UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): March 1, 2022

Horizon Therapeutics Public Limited Company
(Exact name of registrant as specified in its charter)

Ireland	**001-35238**	**Not Applicable**
(State or other jurisdiction of incorporation)	**(Commission File No.)**	**(IRS Employer Identification No.)**

70 St. Stephen's Green, Dublin, D02 E2X4, Ireland
(Address of principal executive offices)

Registrant's telephone number, including area code: 011-353-1-772-2100

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

Title of each class	Trading Symbol(s)	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 is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 or Rule 12b-2 of the Securities Exchange Act of 1934.

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. ☐

Item 2.02 Results of Operations and Financial Condition.

On March 1, 2022, Horizon Therapeutics plc issued a press release announcing its financial results for the fourth quarter and year ended December 31, 2021. A copy of this press release is attached hereto as Exhibit 99.1.

The information in this Item 2.02 and the exhibit hereto are being furnished and shall not be deemed to be "filed" for purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liability of that section, nor shall they be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as expressly set forth by specific reference in such a filing.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

Exhibit No.	Description
99.1	Press Release of Horizon Therapeutics plc, dated March 1, 2022.
104	Cover Page Interactive Data File (embedded within the Inline XBRL document).

SIGNATURES

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

Date: March 1, 2022

HORIZON THERAPEUTICS PUBLIC LIMITED COMPANY

By: /s/ Paul W. Hoelscher
Paul W. Hoelscher
Executive Vice President and Chief Financial Officer

Horizon Therapeutics plc Reports Fourth-Quarter 2021 and Full-Year 2021 Financial Results; Announces Full-Year 2022 Guidance

Fourth-Quarter 2021 Results:

— Net Sales of $1.01 Billion Increased 36% —
— GAAP Net Income of $173.2 Million; Adjusted EBITDA of $416.0 Million —
— TEPEZZA® (teprotumumab-trbw) Net Sales of $589.6 Million Increased 72% —
— KRYSTEXXA® (pegloticase injection) Net Sales of $170.3 Million Increased 32%; KRYSTEXXA Plus Immunomodulation Use Now Approaching 50% —
— Cash Position of $1.58 Billion as of Dec. 31, 2021 —

Full-Year 2021 Results:

— Record Net Sales of $3.23 Billion Increased 47% —
— GAAP Net Income of $534.5 Million; Adjusted EBITDA of $1.28 Billion —
— Record TEPEZZA Net Sales of $1.66 Billion, Representing Year-Over-Year Growth of 103% —
— Record KRYSTEXXA Net Sales of $565.5 Million, Representing Year-Over-Year Growth of 39% —
— Operating Cash Flow of More Than $1.0 Billion —

Full-Year 2022 Guidance:

— Net Sales Guidance of $3.9 Billion to $4.0 Billion, Representing 22% Growth at the Midpoint —
— Adjusted EBITDA Guidance of $1.63 Billion to $1.70 Billion, Representing 30% Growth and 230 Basis Points of Margin Expansion at the Midpoint —
— Expect TEPEZZA Net Sales Percentage Growth in the Mid-30s —
— Expect KRYSTEXXA Net Sales Growth of More Than 20% —

Company Highlights:

— Initiated Four Clinical Trials, Including TEPEZZA Phase 3 Trial in Japan —
— Submitted Supplemental Biologics License Application (sBLA) to the U.S. FDA to Expand Label for KRYSTEXXA to Include Co-Treatment with Methotrexate Based on Positive Data from MIRROR Trial —
— Advanced Pipeline to Drive Long-Term Growth; Entered into Agreement with Alpine to Develop Novel Therapies for Autoimmune and Inflammatory Diseases —

DUBLIN – March 1, 2022 – Horizon Therapeutics plc (Nasdaq: HZNP) today announced fourth-quarter and record full-year 2021 financial results and provided full-year 2022 net sales and adjusted EBITDA guidance.

“2021 marked a year of tremendous growth for Horizon – we invested significantly in our research and development capabilities and talent, significantly expanded our pipeline, increased our manufacturing capacity to meet growing demand and achieved outstanding financial results,” said Tim Walbert, chairman, president and chief executive officer, Horizon. “I am very proud of what we have accomplished, but I am most excited about the potential for continued growth going forward as we leverage the strong foundation we have built over the past several years. We expect another year of strong double-digit net sales and adjusted EBITDA growth in 2022, as well as meaningful margin expansion, as we continue to execute commercially and build on our momentum in R&D to develop new approaches for patients with rare, autoimmune and severe inflammatory diseases.”

Financial Highlights

(in millions except for per share amounts and percentages)	Q4 21	Q4 20	% Change	FY 21	FY 20	% Change
Net sales	$1,014.5	$745.3	36	$3,226.4	$2,200.4	47
Net income	173.2	190.6	(9)	534.5	389.8	37
Non-GAAP net income (1)	334.0	272.2	23	1,089.7	828.8	31
Adjusted EBITDA (1)	416.0	341.0	22	1,284.3	965.7	33
Earnings per share - diluted	0.73	0.82	(11)	2.27	1.81	25
Non-GAAP earnings per share - diluted	1.41	1.17	21	4.62	3.75	23

(1) Beginning in the fourth quarter of 2021, the Company no longer excludes upfront and milestone payments related to license and collaboration agreements from non-GAAP financial measures. Adjusted EBITDA and non-GAAP net income for the three months ended Dec. 31, 2021 and 2020, includes $36.2 million and $30.0 million, respectively of upfront and milestone payments related to license and collaboration agreements. Adjusted EBITDA and non-GAAP net income for the years ended Dec. 31, 2021 and 2020, includes $89.7 million and $33.0 million, respectively of upfront and milestone payments related to license and collaboration agreements.

Fourth Quarter and Recent Company Highlights

- **Submitted sBLA for Co-Treatment of KRYSTEXXA Plus Methotrexate:** In January, the Company submitted an sBLA to the U.S. Food and Drug Administration (FDA) to expand the label for KRYSTEXXA to include co-treatment with methotrexate. The submission is based on results from the MIRROR Phase 4 randomized, placebo-controlled trial announced in October, which demonstrated that 71% of patients receiving KRYSTEXXA plus methotrexate achieved a complete response, a more than 30 percentage point improvement compared to patients who were randomized to receive KRYSTEXXA plus placebo ($p<0.001$). KRYSTEXXA plus immunomodulation is a core element of the Company's strategy to maximize the value of KRYSTEXXA and enable more patients with uncontrolled gout to benefit from the medicine.
- **Entered into Agreement with Alpine Immune Sciences to Develop Novel Therapies for Autoimmune and Inflammatory Diseases:** In December, the Company entered into an exclusive license and collaboration agreement with Alpine for the development and commercialization of up to four fusion protein-based preclinical candidates, including multi-specific approaches, for autoimmune and inflammatory diseases. The Alpine collaboration is an example of how Horizon continues to execute on its research strategy to drive earlier-stage discovery through internal research and research-based partnerships and collaborations.
- **Added Second TEPEZZA Drug Product Manufacturer:** In December, the U.S. FDA approved Horizon's application for a second drug product manufacturer for TEPEZZA, Patheon (contract development and manufacturing organization services of Thermo Fisher Scientific). The addition of Patheon is part the Company's long-term strategy adopted in early 2020 to support TEPEZZA supply, given the much stronger than expected demand since launch and planned expansion outside of the United States.
- **Received CHMP Positive Opinion for UPLIZNA® (inebilizumab-cdon):** In November, the Committee for Medicinal Products for Human Use (CHMP) of the European Medicines Agency (EMA) issued a positive opinion recommending marketing authorization for UPLIZNA in adult patients with neuromyelitis optica spectrum disorder (NMOSD) who are anti-aquaporin-4 immunoglobulin G seropositive (AQP4-IgG+). The Company expects to launch UPLIZNA in Europe in 2022, beginning with Germany in the second quarter, as well as other international markets in the coming years.

