In August 2022, Selecta announced the completion of enrollment for both DISSOLVE trials, the two clinical studies of the Phase 3 DISSOLVE development program of SEL-212 for chronic refractory gout. In March 2023, Selecta and Sobi announced positive topline data from the DISSOLVE trials. Sobi intends to file a biologics license application, or BLA, in the first half of 2024. SEL-212 is a combination of Selecta's ImmTOR immune tolerance platform and a therapeutic uricase enzyme (pegadricase).

RAVICTI could face competition from a few alternative medicine and treatment options that have been recently approved or are in development, including Pheburane®, a taste-masked formulation of sodium phenylbutyrate for which Medunik USA received approval from the FDA in June 2022, a gene-therapy candidate by Ultragenyx Pharmaceutical Inc., Olpruva™, a taste-masked formulation of sodium phenylbutyrate for which ACER Therapeutics Inc. received approval from the FDA in December 2022, an enzyme replacement for a specific UCD subtype (ARG) by Aeglea Bio Therapeutics Inc. and a mRNA-based therapeutic for a specific UCD subtype (OTC) by Arcturus Therapeutics Holdings Inc. PROCYSBI faces competition from Cystagon® (immediate-release cysteamine bitartrate capsules) for the treatment of cystinosis. Additionally, we are also aware that AVROBIO, Inc. has a gene therapy candidate in development for the treatment of cystinosis.

UPLIZNA faces competition from eculizumab, marketed as Soliris® by AstraZeneca plc, or AstraZeneca, and satralizumab, marketed as Enspryng™ by Genentech/Chugai Pharmaceuticals Co., Ltd., a subsidiary of F. Hoffmann-La Roche Ltd., each for the treatment of patients with NMOSD. AstraZeneca announced in May 2023 that Ultomiris® (ravulizumab) has been approved in the EU for the treatment of adults with anti-aquaporin-4 (AQP4) antibody-positive (Ab+) NMOSD. Ultomiris is currently under regulatory review in the United States and, if approved for this indication, UPLIZNA could face additional competition. UPLIZNA also faces competition from rituximab, an off-label treatment that has been used for years to treat NMOSD given the lack of an approved medicine for this disease prior to 2019. Other novel treatments are under development for NMOSD, including Phase 3 candidates being developed by Beijing Mabworks Biotech Co. Ltd. and RemeGen Co. Ltd., and Phase 2 candidates, including a candidate being developed by Chord Therapeutics SA/Merck KGaA.

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) non-exclusive licenses to manufacture and commercialize generic versions of RAVICTI in the United States after July 1, 2025 and (ii) non-exclusive license to manufacture and commercialize a generic version of PROCYSBI in the United States after March 31, 2030. Under certain circumstances, each of these licenses could become effective on an earlier date.

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 potentially curative treatment of bone marrow transplants for 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, the U.S. patents covering ACTIMMUNE expired on August 30, 2022, and although we are not currently aware of any biosimilar to ACTIMMUNE 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, received FDA approval in January 2021 for carglumic acid for the treatment of acute hyperammonemia due to propionic acidemia or methylmalonic acidemia. Carglumic acid is also approved for chronic and acute hyperammonemia due to N-acetylglutamate synthase deficiency, a rare UCD subtype. 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 biopharmaceutical 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 biopharmaceutical companies in the discovery, development and commercialization of new medicine candidates.

*Our biologic medicines and candidates may face biosimilar competition sooner than anticipated.**

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

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

Data and market exclusivity is available in relation to grant of certain types of marketing authorization for medicinal products in the EU. Upon grant of a marketing authorization, innovative medicinal products are generally entitled to benefit from eight years of data exclusivity and 10 years of market exclusivity in the EU. Data exclusivity, if granted, prevents regulatory authorities in the EU from referencing the innovator's data to assess a generic application or biosimilar application for eight years from the date of authorization of the innovative product. After this period a generic or biosimilar marketing authorization application can be submitted, and the innovator's data may be referenced. The market exclusivity period prevents a successful generic or biosimilar applicant from commercializing its product in the EU until 10 years have elapsed from grant of the initial marketing authorization of the reference product in the EU. The overall ten year period may, occasionally, be extended for a further year to a maximum of 11 years if, during the first eight years of those ten years, the marketing authorization holder obtains an authorization for one or more new therapeutic indications which, during the scientific evaluation prior to their authorization, are held to bring a significant clinical benefit in comparison with existing therapies. However, there is no guarantee that a product will be considered by the EU's regulatory authorities to be a new chemical/biological entity, and products may not qualify for data exclusivity. In the EU, the European Commission has granted marketing authorizations for several biosimilar products pursuant to a set of general and product class-specific guidelines for biosimilar approvals issued over the past few years. In addition, companies may be developing biosimilar products in other countries that could compete with our medicines, if approved.

On April 26, 2023, the European Commission adopted a proposal for a new Directive and Regulation to revise the existing pharmaceutical legislation. If adopted in the form proposed, the recent European Commission proposals to revise the existing EU laws governing authorization of medicinal products may result in a decrease in data and market exclusivity for our product candidates in the EU.

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

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

Under the Orphan Drug Act of 1983, the FDA may designate a medicine as an orphan drug if it is a drug intended to treat a rare disease or condition affecting fewer than 200,000 people in the United States. A company that first obtains FDA approval for a designated orphan drug for the specified rare disease or condition receives orphan drug marketing exclusivity for that drug for a period of seven years from the date of its approval. PROCYSBI received ten years of market exclusivity for the treatment of nephropathic cystinosis, through September 2023, as an orphan drug in the EEA and UK. PROCYSBI received seven years of market exclusivity, until December 22, 2024, for patients one year of age to less than two years of age as an orphan drug in the United States. TEPEZZA has been granted orphan drug exclusivity for treatment of active (dynamic) phase Graves' ophthalmopathy, which we expect will provide orphan drug marketing exclusivity in the United States until January 2027. In addition, UPLIZNA was granted orphan drug exclusivity for the treatment of NMOSD, which we expect will provide orphan drug marketing exclusivity in the United States until June 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. Outside the United States, similar limitations regarding orphan drugs also exist. 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.

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 biopharmaceutical 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. 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. 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.

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.

We have operations in the United States, Ireland and in multiple other jurisdictions, and are pursuing a global expansion strategy, which includes bringing TEPEZZA to patients with TED and UPLIZNA to adult patients with NMOSD outside of the United States.

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, and comparable requirements in foreign countries;
- 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 biopharmaceuticals are employed by their government, and the purchasers of biopharmaceuticals 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 biopharmaceutical 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. In addition, under the transaction agreement with Amgen, we are generally required to conduct our business in the ordinary course, consistent with past practice and are restricted from taking certain specified actions absent Amgen's prior written consent. If the pending Transaction with Amgen is not consummated and 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 biopharmaceutical 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, including 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 June 30, 2023, we employed approximately 2,190 full-time employees, including approximately 370 sales representatives and sales management, 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. We have experienced additional turnover and difficulties in hiring new employees as a result of the pending Transaction with Amgen. 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 biopharmaceutical businesses.

As our commercialization plans and strategies continue to develop, and particularly as we execute on our strategy to expand our commercial team in the United States and establish commercial capabilities outside the United States, we will need to continue to recruit and train sales and marketing personnel. In addition, as we build our R&D and manufacturing capabilities, we will need to continue to recruit and train qualified individuals in these areas. 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 our R&D function in recent years, we may need to enhance our clinical development and regulatory functions to properly evaluate and develop earlier-stage opportunities, which may include recruiting personnel that are knowledgeable in therapeutic areas we have not yet pursued. If we are unable to acquire promising development-stage assets or eventually obtain marketing approval for them, we may not be able to create a meaningful pipeline of new medicines and eventually realize a return on our investments. For example, a core strategic rationale for the Viela acquisition was Viela's pipeline of medicine candidates and R&D capabilities, but if we experience clinical failures with respect to Viela's medicine candidates and research programs or such candidates and programs do not otherwise result in marketed medicines, we will not realize the expected benefits from our substantial investment in the acquisition and subsequent development of the Viela pipeline. As our R&D plans and strategies continue to develop, including as a result of our acquisition of Viela, we will need to continue to recruit and train R&D personnel.

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

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

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

We 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 due to the pending Transaction and the restrictions under the transaction agreement with Amgen, or because our financial resources may be insufficient and/or third parties may not view our commercial and development capabilities as being adequate. Further, increasing regulatory scrutiny of acquisitions may limit our ability to pursue certain acquisitions where we have potentially competing products or clinical programs. 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, including any failures to capitalize on opportunistic strategic transactions due to the restrictions under the transaction agreement with Amgen in the event the Transaction is not ultimately consummated, 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 Ireland and in multiple other jurisdictions. We are able to achieve a favorable tax rate through the performance of certain functions and ownership of certain assets in tax-efficient jurisdictions, including Ireland and Bermuda, together with the use of intercompany service and transfer pricing agreements, each on an arm's length basis. Our effective tax rate may be different than experienced in the past due to numerous factors including, changes to the tax laws of jurisdictions that we operate in, the enactment of new tax treaties or changes to existing tax treaties, changes in the mix of our profitability from jurisdiction to jurisdiction, the implementation of the EU Anti-Tax Avoidance Directive (see further discussion below), the implementation of the Bermuda Economic Substance Act 2018 (effective December 31, 2018) and our inability to secure or sustain acceptable agreements with tax authorities (if applicable). Any of these factors could cause us to experience an effective tax rate significantly different from previous periods or our current expectations. Taxing authorities, such as the U.S. Internal Revenue Service, or IRS, actively audit and otherwise challenge these types of arrangements, and have done so in the biopharmaceutical industry. We expect that these challenges will continue as a result of the recent increase in scrutiny and political attention on corporate tax structures. The IRS and/or the Irish tax authorities may challenge our structure and transfer pricing arrangements through an audit or lawsuit. Responding to or defending such a challenge could be expensive and consume time and other resources, and divert management's time and focus from operating our business. We cannot predict whether taxing authorities will conduct an audit or file a lawsuit challenging this structure, the cost involved in responding to any such audit or lawsuit, or the outcome. If we are unsuccessful in defending such a challenge, we may be required to pay taxes for prior periods, as well as interest, fines or penalties, and may be obligated to pay increased taxes in the future, any of which could require us to reduce our operating expenses, decrease efforts in support of our medicines or seek to raise additional funds, all of which could have a material adverse effect on our business, financial condition, results of operations and growth prospects.

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

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

We do not believe that our classification as a foreign corporation for U.S. federal income tax purposes is affected by Section 7874, 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 Cooperation and Development, or the OECD, released its Base Erosion and Profit Shifting project final report on October 5, 2015. This report provides the basis for international standards for corporate taxation that are designed to prevent, among other things, the artificial shifting of income to tax havens and low-tax jurisdictions, the erosion of the tax base through interest deductions on intercompany debt and the artificial avoidance of permanent establishments (i.e., tax nexus with a jurisdiction). Legislation to adopt these standards has been enacted or is currently under consideration in a number of jurisdictions. On June 7, 2017, several countries, including many countries that we operate and have subsidiaries in, participated in the signing ceremony adopting the OECD's Multilateral Convention to Implement Tax Treaty Related Measures to Prevent Base Erosion and Profit Shifting, commonly referred to as the MLI. The MLI came into effect on July 1, 2018. In January 2019, Ireland deposited the instrument of ratification of Ireland's MLI choices with the OECD. Ireland's MLI came into force on May 1, 2019, however the provisions in respect of withholding taxes and other taxes levied by Ireland did not come into effect for us until January 1, 2020 (with application also depending on whether the MLI has been ratified in other jurisdictions whose tax treaties with Ireland are affected). The MLI may modify affected tax treaties making it more difficult for us to obtain advantageous tax-treaty benefits. The number of affected tax treaties could eventually be in the thousands. As a result, our income may be taxed in jurisdictions where it is not currently taxed and at higher rates of tax than it is currently taxed, which may increase our effective tax rate.

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. Finance Act 2021 introduced further ATAD measures, such as the interest limitation rules and anti-hybrid rules to neutralize reverse-hybrid mismatches into Irish law with effect from January 1, 2022. We do not expect a material impact on our effective tax rate as a result of the introduction of these provisions.

On October 8, 2021, 136 of the 140 members of the OECD/G20 Inclusive Framework on Base Erosion and Profit Shifting, or Inclusive Framework, approved a statement providing a framework for reform of the international tax rules, or Inclusive Framework Statement. The Inclusive Framework Statement sets out the key terms for an agreement on a two-pillar solution to address the tax challenges arising from the digitalization of the economy. Pillar One focuses on nexus and profit allocation and Pillar Two provides for a global minimum effective corporate tax rate of 15%. The Inclusive Framework Statement provides that Pillar One would apply to multinational enterprises with annual global revenue above 20 billion euros and profitability above 10%, with the revenue threshold potentially reduced to 10 billion euros in the future. Based on these thresholds, we would currently be outside the scope of the Pillar One proposals. On December 20, 2021, the Inclusive Framework published detailed rules which define the scope of, and set out the mechanism for introducing, the Pillar Two global minimum effective tax rate proposal. The rules provide for the imposition of the global minimum effective tax rate on certain multinational enterprises that have consolidated revenues of at least 750 million euros in at least two out of the last four years. Based on these thresholds, we currently expect that we could fall within the scope of the Pillar Two proposals. A number of countries are currently proposing to implement core elements of the Pillar Two proposals by the start of 2024 and, on December 15, 2022, the EU adopted a Council Directive requiring aspects of the Pillar Two proposals to be transposed into the national laws of its Member States (including Ireland) by December 31, 2023. Although it is difficult at this stage to determine with precision the impact the Pillar Two proposals would have, their implementation could materially increase our effective tax rate.

On August 16, 2022, President Biden signed into law the Inflation Reduction Act of 2022, or IRA, which includes a minimum tax equal to 15 percent of the adjusted financial statement income of certain corporations, as well as a one percent excise tax on share buybacks. Pending further guidance, it is possible that the IRA could increase our tax liability, which could in turn adversely impact our business and future profitability. The IRA or future changes in U.S. tax laws could have a material adverse impact on the value of our deferred tax assets and liabilities, could result in significant one-time charges, and could increase our future U.S. tax expense.