- **Presented Final Results from KRYSTEXXA PROTECT Trial at Key Medical Meeting:** Final results from the PROTECT open-label trial evaluating KRYSTEXXA to improve management of uncontrolled gout in kidney transplant patients were presented at the American Society of Nephrology (ASN) Kidney Week in November. The data demonstrated that 89% (16 of 18 patients) achieved the primary endpoint at Month 6. The results are encouraging with respect to the ability of KRYSTEXXA to treat uncontrolled gout without compromising kidney function in this very sensitive transplant population.
- **Presented New TEPEZZA Data at Key Medical Meetings:** In February, multiple new data were presented at the 48th Annual Meeting of the North American Neuro-Ophthalmology Society (NANOS 2022), including new data from a post-marketing safety analysis of hearing-related events associated with TEPEZZA that showed rates were comparable to what was seen in the OPTIC Phase 3 and OPTIC-X open-label extension trials. In November, new TEPEZZA real-world data were presented at the American Academy of Ophthalmology Annual Meeting (AAO 2021). The data showed that over 90% of TEPEZZA patients completed all eight infusions, indicating a high level of adherence to TEPEZZA in clinical practice.
- **New TEPEZZA Chronic TED Data Published:** In January, new data from an independent physician case study of six chronic thyroid eye disease (TED) patients who showed benefit after treatment with TEPEZZA were published in *Eye*, the official journal for the Royal College of Ophthalmologists. The case study adds to the growing body of evidence supporting the use of TEPEZZA in chronic TED patients, with nearly 60 chronic TED patients across multiple case studies who have demonstrated benefit.
- **New UPLIZNA Data Published and Presented at Medical Meetings:** New UPLIZNA data from the Phase 3 trial were presented at NANOS 2022 in February, showing treatment with UPLIZNA effectively reduced the severity of attacks in patients with NMOSD. In November, an analysis of UPLIZNA data from the Phase 3 trial was published in *Multiple Sclerosis and Related Disorders* showing that prior rituximab exposure did not impact the efficacy of UPLIZNA, and that UPLIZNA demonstrated comparable efficacy to trial participants without prior exposure to rituximab. Notably, all seven participants who had pre-study attacks despite rituximab use did not experience any attacks after being treated with UPLIZNA. In October, an analysis of data from the Phase 3 trial was published in the *Multiple Sclerosis Journal* highlighting a sustained effect on attack risk in people with NMOSD who were treated with UPLIZNA for four or more years. Multiple new data were also presented at the virtual 37th Congress of the European Committee for Treatment and Research in Multiple Sclerosis (ECTRIMS) in October, including new data showing a link between the depth of b-cell depletion in the blood and long-term clinical outcomes.
- Initiated Enrollment in Four Clinical Trials:
  - In November, the first patient enrolled in a pivotal Phase 2b trial to evaluate HZN-825 in patients with diffuse cutaneous systemic sclerosis, a subset of systemic sclerosis (also known as scleroderma). Systemic sclerosis is a rare, chronic, autoimmune disease marked by fibrosis or skin thickening and can lead to internal organ damage.
  - In November, the first patient enrolled in a Phase 1 exploratory trial to evaluate TEPEZZA in patients with diffuse cutaneous systemic sclerosis.

- In January, the first patient enrolled in a pivotal Phase 2b trial to evaluate HZN-825 in patients with idiopathic pulmonary fibrosis (IPF), the most common form of interstitial lung disease. IPF is a rare, progressive lung disease caused by inflammation and fibrosis, or scarring, of the lungs.
- In February, the first patient enrolled in a Phase 3 trial in Japan to evaluate TEPEZZA in patients with moderate-to-severe active TED, a serious, progressive and potentially vision-threatening rare autoimmune disease. TEPEZZA has not been approved for commercial use in Japan.

- **Expanding East Coast Hub Following Viela Bio Acquisition:** In January, the Company entered into an agreement to lease a new 192,000-square-foot, state-of-the-art facility under construction in Rockville, Maryland that will serve as the Company's primary East Coast research and development and technical operations hub. The Company is significantly expanding and consolidating its East Coast footprint with the new facility, nearly quadrupling its current Maryland footprint acquired in the acquisition of Viela and anticipates adding key R&D talent to support its growing research and development capabilities and expanded pipeline.
- **Sean Clayton Appointed as General Counsel:** In February, the Company named Sean Clayton as executive vice president and general counsel. Mr. Clayton brings nearly 20 years of legal experience and was previously a partner at Cooley LLP where he represented public and private biotechnology companies in general corporate matters and securities laws, as well as a wide range of transactions, including public and private financings. Mr. Clayton led the Cooley team that represented Horizon in its initial public offering in 2011 and has advised Horizon's management team and board of directors on corporate and transactional matters since that time.
- **Continued to Demonstrate Gender and Ethnicity Pay Equity:** A second study conducted by Aon, a leading compensation consulting firm, showed that Horizon continues to demonstrate both gender and ethnicity pay equity. This study was a follow-on study to the gender and ethnicity pay equity study Aon conducted in 2019. The Company maintained its gender and ethnicity pay equity after having grown significantly in the two years since the first study, as well as having completed the acquisition of Viela, which included the addition of a significant number of employees.
- **Received Continued Recognition as a Top Workplace:** In 2021, the Company received 15 workplace-related recognitions, including six in the fourth quarter, reflecting the high level of engagement of its employees. Horizon was named to the following lists in the fourth quarter:
  - Newsweek's inaugural Most Loved Workplaces;
  - Great Place to Work's 2021 Best Workplaces for Parents;
  - *Chicago Tribune* Top Workplaces 2021;
  - National Association for Business Resources' 2021 Best and Brightest Companies to Work For in the Nation;
  - San Francisco Bay Area's 2021 Best and Brightest Companies to Work For; and
  - Dave Thomas Foundation for Adoption's Top 100 Best Adoption-Friendly Workplaces.