Effective January 1, 2022, the Tax Cuts and Jobs Act eliminated the option to deduct R&D expenses for tax purposes in the year incurred and requires taxpayers to capitalize and subsequently amortize such expenses over five years for research activities conducted in the United States and over fifteen years for research activities conducted outside the United States. Unless U.S. Treasury issues regulations that narrow the application of this provision to a smaller subset of our R&D expenses or the provision is deferred, modified, or repealed by Congress, this provision could materially decrease our cash flows from operations with an offsetting similarly sized increase in our net deferred tax assets over these amortization periods. The actual impact of this provision will depend on multiple factors, including the amount of R&D expenses we will incur and whether we conduct our R&D activities inside or outside the United States.

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 biopharmaceuticals industries depends upon our ability to attract and retain highly qualified managerial, manufacturing, 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, development and manufacturing teams may terminate their employment with us on short notice. Although we have written employment arrangements with all of our employees, these employment arrangements in the United States generally provide for at-will employment, which means that our employees can leave our employment at any time, with or without notice. In addition, the pending Transaction with Amgen has made it more difficult to attract and retain qualified employees due to the uncertainty about whether or when the transaction will close and impact of the Transaction on our employees. 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, manufacturing, scientific and medical personnel.

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

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

The United States and some foreign jurisdictions are considering or have enacted a number of legislative and regulatory proposals that change the healthcare system in ways that could impact profitability. In the United States and other countries there is significant interest in implementing regulations and legislation with the stated goals of containing healthcare costs, improving quality, and/or expanding access. The biopharmaceutical industry has been a focus of these efforts and has been significantly affected by major legislative initiatives, particularly in the United States. For example, the ACA, among other things, established an annual, nondeductible fee on any entity that manufactures or imports specified branded prescription drugs and biologic agents; expanded eligibility criteria for Medicaid programs; increased the statutory minimum rebates a manufacturer must pay under the Medicaid Drug Rebate Program; creates a Medicare Part D coverage gap discount program; established a Patient-Centered Outcomes Research Institute to oversee, identify priorities in and conduct comparative clinical effectiveness research, along with funding for such research; and established a Center for Medicare & Medicaid Innovation at CMS to test innovative payment and service delivery models to lower Medicare and Medicaid spending. On June 17, 2021, the U.S. Supreme Court dismissed a challenge on procedural grounds that argued the ACA is unconstitutional in its entirety because the "individual mandate" was repealed by Congress. However, it is possible that the ACA will be subject to additional judicial or Congressional challenges in the future.

Prior to the U.S. Supreme Court ruling, on January 28, 2021, President Biden issued an executive order that initiated a special enrollment period for purposes of obtaining health insurance coverage through the ACA marketplace. The executive order also instructed certain governmental agencies to review and reconsider their existing policies and rules that limit access to healthcare, including among others, reexamining Medicaid demonstration projects and waiver programs that include work requirements, and policies that create unnecessary barriers to obtaining access to health insurance coverage through Medicaid or the ACA.

In addition, on August 16, 2022, President Biden signed the IRA into law, which among other things, extends enhanced subsidies for individuals purchasing health insurance coverage in ACA marketplaces through plan year 2025. The IRA also eliminates the "donut hole" under the Medicare Part D program beginning in 2025 by significantly lowering the beneficiary maximum out-of-pocket costs. Medicare will cap beneficiary costs at $2,000 per year, indexed in future years to the rate of increase in Medicare costs. Further, the IRA restructures liability under Medicare Part D beginning in 2025, through a newly established Manufacturer Discount Program, which in part requires manufacturers to provide a 10% discount in the initial phase and 20% discount in the catastrophic phase for brand drugs. It is unclear how future healthcare reform measures of the Biden administration will impact the many different provisions of the ACA and IRA affecting the health system, the biopharmaceutical sector and our business. It is also likely that the IRA will put pressure on commercial insurers to reduce coverage or reimbursement of branded medicines.

Other legislative changes have also been proposed and adopted since the ACA was enacted. For example, the Budget Control Act of 2011 resulted in aggregate reductions in Medicare payments to providers of up to 2 percent per fiscal year, starting in 2013, and due to subsequent legislative amendments to the statute will remain in effect until 2032, unless additional Congressional action is taken. The American Taxpayer Relief Act of 2012, among other things, reduced Medicare payments to several types of providers and increased the statute of limitations period for the government to recover overpayments to providers from three to five years. Such laws, and others that may affect our business that have been enacted or may in the future be enacted, may result in additional reductions in Medicare and other healthcare funding.

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

In July 2021, the Biden administration released an executive order, "Promoting Competition in the American Economy," with multiple provisions aimed at prescription drugs. In response to President Biden's executive order, on September 9, 2021, HHS released a Comprehensive Plan for Addressing High Drug Prices that outlines principles for drug pricing reform. The plan sets out a variety of potential legislative policies that Congress could pursue as well as potential administrative actions HHS can take to advance these principles. In response to the Biden administration's October 2022 executive order, on February 14, 2023, HHS released a report outlining three new models for testing by the Center for Medicare and Medicaid Innovation which will be evaluated on their ability to lower the cost of drugs, promote accessibility, and improve quality of care. These models target Medicare Part D, cell and gene therapies, and drugs approved on the accelerated approval pathway. It is unclear whether the models will be utilized in any health reform measures in the future.

Congress continues to seek new legislative and/or administrative measures to control drug costs. On March 11, 2021, President Biden signed the American Rescue Plan Act of 2021 into law, which eliminates the statutory Medicaid drug rebate cap, currently set at 100% of a drug's average manufacturer price, for single source and innovator multiple source drugs, beginning January 1, 2024. In addition, the IRA directs the HHS Secretary to establish a Drug Price Negotiation Program, or Program, to lower prices for certain high-expenditure, single-source prescription drugs and biologics covered under Medicare Part B and Part D that have been approved by the FDA for at least 7 years for prescription drugs and at least 11 years for biologics when the drug or biologic, as applicable, is eligible for selection for the Program. Under the Program, the HHS Secretary will publish a list of "selected drugs," and will then negotiate maximum fair prices with their manufacturers. The Program will be implemented in stages. Beginning in 2026, 10 Medicare Part D "selected drugs" will be subject to price negotiations. By 2029, and in subsequent years thereafter, the number will increase to 20 drugs and biologics covered under Medicare Part B and Part D. Agreements between HHS and manufacturers will remain in place until a drug or biologic is no longer considered a "selected drug" for negotiation purposes. Manufacturers who do not comply with the negotiated prices set under the Program will be subject to an excise tax based on a percentage of total sales of a "selected drug" up to 95%, or they have the option to withdraw from the Medicare and Medicaid markets. Orphan drugs approved for only one rare disease or condition, among others, are exempt from negotiation. Further, the IRA now requires manufacturers that increase prices of certain Medicare Part B and Part D drugs or biologics at a rate greater than inflation to pay rebates to CMS or be subject to civil monetary penalties. Inflation penalties for Part B drugs will be assessed beginning in the fall of 2025, and inflation penalties for Part D drugs will be assessed starting at the end of 2025. The IRA permits HHS to implement many of these provisions through guidance, as opposed to regulation, for the initial years. HHS has and will continue to issue and update guidance as these programs are implemented. These provisions will take effect progressively starting in fiscal year 2023, although the Program is currently subject to legal challenges. The IRA is likely to have a significant negative impact on the pharmaceutical industry.

In EU countries and Japan, 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. Certain of these changes could impose limitations on the prices we will be able to charge for our medicines and any approved medicine candidates or the amounts of reimbursement available for these medicines from governmental agencies or third-party payers, may increase the tax obligations on biopharmaceutical companies such as ours, or may facilitate the introduction of generic competition with respect to our medicines.

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

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

In the United States, we are subject directly, or indirectly through our customers and other third parties, to various state and federal fraud and abuse and transparency laws, including, without limitation, the federal Anti-Kickback Statute, the federal False Claims Act, the Civil Monetary Penalties Law prohibiting, among other things, beneficiary inducements, and similar state and local laws, federal and state privacy and security laws, such as the Health Insurance Portability and Accountability Act of 1996, as amended by the Health Information Technology for Economic and Clinical Health Act, 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 biopharmaceutical representatives to be licensed and comply with codes of conduct, transparency reporting, and other obligations. Collectively, these laws may affect, among other things, our current and proposed research, sales, marketing and educational programs, as well as other possible relationships with customers, pharmacies, physicians, payers, and patients. We are subject to similar laws in the EEA.

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

There has also been a trend of increased federal and state regulation of payments made to physicians and other healthcare providers. The ACA, among other things, imposed reporting requirements on drug manufacturers for payments made by them to physicians (defined to include doctors, dentists, podiatrists, optometrists and licensed chiropractors), certain other healthcare providers (including, for example, physician assistants and nurse practitioners), and teaching hospitals, as well as ownership and investment interests held by physicians, and their immediate family members. Failure to submit required information may result in significant civil monetary penalties.

On August 3, 2022, we received a civil investigative demand from the United States Department of Justice, or DOJ, pursuant to the Federal False Claims Act regarding an investigation concerning potentially false information in prior authorization forms. A prior authorization form is a managed care practice whereby the payer (either a commercial insurer or a government health program) requires that the prescribing physician provide additional justification or information supporting the physician’s decision to prescribe a particular medicine. The civil investigative demand requests certain documents and information related to DUEXIS, PENNSAID 2%, VIMOVO and RAYOS. We are cooperating with the investigation and the DOJ has not indicated to us whether it believes we engaged in any wrongdoing or if we are the subject of the investigation. While we are not aware of any fraudulent scheme to provide false information in prior authorization forms for our medicines that resulted in improper payments from government healthcare programs, no assurance can be given as to the timing or outcome of the DOJ’s investigation, or that it will not result in a material adverse effect on our business.

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

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

Undesirable side effects caused by any medicine candidate that we develop could result in the denial of regulatory approval by the FDA or other comparable foreign regulatory authorities for any or all targeted indications, or cause us to evaluate the future of our development programs. In our clinical trials that supported the initial U.S. approval of TEPEZZA for the treatment of TED, the most commonly reported treatment-emergent adverse events were muscle spasms, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache, dry skin, weight decreased, nail disorder, and menstrual disorders. While our post-marketing studies and pharmacovigilance reporting data have shown similar rates of hearing impairment as compared to the initial TEPEZZA pivotal clinical trials, which was reflected in the initial FDA-approved label, there have been third party reports that have purported to show higher rates of hearing impairment. In addition, an analysis of safety data as part of our ongoing pharmacovigilance program indicated a signal of hearing impairment events of greater severity, in limited cases, than those observed in the TEPEZZA pivotal clinical trials and described in the approved product label. Based on this analysis, we initiated discussions with the FDA regarding potential updates to the warnings and precautions, adverse reactions and patient counseling information sections of the TEPEZZA label as part of a supplemental biologic license application, or sBLA. On July 17, 2023, the FDA approved the sBLA to include additional information on hearing impairment, including the possibility of severe hearing impairment, which in some cases may be permanent. To the extent healthcare providers or patients become concerned with adverse events associated with TEPEZZA, including the potential for hearing impairment, it could negatively impact our ability to increase adoption of the medicine. With respect to KRYSTEXXA, the most commonly reported adverse reactions in the pivotal trial were gout flares, infusion reactions, nausea, contusion or ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting. When administering KRYSTEXXA with methotrexate, the most commonly reported adverse events in the MIRROR randomized control trial were gout flares, arthralgia, COVID-19, nausea and fatigue. 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. With respect to UPLIZNA, the most common adverse reactions across both the randomized and open-label treatment in our N-MOmentum trial for UPLIZNA were urinary tract infection, nasopharyngitis, arthralgia, upper respiratory tract infection, headache, back pain, and infusion related reaction. The most common infections reported by treated patients in the randomized and open-label periods included urinary tract infection, nasopharyngitis, upper respiratory tract infection and influenza. In addition, three deaths were reported in the ongoing open-label period. One death occurred in a patient experiencing a myelitis attack and was considered unrelated to UPLIZNA by the investigator. The second death was due to complications from mechanical ventilator-associated pneumonia in a patient who developed new neurological symptoms and seizures, the cause of which could not be definitively established. The possibility that the death was treatment-related could not be ruled out, and as a result, under the terms of the protocol for the trial, the death was assessed as treatment-related. The third death was due to COVID-19 pneumonia and was considered unrelated to UPLIZNA by the investigator. There can be no assurance a foreign regulatory authority will agree with the classifications of the deaths made by the investigators or that we will not be required to conduct additional clinical trials of UPLIZNA in order to establish an adequate safety database. With respect to PROCYSBI, the most common side effects include vomiting, nausea, abdominal pain, breath odor, diarrhea, skin odor, fatigue, rash and headache. The most common side effects observed in pivotal trials for ACTIMMUNE were "flu-like" or constitutional symptoms such as fever, headache, chills, myalgia and fatigue.

The FDA or other comparable foreign 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, we or others may identify undesirable side effects caused by our medicines or any other medicine candidate that we may develop that receives marketing approval, or there could be perceptions that the medicine is associated with undesirable side effects. For example, product liability suits have been filed against us alleging that TEPEZZA is defectively designed and/or that we failed to include proper warnings regarding potential adverse events associated with hearing impairment. As a result of any such events it is possible that:

- regulatory authorities may require the addition of labeling statements, such as a “black box” warning or a contraindication;
- regulatory authorities may withdraw, suspend or vary 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 recent and potential future product liability and/or personal injury claims.

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

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

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

*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.

In some instances, there can be significant variability in safety and efficacy results between different clinical trials of the same medicine candidate due to numerous factors, including changes in trial protocols, differences in size and type of the patient populations, differences in and adherence to the dosing regimen and other trial protocols and the rate of dropout among clinical trial participants. For example, we recently announced that daxdilimab failed to meet the primary endpoint in a Phase 2 clinical trial in systemic lupus erythematosus, and cannot guarantee that our trials of daxdilimab in other indications will have different outcomes. In addition, while we have announced that dazodalibep met the primary endpoint in a Phase 2 clinical trial in Sjögren's syndrome in both populations and that we plan on initiating a Phase 3 development program in this indication, there is no assurance that dazodalibep will demonstrate similar results in the planned Phase 3 trials, or demonstrate successful results in our planned trial in focal segmental glomerulosclerosis. As another example, while TEPEZZA is approved in the United States in TED and we have also recently announced that TEPEZZA met the primary endpoint in a Phase 4 clinical trial in chronic/low CAS TED, there is no assurance that TEPEZZA will demonstrate similar results in our ongoing Phase 3 trial in chronic/low CAS TED in Japanese patients.