Key Clinical Development Programs

- **Daxdilimab (HZN-7734)**, an anti-ILT7 human monoclonal antibody that depletes certain dendritic cells. Depleting these cells may interrupt the cycle of inflammation that causes tissue damage in diseases such as lupus, and a variety of other autoimmune conditions.
    - **Systemic Lupus Erythematosus (SLE) Trial:** Phase 2 randomized, placebo-controlled trial underway to evaluate daxdilimab in patients with SLE, a disease in which the body's immune system attacks its own tissues and organs.
    - **Alopecia Areata Trial:** Phase 2 trial to evaluate daxdilimab in patients with alopecia areata, an autoimmune disorder characterized by nonscarring hair loss, expected to initiate in the second quarter of 2022.
    - **Discoid Lupus Erythematosus (DLE) Trial:** Phase 2 trial to evaluate daxdilimab in patients with DLE, a rare, chronic, inflammatory skin condition characterized by lesions that result in scarring, expected to initiate by mid-year 2022.
    - **Lupus Nephritis Trial:** Phase 2 trial to evaluate daxdilimab in patients with lupus nephritis, a rare, autoimmune and inflammatory condition of the kidney, expected to initiate in the third quarter of 2022.
    - **Dermatomyositis Trial:** Phase 2 trial to evaluate daxdilimab in patients with dermatomyositis, a rare, autoimmune disorder characterized by rashes, debilitating muscle weakness and interstitial lung disease, expected to initiate in the fourth quarter of 2022.
- **Dazodalibep (HZN-4920)**, a CD40 ligand antagonist that blocks T cell interaction with CD40-expressing B cells, disrupting the overactivation of the CD40 ligand co-stimulatory pathway. Several autoimmune diseases are associated with the overactivation of this pathway.
    - **Sjögren's Syndrome Trial:** Phase 2b randomized, placebo-controlled trial underway to evaluate dazodalibep in patients with Sjögren's syndrome, a chronic, systemic autoimmune condition that impacts exocrine glands, including the salivary and tear glands.
    - **Rheumatoid Arthritis Trial:** Phase 2 randomized, placebo-controlled trial underway to evaluate dazodalibep in patients with rheumatoid arthritis.
    - **Kidney Transplant Rejection Trial:** Phase 2 open-label trial underway to evaluate dazodalibep in kidney transplant rejection patients.
    - **Focal Segmental Glomerulosclerosis (FSGS) Trial:** Phase 2 trial to evaluate dazodalibep in patients with FSGS, a rare kidney disorder characterized by scarring of glomeruli, expected to initiate in the fourth quarter of 2022.
- **HZN-825**, an oral lysophosphatidic acid receptor 1 ($LPAR_1$) antagonist that prevents gene activation.
    - **Diffuse Cutaneous Systemic Sclerosis Trial:** Pivotal Phase 2b trial initiated in November 2021 to evaluate HZN-825 in diffuse cutaneous systemic sclerosis.
    - **Idiopathic Pulmonary Fibrosis Trial:** Pivotal Phase 2b trial initiated in January 2022 to evaluate HZN-825 in idiopathic pulmonary fibrosis, the most common form of interstitial lung disease.

- **UPLIZNA**, an anti-CD19 humanized monoclonal antibody that depletes B cells, including the pathogenic cells that produce autoantibodies.
    - **Myasthenia Gravis Trial:** Phase 3 randomized, placebo-controlled trial underway to evaluate UPLIZNA in patients with myasthenia gravis, a chronic, rare, autoimmune neuromuscular disease that affects voluntary muscles, especially those that control the eyes, mouth, throat and limbs.
    - **IgG4-Related Disease Trial:** Phase 3 randomized, placebo-controlled trial underway to evaluate UPLIZNA in patients with IgG4-related disease, which is a group of disorders marked by tumor-like swelling and fibrosis of affected organs, such as the pancreas, salivary glands and kidneys.
- **TEPEZZA**, an insulin-like growth factor type 1 receptor (IGF-1R) antagonist monoclonal antibody.
    - **Chronic TED Trial:** Phase 4 randomized, placebo-controlled trial underway to evaluate TEPEZZA in chronic TED.
    - **TED in Japan (OPTIC-J) Trial:** Phase 3 randomized, placebo-controlled trial in Japan initiated in February 2022 to evaluate TEPEZZA in patients with moderate-to-severe active TED.
    - **Subcutaneous (SC) Administration Trial:** Phase 1b trial to explore the pharmacokinetics, safety, tolerability, efficacy, and immunogenicity of subcutaneous administration of TEPEZZA in patients with TED, expected to initiate by mid-year 2022.
    - **Diffuse Cutaneous Systemic Sclerosis Exploratory Trial:** Phase 1 exploratory trial initiated in November 2021 to evaluate TEPEZZA in diffuse cutaneous systemic sclerosis.
- **KRYSTEXXA,** a recombinant uricase enzyme that converts urate into a water-soluble liquid, allantoin, that can be easily excreted from the body.
    - **Shorter Infusion Duration Trial:** Phase 4 open-label trial underway to evaluate the impact of administering KRYSTEXXA plus methotrexate over a shorter infusion duration in patients with uncontrolled gout.
    - **Monthly Dosing Trial:** Phase 4 open-label trial underway to evaluate monthly dosing of KRYSTEXXA plus methotrexate in patients with uncontrolled gout.
    - **Retreatment Trial:** Phase 4 open-label trial underway to evaluate KRYSTEXXA plus methotrexate in patients who were not complete responders to KRYSTEXXA monotherapy.
- **HZN-1116,** a fully human monoclonal antibody that binds and neutralizes the function of the FLT3-ligand, thereby reducing both conventional and plasmacytoid dendritic cells.
    - **Autoimmune Disease Trial:** Phase 1 trial underway to evaluate HZN-1116 in patients with autoimmune diseases.

Fourth-Quarter Financial Results

Note: For additional detail and reconciliation of non-GAAP financial measures to the most directly comparable GAAP financial measures, please refer to the tables at the end of this release.

- **Net Sales:** Fourth-quarter 2021 net sales were $1.014 billion, an increase of 36% compared to the fourth quarter of 2020.
- **Gross Profit:** Under U.S. GAAP, the fourth-quarter 2021 gross profit ratio was 76.2% compared to 78.2% in the fourth quarter of 2020. The non-GAAP gross profit ratio in the fourth quarter of 2021 was 86.5% compared to 87.1% in the fourth quarter of 2020.
- **Operating Expenses:** R&D expenses were 13.9% of net sales and SG&A expenses were 39.3% of net sales. Non-GAAP R&D expenses were 11.4% of net sales and non-GAAP SG&A expenses were 34.0% of net sales. Fourth-quarter 2021 GAAP and non-GAAP R&D expenses include $36.2 million of upfront and milestone payments primarily related to the collaboration agreement with Alpine. Beginning in the fourth quarter of 2021, the Company no longer excludes upfront and milestone payments related to license and collaboration agreements from non-GAAP financial measures and line item components.
- **Income Tax Expense:** On a GAAP basis in the fourth quarter of 2021, income tax expense was $37.9 million. Fourth-quarter non-GAAP income tax expense was $61.4 million.
- **Net Income:** In the fourth-quarter of 2021, net income on a GAAP and non-GAAP basis was $173.2 million and $334.0 million, respectively.
- **Adjusted EBITDA:** Fourth-quarter 2021 adjusted EBITDA was $416.0 million and includes $36.2 million of upfront and milestone payments primarily related to the collaboration agreement with Alpine. Beginning in the fourth quarter of 2021, the Company no longer excludes upfront and milestone payments related to license and collaboration agreements from non-GAAP financial measures.
- **Earnings per Share:** On a GAAP basis, diluted earnings per share in the fourth quarter of 2021 and 2020 were $0.73 and $0.82, respectively. Non-GAAP diluted earnings per share in the fourth quarter of 2021 and 2020 were $1.41 and $1.17, respectively. Weighted average shares outstanding used for calculating GAAP and non-GAAP diluted earnings per share in the fourth quarter of 2021 were 236.8 million.

Fourth-Quarter Segment Results

Management uses net sales and segment operating income to evaluate the performance of the Company's two segments, the orphan segment and the inflammation segment. While segment operating income contains certain adjustments to the directly comparable GAAP figures in the Company's consolidated financial results, it is considered to be prepared in accordance with GAAP for purposes of presenting the Company's segment operating results. The Company continues to exclude upfront and milestone payments related to license and collaboration agreements from its segment operating income.

Orphan Segment

(in millions except for percentages)	Q4 21	Q4 20	% Change	FY 21	FY 20	% Change
TEPEZZA®	$589.6	$343.7	72	$1,661.3	$ 820.0	103
KRYSTEXXA®	170.3	128.9	32	565.5	405.9	39
RAVICTI®(1)	74.4	70.2	6	291.9	261.6	12
PROCYSBI®	47.4	47.3	0	189.9	170.1	12
ACTIMMUNE®	30.6	35.7	(14)	117.2	118.8	(1)
UPLIZNA®(2)	25.8	—	NM	60.8	—	NM
BUPHENYL®(1)	2.1	2.2	(4)	7.9	10.6	(26)
QUINSAIR™	0.3	0.2	48	1.0	0.7	47
Orphan Net Sales	**$940.5**	**$628.2**	**50**	**$2,895.5**	**$1,787.7**	**62**
Orphan Segment Operating Income	**$420.8**	**$303.0**	**39**	**$1,219.3**	**$ 783.6**	**56**

(1) On Oct. 27, 2020, the Company sold its rights to develop and commercialize RAVICTI and BUPHENYL in Japan to Medical Need Europe AB, part of the Immedica Group. The Company has retained the rights to RAVICTI and BUPHENYL in North America.
(2) UPLIZNA was acquired on March 15, 2021. Fourth-quarter 2021 UPLIZNA net sales included $3.7 million of revenue from Mitsubishi Tanabe Pharma Corporation, the Company's Japanese partner.

- Fourth-quarter 2021 net sales of the orphan segment, the Company's strategic growth segment, were $940.5 million, an increase of 50% over the prior year's quarter, driven by the strong performance of TEPEZZA, KRYSTEXXA and RAVICTI. The orphan segment represented 93% of total company fourth-quarter net sales.
- KRYSTEXXA fourth-quarter 2021 net sales increased 32% year-over-year driven by increased adoption of KRYSTEXXA plus immunomodulation, which is now approaching 50%. In addition, the Company continues to see strong uptake of KRYSTEXXA from both rheumatologists and nephrologists.
- Fourth-quarter 2021 orphan segment operating income was $420.8 million, which includes additional investment associated with TEPEZZA, UPLIZNA and the Company's pipeline programs.

Inflammation Segment

(in millions except for percentages)	Q4 21	Q4 20	% Change	FY 21	FY 20	% Change
PENNSAID 2%®	$48.9	$ 51.1	(4)	$191.6	$178.0	8
RAYOS®	13.3	21.0	(37)	56.9	71.8	(21)
DUEXIS®(1)	11.5	38.3	(70)	74.0	125.3	(41)
VIMOVO®(2)	0.3	6.7	(96)	8.4	37.6	(78)
Inflammation Net Sales	**$74.0**	**$117.1**	**(37)**	**$330.9**	**$412.7**	**(20)**
Inflammation Segment Operating Income	**$32.6**	**$ 66.9**	**(51)**	**$156.2**	**$212.1**	**(26)**

(1) On Aug. 4, 2021, Alkem Laboratories, Inc. initiated an at-risk launch of generic DUEXIS in the United States.
(2) On Feb. 27, 2020, Dr. Reddy's Laboratory initiated an at-risk launch of generic VIMOVO in the United States.

- Fourth-quarter 2021 net sales of the inflammation segment were $74.0 million, and segment operating income was $32.6 million.

Cash Flow Statement and Balance Sheet Highlights

- In the fourth-quarter of 2021, operating cash flow on a GAAP and non-GAAP basis was $538.6 million and $554.4 million, respectively. Full-year 2021 operating cash flow on a GAAP and non-GAAP basis was $1.035 billion and $1.190 billion, respectively.
- As of Dec. 31, 2021, the Company had cash and cash equivalents of $1.580 billion.
- As of Dec. 31, 2021, the total principal amount of debt outstanding was $2.606 billion.

2022 Guidance

The Company expects full-year 2022 net sales to range between $3.9 billion and $4.0 billion, representing 22% growth at the midpoint. The Company expects TEPEZZA full-year 2022 net sales percentage growth in the mid-30s and KRYSTEXXA full-year 2022 net sales growth of more than 20%. Full-year 2022 adjusted EBITDA is expected to range between $1.63 billion and $1.70 billion, representing 30% growth and 230 basis points of margin expansion at the midpoint.

Webcast

At 8 a.m. EST / 1 p.m. IST today, the Company will host a live webcast to review its financial and operating results and provide a general business update. The live webcast and a replay may be accessed at http://ir.horizontherapeutics.com. Please connect to the Company's website at least 15 minutes prior to the live webcast to ensure adequate time for any software download that may be needed to access the webcast. A replay of the webcast will be available approximately two hours after the live webcast.

About Horizon

Horizon is 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. For more information on how we go to incredible lengths to impact lives, visit www.horizontherapeutics.com and follow us on Twitter, LinkedIn, Instagram and Facebook.

Note Regarding Use of Non-GAAP Financial Measures

EBITDA, or earnings before interest, taxes, depreciation and amortization, and adjusted EBITDA are used and provided by Horizon as non-GAAP financial measures. Horizon provides certain other financial measures such as non-GAAP net income, non-GAAP diluted earnings per share, non-GAAP gross profit and gross profit ratio, non-GAAP operating expenses, non-GAAP operating income, non-GAAP tax (benefit) and tax rate and non-GAAP operating cash flow, each of which include adjustments to GAAP figures. These non-GAAP measures are intended to provide additional information on Horizon's performance, operations, expenses, profitability and cash flows. Adjustments to Horizons GAAP figures as well as EBITDA exclude acquisition and/or divestiture-related costs, manufacturing plant start-up costs, drug substance harmonization costs, fees related to refinancing activities, restructuring and

realignment costs and litigation settlements, as well as non-cash items such as share-based compensation, inventory step-up expense, depreciation and amortization, non-cash interest expense, long-lived assets impairment charges, loss on debt extinguishments, gain (loss) on sale of assets, gain 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. Horizon maintains an established non-GAAP cost policy that guides the determination of what costs will be excluded in non-GAAP measures. Horizon believes that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of Horizon's financial and operating performance. The non-GAAP financial measures are included with the intent of providing investors with a more complete understanding of the Company's historical and expected financial results and trends and to facilitate comparisons between periods and with respect to projected information. In addition, these non-GAAP financial measures are among the indicators Horizon's management uses for planning and forecasting purposes and measuring the Company's 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 the Company may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies. Horizon has not provided a reconciliation of its full-year 2022 adjusted EBITDA and associated margin expansion outlook to an expected net income (loss) outlook because certain items such as acquisition/divestiture-related expenses and share-based compensation that are a component of net income (loss) cannot be reasonably projected due to the significant impact of changes in Horizon's stock price, the variability associated with the size or timing of acquisitions/divestitures and other factors. These components of net income (loss) could significantly impact Horizon's actual net income (loss).

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to Horizon's full-year 2022 net sales, adjusted EBITDA and margin expansion guidance; expected financial performance and operating results in future periods, including potential growth in net sales of certain of Horizon's medicines; development, manufacturing and commercialization plans; expected timing of clinical trials, availability of clinical data and regulatory submissions; potential market opportunity for and benefits of Horizon's medicines and medicine candidates and business and other statements that are not historical facts. These forward-looking statements are based on Horizon's current expectations and inherently involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such forward-looking statements as a result of these risks and uncertainties, which include, without limitation, risks that Horizon's actual future financial and operating results may differ from its expectations or goals; Horizon's ability to grow net sales from existing medicines; impacts of the COVID-19 pandemic and actions taken to slow its spread, including impacts on supplies and net sales of Horizon's medicines and potential delays in clinical trials; the fact that Horizon's full-year 2022 net sales, adjusted EBITDA and TEPEZZA net sales guidance and the expected timing of certain TEPEZZA clinical trials assume that future committed manufacturing slots for TEPEZZA are not cancelled and are run successfully, which could be impacted by additional government-mandated COVID-19 vaccine production orders and other risks associated with the manufacture of biologic medicines; risks associated with acquisitions, such as the risk that the businesses will not be integrated successfully, that such integration may be more difficult, time-consuming or costly than expected or that the expected benefits of the transaction will not occur; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; risks relating to Horizon's ability to successfully implement its business strategies, including its manufacturing and global expansion strategy; risks inherent in developing novel medicine candidates and existing medicines for new indications; risks associated with regulatory approvals; risks in the ability to recruit, train and retain qualified personnel; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information.