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 approval or positive Ethics Committee opinions as part of the single decision on the authorization of the clinical trial issued by EU Member States including input from the national competent authorities and Ethics Committee in relation to 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;
- war or geopolitical issues in areas where we have clinical sites, including in Russia and Ukraine;
- adding new sites or countries; or
- manufacturing sufficient quantities of medicine candidates for use in clinical trials.

Our clinical trials have been and may also in the future be affected by public health epidemics or outbreaks. For example, while the clinical trial has since completed, we experienced enrollment delays in our TEPEZZA clinical trial in chronic/low CAS TED due to the impacts of the omicron variant of COVID-19. We also experienced enrollment delays in our UPLIZNA clinical trial in myasthenia gravis due to government ordered COVID-19 lockdowns in China, combined with other negative impacts related to the conflict in Ukraine. As a result, we expect topline data for our clinical trial of UPLIZNA in myasthenia gravis in 2024. The availability of supplies needed for the conduct of preclinical studies and clinical trials may be impacted by supply disruptions. For example, we depend on the availability of non-human primates to conduct certain preclinical studies that we are required to complete prior to submitting an IND and initiating clinical development. There is currently a global shortage of non-human primates available for drug development. If the shortage continues, this could substantially increase the cost of conducting our preclinical development and could also result in delays to our development timelines. 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 impacted by local disruptions, the integrity of data from our trials may be compromised or not accepted by the FDA or other comparable foreign 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 comparable foreign 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 comparable foreign regulatory authorities resulting in the imposition of a clinical hold, unforeseen safety issues or adverse side effects, failure to demonstrate a benefit from using a medicine candidate, changes in governmental regulations or administrative actions or lack of adequate funding to continue the clinical trial. If we experience delays in the completion of, or if we terminate, any clinical trial of our medicine candidates, the commercial prospects of our medicine candidates will be harmed, and our ability to generate medicine revenues from any of these medicine candidates will be delayed or reduced. In addition, any delays in completing our clinical trials will increase our costs, slow down our medicine development and approval process and jeopardize our ability to commence medicine sales and generate revenues.

Moreover, principal investigators for our clinical trials may serve as scientific advisors or consultants to us from time to time and receive compensation in connection with such services. Under certain circumstances, we may be required to report some of these relationships to the FDA or comparable foreign regulatory authorities. The FDA or comparable foreign regulatory authorities 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 or comparable foreign regulatory authorities 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 or comparable foreign regulatory authorities and may ultimately lead to the denial of marketing approval of one or more of our medicine candidates.

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

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

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

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

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

*Actual or threatened public health pandemics or outbreaks may adversely impact our industry, including the commercialization of our medicines, our supply chain, our clinical trials, our liquidity and access to capital markets and our business development activities.**

While many health organizations have declared that the COVID-19 pandemic has ended, the pandemic and previous actions to slow its spread had an adverse impact on our operations, including the commercialization of our medicines, and we cannot predict if or when other similar disease outbreaks will emerge that cause similar disruptions. The extent to which future pandemics 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 timing and duration of future pandemics, the transmissibility and severity of illness caused by future pandemics, the efforts by governments and businesses to contain the spread of future pandemics, business closures or business disruptions and the impact on the economy and capital markets.

*If our information technology systems or data, or those of third parties upon which we rely, are or were compromised or threatened to be compromised, we could experience adverse consequences resulting from such compromise, including but not limited to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of sales; and other adverse consequences.**

In the ordinary course of our business, we may collect, receive, store, generate, use, protect, secure, dispose of, transmit, disclose, or otherwise make accessible (collectively "process") proprietary, confidential, and sensitive data, including personal data (such as health-related data), intellectual property, and trade secrets. We may rely upon third parties (such as service providers) for our data processing-related activities. We may share or receive sensitive data with or from third parties.

Cyberattacks, malicious internet-based activity, and online and offline fraud are prevalent and continue to increase. These threats are becoming increasingly difficult to detect. These threats come from a variety of sources. In addition to traditional computer "hackers," threat actors, personnel misconduct, or error (such as theft or misuse), sophisticated nation-state and nation-state supported actors now engage in attacks. Some actors now engage and are expected to continue to engage in cyber-attacks, including without limitation nation-state actors for geopolitical reasons and in conjunction with military conflicts and defense activities. During times of war and other major conflicts, we, and the third parties upon which we rely, may be vulnerable to a heightened risk of these attacks, including retaliatory cyber-attacks, that could materially disrupt our systems and operations, and ability to produce, sell and distribute our medicines. We may be subject to a variety of evolving threats, including but not limited to social engineering attacks, malware, denial-of-service attacks, ransomware, supply-chain attacks, software bugs, server malfunction, software or hardware failures, loss of data or other information technology assets, adware, telecommunications failures, earthquakes, fire, flood, and other similar threats. Ransomware attacks, including those perpetrated by organized criminal threat actors, nation-states, and nation-state supported actors, are becoming increasingly prevalent and severe and can lead to significant interruptions in our operations, loss or misuse of data and income, reputational harm, and diversion of funds. Extortion payments may alleviate the negative impact of a ransomware attack, but we may be unwilling or unable to make such payments due to, for example, applicable laws or regulations prohibiting payments. Similarly, supply-chain attacks have increased in frequency and severity, and we cannot guarantee that third parties and infrastructure in our supply chain have not been compromised or that they do not contain exploitable defects or bugs that could result in a breach of or disruption to our information technology systems or the third-party information technology systems that support us and our services. Further, as the majority of our employees work remotely for some portion of their jobs, this has increased risk to our information technology systems and data with the utilization of network connections outside our premises. Future business transactions (such as acquisitions or integrations) could expose us to additional cybersecurity risks and vulnerabilities, as our systems could be negatively affected by vulnerabilities present in acquired or integrated entities' systems and technologies.

Any of the previously identified or similar threats could cause a security incident. A security incident could result in unauthorized, unlawful or accidental acquisition, modification, destruction, loss, alteration, encryption, disclosure of or access to data. A security incident could disrupt our (and third parties upon whom we rely) ability to provide our products and services. We may expend significant resources or modify our business activities (including our clinical trial activities) in an effort to protect against security incidents. Certain data privacy and security obligations may require us to implement and maintain specific security measures, industry-standard or reasonable security measures to protect our information technology systems and data.

While we have implemented security measures designed to protect against a security incident, there can be no assurance that these measures will be effective. We have not always been able in the past and may be unable in the future to detect vulnerabilities in our information technology systems because such threats and techniques change frequently, are often sophisticated in nature, and may not be detected until after a security incident has occurred. Despite our efforts to identify and remediate vulnerabilities, if any, in our information technology systems, our efforts may not be successful. Further, we may experience, delays in developing and deploying remedial measures designed to address any such identified vulnerabilities.