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Horizon Therapeutics plc
Condensed Consolidated Statements of Operations
(in thousands, except share and per share data)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
	(Unaudited)			
Net sales	$ 1,014,464	$ 745,314	$ 3,226,410	$ 2,200,429
Cost of goods sold	241,509	162,289	794,512	532,695
Gross profit	**772,955**	**583,025**	**2,431,898**	**1,667,734**
OPERATING EXPENSES:				
Research and development	140,914	70,881	431,990	209,364
Selling, general and administrative	398,954	276,956	1,446,410	973,227
Impairment of long-lived asset	—	—	12,371	—
Gain on sale of assets	—	(4,883)	(2,000)	(4,883)
Total operating expenses	**539,868**	**342,954**	**1,888,771**	**1,177,708**
Operating income	**233,087**	**240,071**	**543,127**	**490,026**
OTHER EXPENSE, NET:				
Interest expense, net	(22,045)	(11,516)	(81,063)	(59,616)
Loss on debt extinguishment	—	—	—	(31,856)
Foreign exchange gain (loss)	335	(603)	(1,028)	(297)
Other (expense) income, net	(322)	1,597	1,791	3,388
Total other expense, net	**(22,032)**	**(10,522)**	**(80,300)**	**(88,381)**
Income before expense (benefit) for income taxes	**211,055**	**229,549**	**462,827**	**401,645**
Expense (benefit) for income taxes	37,873	38,992	(71,664)	11,849
Net income	**$ 173,182**	**$ 190,557**	**$ 534,491**	**$ 389,796**
Net income per ordinary share - basic	$ 0.76	$ 0.86	$ 2.37	$ 1.91
Weighted average ordinary shares outstanding - basic	227,028,298	220,929,626	225,551,410	203,967,246
Net income per ordinary share - diluted	$ 0.73	$ 0.82	$ 2.27	$ 1.81
Weighted average ordinary shares outstanding - diluted	236,806,923	232,886,942	235,680,483	215,308,768

Horizon Therapeutics plc
Condensed Consolidated Balance Sheets
(in thousands, except share data)

	As of	
	December 31, 2021	December 31, 2020
ASSETS		
CURRENT ASSETS:		
Cash and cash equivalents	$ 1,580,317	$ 2,079,906
Restricted cash	3,839	3,573
Accounts receivable, net	632,775	659,701
Inventories, net	225,730	75,283
Prepaid expenses and other current assets	357,106	251,945
Total current assets	**2,799,767**	**3,070,408**
Property, plant and equipment, net	292,298	189,037
Developed technology and other intangible assets, net	2,960,118	1,782,962
In-process research and development	880,000	—
Goodwill	1,066,709	413,669
Deferred tax assets, net	538,098	560,841
Other assets	140,738	55,699
Total assets	**$ 8,677,728**	**$ 6,072,616**
LIABILITIES AND SHAREHOLDERS' EQUITY		
CURRENT LIABILITIES:		
Accounts payable	$ 30,125	$ 37,710
Accrued expenses and other current liabilities	523,015	485,567
Accrued trade discounts and rebates	317,431	352,463
Long-term debt - current portion	16,000	—
Total current liabilities	**886,571**	**875,740**
LONG-TERM LIABILITIES:		
Long-term debt, net	2,555,233	1,003,379
Deferred tax liabilities, net	390,455	66,474
Other long-term liabilities	173,076	101,672
Total long-term liabilities	**3,118,764**	**1,171,525**
COMMITMENTS AND CONTINGENCIES		
SHAREHOLDERS' EQUITY:		
Ordinary shares, $0.0001 nominal value; 600,000,000 shares authorized at December 31, 2021 and December 31, 2020; 227,760,936 and 221,721,674 shares issued at December 31, 2021 and December 31, 2020, respectively; and 227,376,570 and 221,337,308 shares outstanding at December 31, 2021 and December 31, 2020, respectively	23	22
Treasury stock, 384,366 ordinary shares at December 31, 2021 and December 31, 2020	(4,585)	(4,585)
Additional paid-in capital	4,373,337	4,245,945
Accumulated other comprehensive loss	(14,987)	(145)
Retained earnings (accumulated deficit)	318,605	(215,886)
Total shareholders' equity	**4,672,393**	**4,025,351**
Total liabilities and shareholders' equity	**$ 8,677,728**	**$ 6,072,616**

Horizon Therapeutics plc
Condensed Consolidated Statements of Cash Flows
(in thousands)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
	(Unaudited)			
CASH FLOWS FROM OPERATING ACTIVITIES:				
Net income	$ 173,182	$ 190,557	$ 534,491	$ 389,796
Adjustments to reconcile net income to net cash provided by operating activities:				
Depreciation and amortization expense	96,535	69,545	353,751	279,451
Equity-settled share-based compensation	48,692	32,793	219,086	146,627
Acquired in-process research and development expense	30,072	30,000	76,572	77,517
Loss on debt extinguishment	—	—	—	31,856
Impairment of long-lived asset	—	—	12,371	—
Amortization of debt discount and deferred financing costs	1,449	615	5,189	12,640
Gain on sale of assets	—	(4,883)	(2,000)	(4,883)
Deferred income taxes	46,918	(25,412)	(101,016)	(33,453)
Foreign exchange and other adjustments	61	728	(1,433)	1,812
Changes in operating assets and liabilities:				
Accounts receivable	142,572	46,219	34,796	(251,173)
Inventories	11,761	1,878	1,267	(21,451)
Prepaid expenses and other current assets	(27,403)	(31,562)	(88,193)	(114,788)
Accounts payable	(19,837)	(1,694)	(12,197)	16,015
Accrued trade discounts and rebates	13,909	29,560	(36,929)	(113,991)
Accrued expenses and other current liabilities	16,242	57,791	50,622	114,621
Other non-current assets and liabilities	4,404	13,682	(11,106)	25,092
Net cash provided by operating activities	**538,557**	**409,817**	**1,035,271**	**555,688**
CASH FLOWS FROM INVESTING ACTIVITIES:				
Purchases of property, plant and equipment	(16,901)	(36,453)	(76,596)	(169,852)
Payments for long-term investments, net	(14,871)	(4,377)	(24,668)	(13,314)
Payments for acquisitions, net of cash acquired	(2,000)	—	(2,845,275)	(262,305)
Change in escrow deposit for property purchase	—	—	—	6,000
Proceeds from sale of assets	—	5,400	2,000	5,400
Payments related to license agreements	(3,072)	(30,000)	(49,572)	(30,000)
Net cash used in investing activities	**(36,844)**	**(65,430)**	**(2,994,111)**	**(464,071)**
CASH FLOWS FROM FINANCING ACTIVITIES:				
Repayment of senior notes	—	—	—	(1,739)
Net proceeds from the issuance of ordinary shares	—	(209)	—	919,786
Net proceeds from term loans	—	—	1,574,993	—
Repayment of term loans	(4,000)	—	(12,000)	—
Proceeds from the issuance of ordinary shares in conjunction with ESPP program	11,046	8,189	22,528	16,168
Proceeds from the issuance of ordinary shares in connection with stock option exercises	10,553	2,870	50,566	36,869
Payment of employee withholding taxes relating to share-based awards	(7,887)	(6,753)	(165,964)	(66,505)
Net cash provided by financing activities	**9,712**	**4,097**	**1,470,123**	**904,579**
Effect of foreign exchange rate changes on cash, cash equivalents and restricted cash	**345**	**6,019**	**(10,606)**	**7,244**
Net increase (decrease) in cash, cash equivalents and restricted cash	511,770	354,503	(499,323)	1,003,440
Cash, cash equivalents and restricted cash, beginning of the period(1)	1,072,386	1,728,976	2,083,479	1,080,039
Cash, cash equivalents and restricted cash, end of the period(1)	**$1,584,156**	**$2,083,479**	**$ 1,584,156**	**$2,083,479**

(1) Amounts include restricted cash balance in accordance with ASU No. 2016-18. Cash and cash equivalents excluding restricted cash are shown on the balance sheet.

Horizon Therapeutics plc
GAAP to Non-GAAP Reconciliations
Net Income and Earnings Per Share (Unaudited)
(in thousands, except share and per share data)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
GAAP net income	**$ 173,182**	**$ 190,557**	**$ 534,491**	**$ 389,796**
Non-GAAP adjustments:				
Acquisition/divestiture-related costs	7,763	1,900	95,929	49,196
Gain on equity security investments	(1,257)	—	(1,257)	—
Restructuring and realignment costs	18,606	(141)	26,309	(141)
Manufacturing plant start-up costs	1,910	—	3,622	—
Amortization and step-up:				
Intangible amortization expense	91,017	64,471	336,277	255,148
Inventory step-up expense	10,658	—	27,572	—
Amortization of debt discount and deferred financing costs	1,449	615	5,189	12,640
Impairment of long-lived assets	—	641	12,371	1,713
Gain on sale of assets	—	(4,883)	(2,000)	(4,883)
Share-based compensation	48,692	32,793	219,086	146,627
Depreciation	5,519	5,074	17,475	24,303
Litigation settlement	—	—	5,000	—
Fees related to refinancing activities	—	—	—	54
Loss on debt extinguishment	—	—	—	31,856
Drug substance harmonization costs	—	59	—	542
Total of pre-tax non-GAAP adjustments	**184,357**	**100,529**	**745,573**	**517,055**
Income tax effect of pre-tax non-GAAP adjustments	(27,889)	(18,881)	(169,554)	(98,628)
Other non-GAAP income tax adjustments	4,326	—	(20,800)	20,541
Total of non-GAAP adjustments	**160,794**	**81,648**	**555,219**	**438,968**
Non-GAAP net income	**$ 333,976**	**$ 272,205**	**$ 1,089,710**	**$ 828,764**
Non-GAAP Earnings Per Share:				
Weighted average ordinary shares - Basic	**227,028,298**	**220,929,626**	**225,551,410**	**203,967,246**
Non-GAAP Earnings Per Share - Basic:				
GAAP earnings per share - Basic	**$ 0.76**	**$ 0.86**	**$ 2.37**	**$ 1.91**
Non-GAAP adjustments	0.71	0.37	2.46	2.15
Non-GAAP earnings per share - Basic	**$ 1.47**	**$ 1.23**	**$ 4.83**	**$ 4.06**
Non-GAAP net income	**$ 333,976**	**$ 272,205**	**$ 1,089,710**	**$ 828,764**
Effect of assumed exchange of Exchangeable Senior Notes, net of tax	—	—	—	3,789
Numerator - non-GAAP net income	**$ 333,976**	**$ 272,205**	**$ 1,089,710**	**$ 832,553**
Weighted average ordinary shares - Diluted				
Weighted average ordinary shares - Basic	227,028,298	220,929,626	225,551,410	203,967,246
Ordinary share equivalents	9,778,625	11,957,316	10,129,073	18,203,897
Denominator - weighted average ordinary shares - Diluted	**236,806,923**	**232,886,942**	**235,680,483**	**222,171,143**
Non-GAAP Earnings Per Share - Diluted				
GAAP earnings per share - Diluted	**$ 0.73**	**$ 0.82**	**$ 2.27**	**$ 1.81**
Non-GAAP adjustments	0.68	0.35	2.35	1.94
Non-GAAP earnings per share - Diluted	**$ 1.41**	**$ 1.17**	**$ 4.62**	**$ 3.75**

Horizon Therapeutics plc
GAAP to Non-GAAP Reconciliations
EBITDA and Adjusted EBITDA (Unaudited)
(in thousands)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
GAAP net income	**$173,182**	**$190,557**	**$ 534,491**	**$389,796**
Depreciation	5,519	5,074	17,475	24,303
Amortization and step-up:				
Intangible amortization expense	91,017	64,471	336,277	255,148
Inventory step-up expense	10,658	—	27,572	—
Interest expense, net (including amortization of debt discount and deferred financing costs)	22,045	11,516	81,063	59,616
Expense (benefit) for income taxes	37,873	38,992	(71,664)	11,849
EBITDA	**$340,294**	**$310,610**	**$ 925,214**	**$740,712**
Other non-GAAP adjustments:				
Acquisition/divestiture-related costs	7,763	1,900	95,929	49,196
Gain on equity security investments	(1,257)	—	(1,257)	—
Restructuring and realignment costs	18,606	(141)	26,309	(141)
Manufacturing plant start-up costs	1,910	—	3,622	—
Impairment of long-lived assets	—	641	12,371	1,713
Gain on sale of assets	—	(4,883)	(2,000)	(4,883)
Share-based compensation	48,692	32,793	219,086	146,627
Litigation settlement	—	—	5,000	—
Fees related to refinancing activities	—	—	—	54
Loss on debt extinguishment	—	—	—	31,856
Drug substance harmonization costs	—	59	—	542
Total of other non-GAAP adjustments	**75,714**	**30,369**	**359,060**	**224,964**
Adjusted EBITDA	**$416,008**	**$340,979**	**$1,284,274**	**$965,676**

Horizon Therapeutics plc
GAAP to Non-GAAP Reconciliations
Operating Income (Unaudited)
(in thousands)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
GAAP operating income	**$233,087**	**$240,071**	**$ 543,127**	**$490,026**
Non-GAAP adjustments:				
Acquisition/divestiture-related costs	9,019	1,816	98,260	49,232
Gain on equity security investments	(1,257)	—	(1,257)	—
Restructuring and realignment costs	18,606	(141)	26,309	(141)
Manufacturing plant start-up costs	1,910	—	3,622	—
Amortization and step-up:				
Intangible amortization expense	91,017	64,471	336,277	255,148
Inventory step-up expense	10,658	—	27,572	—
Impairment of long-lived assets	—	641	12,371	1,713
Gain on sale of assets	—	(4,883)	(2,000)	(4,883)
Share-based compensation	48,692	32,793	219,086	146,627
Depreciation	5,520	5,074	17,475	24,303
Litigation settlement	—	—	5,000	—
Fees related to refinancing activities	—	—	—	54
Drug substance harmonization costs	—	59	—	542
Total of non-GAAP adjustments	**184,165**	**99,830**	**742,715**	**472,595**
Non-GAAP operating income	**$417,252**	**$339,901**	**$1,285,842**	**$962,621**
Foreign exchange gain (loss)	335	(603)	(1,028)	(297)
Other (expense) income, net	(1,579)	1,681	(540)	3,352
Adjusted EBITDA	**$416,008**	**$340,979**	**$1,284,274**	**$965,676**

Horizon Therapeutics plc
GAAP to Non-GAAP Reconciliations
Gross Profit and Operating Cash Flow (Unaudited)
(in thousands, except percentages)