Applicable data privacy and security obligations may require us to notify relevant stakeholders of security incidents. Such disclosures are costly, and the disclosures or the failure to comply with such requirements, could lead to adverse impacts. If we (or a third party upon whom we rely) experience a security incident or are perceived to have experienced a security incident, we may experience adverse consequences. These consequences may include: government enforcement actions; additional reporting requirements and/or oversight; restrictions on processing data; litigation; indemnification obligations; negative publicity; reputational harm; monetary fund diversions; interruptions in our operations; financial loss; and other similar harms. Security incidents and attendant consequences may cause customers to stop using our products and services, deter new customers for using our products and services, and negatively impact our ability to grow and operate our business.

Our contracts may not contain limitations of liability, and even where they do, there can be no assurance that limitations of liability in our contracts are sufficient to protect us from liabilities, damages, or claims related to our data privacy and security obligations. We cannot be certain that (a) our liability insurance will be sufficient in type or amount to cover us against claims related to security incidents; (b) such coverage will cover any indemnification claims against us relating to any security incident, will continue to be available to us on economically reasonable terms, or at all; or (c) any insurer will not deny coverage as to any future claim. The successful assertion of one or more claims against us that exceed available insurance coverage, or the occurrence of changes in our insurance policies, including premium increases or the imposition of large deductible or co-insurance requirements, could adversely affect our reputation, business, financial condition and results of operations.

*We are subject to stringent and evolving U.S. and foreign laws, regulations, rules, contractual obligations, policies, standards and other obligations related to data privacy and security. Our actual or perceived failure to comply with such obligations could lead to regulatory investigations or actions; litigation; fines and penalties; disruptions of our business operations; reputational harm; loss of revenue or profits; loss of customers or sales; and other adverse business consequences.**

In the ordinary course of business, we may process personal data and other sensitive information, including proprietary and confidential business data, trade secrets, intellectual property, data we collect about trial participants in connection with clinical trials, and sensitive third-party data. Our data processing activities may subject us to numerous data privacy and security obligations, such as various laws, regulations, guidance, industry standards, external and internal privacy and security policies, contractual requirements, and other obligations relating to data privacy and security.

In the United States, federal, state, and local governments have enacted numerous data privacy and security laws, including data breach notification laws, personal data privacy laws, and consumer protection laws (e.g., Section 5 of the Federal Trade Commission Act). For example, the California Consumer Privacy Act of 2018, or CCPA, requires businesses to provide specific disclosures in privacy notices and honor requests of California residents to exercise certain privacy rights. The CCPA provides for civil penalties of up to $7,500 per violation and allows private litigants affected by certain data breaches to recover significant statutory damages. Although the CCPA exempts some data processed in the context of clinical trials, the CCPA may increase compliance costs and potential liability with respect to other personal data we may maintain about California residents. In addition, the California Privacy Rights Act of 2020, which became effective January 1, 2023, expanded the CCPA's requirements and establishes a new regulatory agency to implement and enforce the law. Other states, such as Virginia, Colorado, Utah and Connecticut, have also passed comprehensive privacy laws, and similar laws are being considered in several other states. In addition, data privacy and security laws have been proposed at the federal and local levels in recent years, which could further complicate compliance efforts and may increase legal risk and compliance costs for us and the third parties upon whom we rely.

Outside the United States, an increasing number of laws, regulations, and industry standards apply to data privacy and security. For example, the EU's General Data Protection Regulation, or the EU GDPR, and the UK's GDPR, impose strict requirements for processing personal data, and violators of these laws face significant penalties. Under the EU GDPR, companies may face temporary or definitive bans on data processing and other corrective actions; fines of up to 20 million Euros or 4% of annual global revenue, whichever is greater; or private litigation related to processing of personal data brought by classes of data subjects or consumer protection organizations authorized at law to represent their interests.

Certain jurisdictions have enacted data localization laws and cross-border personal data transfer laws, which could make it more difficult to transfer information across jurisdictions (such as transferring or receiving personal data that originates in the EU or in other foreign jurisdictions). In particular, the EEA and the UK have historically restricted the transfer of personal data to the United States and other countries whose privacy laws it believes are inadequate. Other jurisdictions may adopt similarly stringent interpretations of their data localization and cross-border data transfer laws.

A recent decision by the European Commission has implemented new laws approving transfers of personal data between the EU and the United States, known as the EU-US Data Privacy Framework, or Framework. The Framework establishes a legal basis for us to transfer personal data between the EU and the United States that is compliant with the EU GDPR, without the need to implement any additional safeguards. The Framework therefore represents an alternative opportunity for us to manage the export of data between the EEA and the U.S. and we are currently assessing our transfer strategy in light of these developments. All international data transfer mechanisms are subject to legal challenges, and there is no certainty that we can continue to rely on these measures to lawfully transfer personal data to the United States if the current legal position changes.

In addition to data privacy and security laws, we may be contractually subject to industry standards adopted by industry groups and may become subject to such obligations in the future. We may also be bound by contractual obligations related to data privacy and security, and our efforts to comply with such obligations may not be successful. For example, certain privacy laws, such as the GDPR and the CCPA, require companies to impose specific contractual restrictions on their service providers. We publish privacy policies, marketing materials and other statements regarding data privacy and security. If these policies, materials, or statements are found to be deficient, lacking in transparency, deceptive, unfair, or misrepresentative of our practices, we may be subject to investigation, enforcement actions by regulators or other adverse consequences.

Obligations related to data privacy and security are quickly changing, becoming increasingly stringent, and creating regulatory uncertainty. Additionally, these obligations may be subject to differing applications and interpretations, which may be inconsistent or conflict among jurisdictions. Preparing for and complying with these obligations requires us to devote significant resources. These obligations may necessitate changes to our services, information technologies, systems, and practices and to those of any third parties that process personal data on our behalf. We may at times fail (or be perceived to have failed) in our efforts to comply with our data privacy and security obligations. Moreover, despite our efforts, our personnel or third parties on whom we rely may fail to comply with such obligations, which could negatively impact our business operations. If we or the third parties on which we rely fail, or are perceived to have failed, to address or comply with applicable data privacy and security obligations, we could face significant consequences, including but not limited to: government enforcement actions; litigation; additional reporting requirements and/or oversight; bans on processing personal data; orders to destroy or not use personal data; and imprisonment of company officials.

Any of these events could have a material adverse effect on our reputation, business, or financial condition, including but not limited to: loss of customers; interruptions or stoppages in our business operations, including clinical trials; inability to process personal data or to operate in certain jurisdictions; limited ability to develop or commercialize our medicines; expenditure of time and resources to defend any claim or inquiry; adverse publicity; or substantial changes to our business model or operations.

We are subject to various laws and regulations pertaining to export controls and trade and economic sanctions, which can impact our business activities and subject us to liability for noncompliance.

Our activities are subject to various U.S. and foreign export control and sanctions laws and regulations, including the U.S. Department of Commerce’s Export Administration Regulations and the U.S. Department of the Treasury’s Office of Foreign Assets Control economic and trade sanctions programs. Export control laws may restrict our ability to export, reexport, or transfer our medicines outside of the United States without authorization. Sanctions laws may prohibit or restrict our ability to provide medicines and services to certain countries, territories, entities, or individuals.