	Three Months Ended December 31,		Twelve Months Ended December 31,	
	2021	2020	2021	2020
Non-GAAP Gross Profit:				
GAAP gross profit	**$772,955**	**$583,025**	**$2,431,898**	**$1,667,734**
Non-GAAP gross profit adjustments:				
Acquisition/divestiture-related costs	1,600	—	1,525	—
Intangible amortization expense	90,466	64,267	334,848	254,337
Inventory step-up expense	10,658	—	27,572	—
Share-based compensation	1,824	1,660	8,699	7,203
Depreciation	55	(96)	282	339
Drug substance harmonization costs	—	59	—	542
Total of Non-GAAP adjustments	**104,603**	**65,890**	**372,926**	**262,421**
Non-GAAP gross profit	**$877,558**	**$648,915**	**$2,804,824**	**$1,930,155**
GAAP gross profit %	76.2%	78.2%	75.4%	75.8%
Non-GAAP gross profit %	86.5%	87.1%	86.9%	87.7%
GAAP cash provided by operating activities	**$538,557**	**$409,817**	**$1,035,271**	**$ 555,688**
Cash payments for acquisition/divestiture-related costs	8,376	1,084	144,449	1,164
Cash payments for restructuring and realignment costs	579	—	2,382	189
Cash payments for manufacturing start-up costs	1,857	—	2,726	—
Cash payments for litigation settlements	5,000	—	5,000	—
Cash payments drug substance harmonization costs	—	252	—	542
Cash payments relating to refinancing activities	—	—	—	73
Non-GAAP operating cash flow	**$554,369**	**$411,153**	**$1,189,828**	**$ 557,656**

Horizon Therapeutics plc
GAAP to Non-GAAP Tax Rate Reconciliation (Unaudited)
(in millions, except percentages and per share amounts)

	Q4 2021				
	Pre-tax Net Income	Income Tax (Benefit) Expense	Tax Rate	Net Income	Diluted Earnings Per Share
As reported - GAAP	$ 211.1	$ 37.9	17.9%	$ 173.2	$ 0.73
Non-GAAP adjustments	184.4	23.6		160.8	
Non-GAAP	**$ 395.4**	**$ 61.4**	**15.5%**	**$ 334.0**	**$ 1.41**

	Q4 2020				
	Pre-tax Net Income	Income Tax (Benefit) Expense	Tax Rate	Net Income	Diluted Earnings Per Share
As reported - GAAP	$ 229.5	$ 39.0	17.0%	$ 190.6	$ 0.82
Non-GAAP adjustments	100.5	18.9		81.6	
Non-GAAP	**$ 330.1**	**$ 57.9**	**17.5%**	**$ 272.2**	**$ 1.17**

	FY 2021				
	Pre-tax Net Income	Income Tax (Benefit) Expense	Tax Rate	Net Income	Diluted Earnings Per Share
As reported - GAAP	$ 462.8	$ (71.7)	(15.5)%	$ 534.5	$ 2.27
Non-GAAP adjustments	745.6	190.4		555.2	
Non-GAAP	**$ 1,208.4**	**$ 118.7**	**9.8%**	**$ 1,089.7**	**$ 4.62**

	FY 2020				
	Pre-tax Net Income	Income Tax (Benefit) Expense	Tax Rate	Net Income	Diluted Earnings Per Share
As reported - GAAP	$ 401.6	$ 11.8	3.0%	$ 389.8	$ 1.81
Non-GAAP adjustments	517.1	78.1		439.0	
Non-GAAP	**$ 918.7**	**$ 89.9**	**9.8%**	**$ 828.8**	**$ 3.75**

Horizon Therapeutics plc
Upfront, Progress and Milestone Payments Related to License and Collaboration Agreements
(in millions)

	Q1 2021	Q2 2021	Q3 2021	Q4 2021	FY 2021
Adjusted EBITDA	**$ 42.8**	**$320.4**	**$505.0**	**$416.0**	**$1,284.3**
Upfront, progress and milestone payments related to license and collaboration agreements included in adjusted EBITDA	3.0	46.5	4.0	36.2	89.7

	Q1 2020	Q2 2020	Q3 2020	Q4 2020	FY 2020
Adjusted EBITDA	**$107.2**	**$187.7**	**$329.8**	**$341.0**	**$ 965.7**
Upfront, progress and milestone payments related to license and collaboration agreements included in adjusted EBITDA	—	3.0	—	30.0	33.0

Beginning in the fourth quarter of 2021, following consultation with the staff of the Division of Corporation Finance of the U.S. Securities and Exchange Commission, the Company no longer excludes upfront and milestone payments related to license and collaboration agreements from its non-GAAP financial measures and its line item components, including non-GAAP R&D and SG&A expenses, adjusted EBITDA, non-GAAP net income and non-GAAP earnings per share. Prior period results have also been updated to reflect this adjustment.

Fourth-quarter 2021 upfront and milestone payments of $36.2 million primarily relate to the collaboration agreement with Alpine.

Full-year 2021 upfront and milestone payments $89.7 million relate to license and collaboration agreements with Alpine and Arrowhead Pharmaceuticals, as well as payments related to daxdilimab and HemoShear.

Fourth-quarter 2020 upfront and milestone payments of $30.0 million relate to a license agreement entered into with Halozyme.

Full-year 2020 upfront and milestone payments of $33.0 million relate to a license agreement entered into with Halozyme as well as payments to HemoShear.

Horizon Therapeutics plc
Certain Income Statement Line Items - Non-GAAP Adjusted
For the Three Months Ended Dec. 31, 2021 and Dec. 31, 2020 (Unaudited)
(in thousands)

	COGS	Research & Development	Selling, General & Administrative	Interest Expense	Other Expense, net	Income Tax Benefit (Expense)
GAAP as reported	**$(241,509)**	**$ (140,914)**	**$ (398,954)**	**$(22,045)**	**$ (322)**	**$ (37,873)**
Non-GAAP Adjustments:						
Acquisition/divestiture-related costs[1]	1,600	18,647	(12,484)	—	—	—
Gain on equity security investments[2]	—	—	—	—	(1,257)	—
Restructuring and realignment costs[3]	—	—	18,606	—	—	—
Manufacturing plant start-up costs[4]	—	—	1,910	—	—	—
Amortization and step-up:						
Intangible amortization expense[5]	90,466	—	551	—	—	—
Inventory step-up expense[6]	10,658	—	—	—	—	—
Amortization of debt discount and deferred financing costs[7]	—	—	—	1,449	—	—
Share-based compensation[8]	1,824	6,693	40,175	—	—	—
Depreciation[9]	55	150	5,314	—	—	—
Income tax effect on pre-tax non-GAAP adjustments[10]	—	—	—	—	—	(27,889)
Other non-GAAP income tax adjustments[11]	—	—	—	—	—	4,326
Total of non-GAAP adjustments [18]	**104,603**	**25,490**	**54,072**	**1,449**	**(1,257)**	**(23,563)**
Non-GAAP [18]	**$(136,906)**	**$ (115,424)**	**$ (344,882)**	**$(20,596)**	**$(1,579)**	**$ (61,436)**

Horizon Therapeutics plc
Certain Income Statement Line Items - Non-GAAP Adjusted
For the Three Months Ended December 31, 2020 (Unaudited)
(in thousands)