These laws and regulations are subject to frequent change which may impact the global economy and supply chains in ways that impact our business. Notably, in response to Russia’s invasion of Ukraine in February 2022, the United States and its allies significantly expanded export control and sanctions prohibitions and restrictions aimed at Russia, Belarus, and certain regions in Ukraine. We have a limited number of ongoing clinical research studies in Russia, Belarus, and non-restricted regions in Ukraine, and are monitoring the potential impact of the conflict on our clinical trial activities. We are no longer initiating new clinical trials or opening new investigator sites in these countries. With respect to our clinical trial of UPLIZNA in myasthenia gravis, disruptions in payment systems and other logistical challenges related to the conflict in Ukraine have negatively impacted enrollment and operations of clinical sites in the region which, combined with other negative impacts related to COVID-19, has delayed our expected timeline for topline data to 2024. Although we continue to work diligently with patients and sites across the impacted regions and are putting the appropriate measures in place to meet enrollment targets, further escalation of the conflict and any additional export controls and sanctions or adverse regulatory developments could restrict, prohibit, or otherwise impair our studies.

Compliance with these laws and regulations can be time- and resource-intensive. Although we are committed to complying with all applicable export control and sanctions laws and regulations, we cannot guarantee full compliance. Violations of these regimes can result in significant financial penalties, loss of licensing privileges, other administrative penalties, reputational harm, and adverse business impact.

*Product liability lawsuits may cause us to incur substantial liabilities or could require us 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. In particular, we have been and may continue to 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. For example, several product liability suits have been filed against us alleging that TEPEZZA is defectively designed and/or that we failed to include proper warnings regarding potential adverse events associated with hearing impairment. While we intend to vigorously defend ourselves in the lawsuits, no assurance can be given as to the outcome of the litigation, whether additional similar lawsuits will be initiated or whether our insurance coverage will be adequate to cover the costs of the litigation or any resulting settlements or judgments. 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 will 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 or the reputation of our medicines;
- 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 Environmental Pollution Liability insurance coverage related to our South San Francisco facility and our Rockville, Maryland facility. If we are subject to any liability as a result of our third-party manufacturers' activities involving hazardous materials, our business and financial condition may be adversely affected. In the future we may seek to establish longer-term third-party manufacturing arrangements, pursuant to which we would seek to obtain contractual indemnification protection from such third-party manufacturers potentially limiting this liability exposure.

Risks Related to our Financial Position and Capital Requirements

We may not remain profitable in future periods.

Although we recorded operating income and net income for the last several years, we may incur operating losses in the future. Losses in prior periods resulted principally from costs incurred in our development activities for our medicines and medicine candidates, commercialization activities related to our medicines and costs associated with our acquisition transactions. Our prior losses, combined with possible future losses, have had and may continue to have an adverse effect on our shareholders' equity and working capital. Our ability to maintain profitability will depend on the revenues we generate from the sale of our medicines being sufficient to cover our operating expenses. We also expect our operating expenses to increase substantially as a result of continuing to develop our pipeline of medicine candidates, which will negatively impact our future profitability until such time, if ever, that these potential medicine candidates are approved and successfully commercialized, as well as developing our manufacturing and international sales and marketing capabilities.

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

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

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

Even if we do generate additional medicine sales, we may not be able to sustain profitability on a quarterly or annual basis. Our failure to 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 commercial medicine portfolio, including costs associated with refinancing debt of acquired companies;
- expand our manufacturing capabilities, including the planned expansion of our facility in Waterford, Ireland;
- satisfy progress and milestone payments under our existing and future license, collaboration and acquisition agreements; and
- conduct clinical trials with respect to potential additional indications, as well as conduct post-marketing requirements and commitments, with respect to our medicines and medicines we acquire.

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

We cannot be certain that additional funding will be available on acceptable terms, or at all. As a result of the COVID-19 pandemic and actions taken to slow its spread, current and potential future bank failures, the military conflict between Ukraine and Russia, actual or anticipated changes in interest rates and economic inflation, the global credit and financial markets have at times experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly and more dilutive. In particular, rising interest rates have made debt financing more expensive which may limit our ability to finance future acquisitions through additional borrowing. In addition, the transaction agreement with Amgen contains restrictions on our ability to incur additional indebtedness or issue new equity in connection with financing activities or otherwise. If we are unable to raise additional capital in sufficient amounts or on terms acceptable to us, we may have to significantly delay, scale back or discontinue the development or commercialization of one or more of our medicines or medicine candidates or one or more of our other R&D initiatives, or delay, cut back or abandon our plans to grow the business through acquisitions. We also could be required to:

- seek collaborators for one or more of our current or future medicine candidates at an earlier stage than otherwise would be desirable or on terms that are less favorable than might otherwise be available; or
- relinquish or license on unfavorable terms our rights to technologies or medicine candidates that we would otherwise seek to develop or commercialize ourselves.

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

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

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

As of June 30, 2023, we had $2.6 billion book value, or $2.6 billion aggregate principal amount of indebtedness, including $2.0 billion 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, R&D and future business opportunities;
- exposing us to the risk of increased interest rates to the extent of any future borrowings, including borrowings under our credit agreement, at variable rates of interest;
- making it more difficult for us to satisfy our obligations with respect to our indebtedness, including our outstanding notes, our credit agreement, and any failure to comply with the obligations of any of our debt instruments, including restrictive covenants and borrowing conditions, could result in an event of default under the agreements governing such indebtedness;
- increasing our vulnerability to, and reducing our flexibility to respond to, changes in our business or general adverse economic and industry conditions;
- limiting our ability to obtain additional financing for working capital, capital expenditures, debt service requirements, acquisitions, and general corporate or other purposes and increasing the cost of any such financing;
- limiting our flexibility in planning for, or reacting to, changes in our business and the industry in which we operate; and placing us at a competitive disadvantage as compared to our competitors, to the extent they are not as highly leveraged and who, therefore, may be able to take advantage of opportunities that our leverage may prevent us from exploiting; and
- restricting us from pursuing certain business opportunities.

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

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

As a result of the COVID-19 pandemic and actions taken to slow its spread, bank failures, actual or anticipated changes in interest rates and economic inflation, the global credit and financial markets have experienced extreme volatility and disruptions, including diminished liquidity and credit availability, declines in consumer confidence, declines in economic growth, increases in unemployment rates and uncertainty about economic stability. In addition, government efforts to stimulate economic activity in the face of the COVID-19 pandemic have caused interest rates to fluctuate and created uncertainty as to future fluctuations. If the equity and credit markets deteriorate, it may make any additional debt or equity financing more difficult, more costly or more dilutive.

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

Our ability to make scheduled payments under or to refinance our debt obligations depends on our financial condition and operating performance, which is subject to prevailing economic, industry and competitive conditions and to certain financial, business and other factors beyond our control. Our ability to generate cash flow to meet our payment obligations under our debt may also depend on the successful implementation of our operating and growth strategies. Any refinancing of our debt could be at higher interest rates and may require us to comply with more onerous covenants, which could further restrict our business operations. We cannot assure that we will maintain a level of cash flows from operating activities sufficient to pay the principal, premium, if any, and interest on our indebtedness.

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

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

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

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

Subject to the restrictions under the transaction agreement with Amgen, 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% 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. Certain net operating losses generated before an August 2, 2012 ownership change and federal net operating losses and federal tax credits acquired through the Viela acquisition are subject to an annual limitation. 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.

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

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

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

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

At June 30, 2023, we had $2.5 billion of cash and cash equivalents consisting of cash, money market funds, time deposits and U.S. federal government securities. While we are not aware of any downgrades, material losses, or other significant deterioration in the fair value of our cash equivalents since June 30, 2023, no assurance can be given that deterioration in conditions of the global credit and financial markets or bank failures would not negatively impact our current portfolio of cash equivalents or our ability to meet our financing objectives. Dislocations in the credit market may adversely impact the value and/or liquidity of marketable securities owned by us.

The UK's referendum to leave the EU and the UK's exit from the EU on January 31, 2020, or "Brexit," has caused and may continue to cause disruptions to capital and currency markets worldwide. The full impact of Brexit, however, remains uncertain. A Trade and Cooperation Agreement, or the TCA, which outlines the trading relationship between the UK and the EU was agreed in December 2020, entered into force provisionally on January 1, 2021, and has been permanently applicable since May 1, 2021.

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

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

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

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

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

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

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

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

These covenants may:

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

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

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

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

In connection with the accounting for our various acquisition transactions, we have recorded significant amounts of intangible assets. Under GAAP, we must assess, at least annually and potentially more frequently, whether the value of goodwill has been impaired. Amortizing intangible assets will be assessed for impairment in the event of an impairment indicator. For example, during the year ended December 31, 2018, we recorded an impairment of $33.6 million to fully write off the book value of developed technology related to PROCYSBI in Canada and Latin America. More recently, our interim goodwill impairment test in the second quarter of 2022 indicated an impairment which represented the difference between the estimated fair value of the former inflammation reporting unit and its carrying value. As a result, we recognized an impairment charge of $56.2 million in June 2022 representing the full amount of goodwill for the former inflammation reporting unit. 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 biopharmaceutical 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.

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.

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

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

We are party to a number of technology licenses that are important to our business and expect to enter into additional licenses in the future. For example, we hold an exclusive, worldwide license from 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. If one or more of these licenses is terminated, it may be impossible for us to continue to commercialize TEPEZZA, which would have a material adverse effect on our business, financial condition and results of operations.

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

In addition, 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 Therapeutics, Inc., or 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.

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

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

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

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

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

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

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

Risks Related to Ownership of Our Ordinary Shares

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

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

- our failure to complete, or further delays in completing, the pending Transaction with Amgen;
- our failure to successfully execute our commercialization strategy with respect to our approved medicines, particularly our commercialization of our medicines in the United States;
- 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 biopharmaceutical 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, the indenture governing the 2027 Senior Notes and the transaction agreement with Amgen. Any return to shareholders will therefore be limited to the increase, if any, of our ordinary share price.

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

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

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

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

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

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

Our articles of association contain provisions which 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 Amgen's offer for our ordinary shares or another third party offer for our ordinary shares.

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

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

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

General Risk Factors

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

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

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

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

Our commercial success depends in part on us avoiding infringement of the patents and proprietary rights of third parties. There is a substantial amount of litigation, both within and outside the United States, involving patent and other intellectual property rights in the biopharmaceutical 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 biopharmaceutical industries expand and more patents are issued, the risk increases that our medicine candidates may be subject to claims of infringement of the patent rights of third parties.

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

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

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

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

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

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

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

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

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

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

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

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

If our existing shareholders sell, or indicate an intention to sell, substantial amounts of our ordinary shares in the public market, the trading price of such ordinary shares could decline. In addition, our ordinary shares that are either subject to outstanding options, RSUs and PSUs 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. If these additional ordinary shares are sold, or if it is perceived that they will be sold, in the public market, the trading price of our ordinary shares could decline.

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

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

ITEM 6. EXHIBITS

Exhibit Number	Description of Document
2.1#	Transaction Agreement, dated December 11, 2022, by and among Amgen Inc., Pillartree Limited and Horizon Therapeutics Public Limited Company (incorporated by reference to Exhibit 2.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on December 12, 2022).
2.2	Appendix 3 to the Rule 2.7 Announcement, dated as of December 12, 2022 (Conditions Appendix) (incorporated by reference to Exhibit 2.2 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on December 12, 2022).
3.1	Memorandum and Articles of Association of Horizon Therapeutics Public Limited Company, as amended (incorporated by reference to Exhibit 3.1 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 8, 2019).
4.1	Indenture dated as of July 16, 2019 by and between Horizon Therapeutics USA, Inc., the guarantors party thereto and U.S. Bank National Association, as trustee (incorporated by reference to Exhibit 4.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on July 16, 2019).
4.2	Form of 5.500% Senior Note due 2027 (incorporated by reference to Exhibit 4.1 to Horizon Therapeutics Public Limited Company's Current Report on Form 8-K, filed on July 16, 2019).
4.3	First Supplemental Indenture, dated November 19, 2019, by and between HZNP Finance Limited and U.S. Bank National Association (incorporated by reference to Exhibit 4.5 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 6, 2020).
4.4	Second Supplemental Indenture, dated April 23, 2020, by and among Horizon Properties Holding LLC, Curzion Pharmaceuticals, Inc. and U.S. Bank National Association (incorporated by reference to Exhibit 4.6 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 6, 2020).
4.5	Third Supplemental Indenture, dated March 15, 2021, by and between Viela Bio, Inc. and U.S. Bank National Association (incorporated by reference to Exhibit 4.5 to Horizon Therapeutics Public Limited Company's Quarterly Report on Form 10-Q, filed on May 5, 2021).
10.1*	Amendment No. 10 to the License Agreement, dated May 22, 2023, by and among F. Hoffmann-La Roche Ltd, Hoffman-La Roche Inc. and Horizon Therapeutics Ireland DAC (as successor in interest to River Vision Development Corp).
10.2	Amendment No. 10, dated June 16, 2023, to the Credit Agreement, dated May 7, 2015, as amended, by and among Horizon Therapeutics USA, Inc., as Borrower, Horizon Therapeutics Public Limited Company, as Irish Holdco and a guarantor, the subsidiary guarantors party thereto, as subsidiary guarantors, the lenders party thereto and Citibank, N.A., as administrative agent and collateral agent.
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.

101. INS	Inline XBRL Instance Document – the instance document does not appear in the Interactive Data File because its XBRL tags are embedded within the Inline XBRL document
101.SCH	Inline XBRL Taxonomy Extension Schema Document
101.CAL	Inline XBRL Taxonomy Extension Calculation Linkbase Document
101.DEF	Inline XBRL Taxonomy Extension Definition Linkbase Document
101.LAB	Inline XBRL Taxonomy Extension Label Linkbase Document
101.PRE	Inline XBRL Taxonomy Extension Presentation Linkbase Document
104	Cover Page Interactive Data File (formatted as Inline XBRL and contained in Exhibit 101)

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

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: August 8, 2023

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

Date: August 8, 2023

By: /s/ Aaron L. Cox
Aaron L. Cox
Executive Vice President, Chief Financial Officer (Principal Financial Officer)