	COGS	Research & Development	Selling, General & Administrative	Gain on Sale of Assets	Interest Expense	Other Income, net	Income Tax Benefit (Expense)
GAAP as reported	**$(162,289)**	**$ (70,881)**	**$ (276,956)**	**$ 4,883**	**$ (11,516)**	**$1,597**	**$ (38,992)**
Non-GAAP Adjustments:							
Acquisition/divestiture-related costs[1]	—	(141)	1,957	—	—	84	—
Restructuring and realignment costs[3]	—	—	(141)	—	—	—	—
Amortization and step-up:							
Intangible amortization expense[5]	64,267	—	204	—	—	—	—
Amortization of debt discount and deferred financing costs[7]	—	—	—	—	615	—	—
Impairment of long lived assets[12]	—	—	641	—	—	—	—
Gain on sale of assets[13]	—	—	—	(4,883)	—	—	—
Share-based compensation[8]	1,660	2,592	28,541	—	—	—	—
Depreciation[9]	(96)	32	5,138	—	—	—	—
Drug substance harmonization costs[14]	59	—	—	—	—	—	—
Income tax effect on pre-tax non-GAAP adjustments[10]	—	—	—	—	—	—	(18,881)
Total of non-GAAP adjustments [18]	**65,890**	**2,483**	**36,340**	**(4,883)**	**615**	**84**	**(18,881)**
Non-GAAP [18]	**$ (96,399)**	**$ (68,398)**	**$ (240,616)**	**$ —**	**$(10,901)**	**$1,681**	**$ (57,873)**

Horizon Therapeutics plc
Certain Income Statement Line Items - Non-GAAP Adjusted
For the Twelve Months Ended Dec. 31, 2021 and Dec. 31, 2020 (Unaudited)
(in thousands)

	COGS	Research & Development	Selling, General & Administrative	Gain on Sale of Assets	Impairment of Long-lived assets	Interest Expense	Other Income (Expense), net	Income Tax Benefit (Expense)
GAAP as reported	**$(794,512)**	**$ (431,990)**	**$ (1,446,410)**	**$ 2,000**	**$ (12,371)**	**$(81,063)**	**$ 1,791**	**$ 71,664**
Non-GAAP Adjustments:								
Acquisition/divestiture-related costs(1)	1,525	18,665	76,816	—	—	—	(1,077)	—
Gain on equity security investments(2)	—	—	—	—	—	—	(1,257)	—
Restructuring and realignment costs(3)	—	—	26,309	—	—	—	—	—
Manufacturing plant start-up costs(4)	—	—	3,622	—	—	—	—	—
Amortization and step-up:								
Intangible amortization expense(5)	334,848	—	1,429	—	—	—	—	—
Inventory step-up expense(6)	27,572	—	—	—	—	—	—	—
Amortization of debt discount and deferred financing costs(7)	—	—	—	—	—	5,189	—	—
Impairment of long lived assets(12)	—	—	—	—	12,371	—	—	—
Gain on sale of assets(13)	—	—	—	(2,000)	—	—	—	—
Share-based compensation(8)	8,699	39,544	170,843	—	—	—	—	—
Depreciation(9)	282	442	16,751	—	—	—	—	—
Litigation settlement(15)	—	—	5,000	—	—	—	—	—
Income tax effect on pre-tax non-GAAP adjustments(10)	—	—	—	—	—	—	—	(169,554)
Other non-GAAP income tax adjustments(11)	—	—	—	—	—	—	—	(20,800)
Total of non-GAAP adjustments (18)	**372,926**	**58,651**	**300,770**	**(2,000)**	**12,371**	**5,189**	**(2,334)**	**(190,354)**
Non-GAAP (18)	**$(421,586)**	**$ (373,339)**	**$ (1,145,640)**	**$ —**	**$ —**	**$(75,874)**	**$ (543)**	**$(118,690)**

Horizon Therapeutics plc
Certain Income Statement Line Items - Non-GAAP Adjusted
For the Twelve Months Ended December 31, 2020 (Unaudited)
(in thousands)

	COGS	Research & Development	Selling, General & Administrative	Loss on Debt Extinguishment	Gain on Sale of Assets	Interest Expense	Other Income (Expense), net	Income Tax Benefit (Expense)
GAAP as reported	**$(532,695)**	**$ (209,364)**	**$ (973,227)**	**$ (31,856)**	**$ 4,883**	**$(59,616)**	**3,388**	**$(11,849)**
Non-GAAP Adjustments:								
Acquisition/divestiture-related costs(1)	—	47,223	2,008	—	—	—	(35)	—
Restructuring and realignment costs(3)	—	—	(141)	—	—	—	—	—
Amortization and step-up:					—			
Intangible amortization expense(5)	254,337	—	811	—	—	—	—	—
Amortization of debt discount and deferred financing costs(7)	—	—	—	—	—	12,640		—
Impairment of long lived assets(12)	—	—	1,713	—	—	—	—	—
Gain on sale of assets(13)	—	—	—	—	(4,883)	—	—	—
Share-based compensation(8)	7,203	13,973	125,451	—	—	—	—	—
Depreciation(9)	339	104	23,860	—		—	—	—
Fees related to refinancing activities(16)	—	—	54	—	—	—	—	—
Loss on debt extinguishment(17)	—	—	—	31,856	—	—	—	—
Drug substance harmonization costs(14)	542	—	—	—	—	—	—	—
Income tax effect on pre-tax non-GAAP adjustments(10)	—	—	—	—	—	—	—	(98,628)
Other non-GAAP income tax adjustments(11)	—	—	—	—	—	—	—	20,541
Total of non-GAAP adjustments (18)	**262,421**	**61,300**	**153,756**	**31,856**	**(4,883)**	**12,640**	**(35)**	**(78,087)**
Non-GAAP (18)	**$(270,274)**	**$ (148,064)**	**$ (819,471)**	**$ —**	**$ —**	**$(46,976)**	**$ 3,353**	**$(89,936)**

NOTES FOR CERTAIN INCOME STATEMENT LINE ITEMS - NON-GAAP

1. Primarily represents transaction and integration costs, including, advisory, legal, consulting and certain employee-related costs, incurred in connection with our acquisitions and divestitures. Costs recovered from subleases of acquired facilities and reimbursed expenses incurred under transition arrangements for divestitures are also reflected in this line item. In addition, the year ended December 31, 2020 amounts include the Curzion acquisition payment of $45.0 million, which was recorded as a research and development expense.

2. We held investments in equity securities with readily determinable fair values of $13.2 million as of December 31, 2021 which are included in other assets in the consolidated balance sheet. For the year ended December 31, 2021, we recognized net unrealized gains of $1.3 million due to the change in fair value of these securities.

3. Since 2020, we have been working to expand our TEPEZZA drug substance manufacturing capacity in the external Copenhagen, Denmark, Boulder, Colorado, and Seattle, Washington facilities. During the fourth quarter of 2021, we ended further TEPEZZA drug substance manufacturing development activities in the Seattle facility and recorded a charge of $16.6 million to research and development expense related to manufacturing development activities in this facility. We expect existing and planned future production capacity at the Copenhagen and Boulder facilities to produce sufficient TEPEZZA drug substance to meet our future needs. In addition, rent and maintenance charges of $9.7 million were recorded for the leased Lake Forest office that we vacated in the first quarter of 2021.

4. During the year ended December 31, 2021, we recorded $3.6 million of manufacturing plant start-up costs related to the purchase of a biologic drug product manufacturing facility from EirGen in July 2021.

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

6. During the three and twelve months ended December 31, 2021, we recognized in cost of goods sold $10.7 million and $27.6 million, respectively, for inventory step-up expense related to UPLIZNA inventory revalued in connection with the Viela acquisition. Because inventory step-up expense is related to an acquisition, will not continue indefinitely and has a significant effect on our gross profit, gross margin percentage and net income for all affected periods, we exclude inventory step-up expense from our non-GAAP financial measures.

7. Represents amortization of debt discount and deferred financing costs associated with our debt.

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

9. Represents depreciation expense related to our property, plant, equipment, software and leasehold improvements.

10. 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.

11. During the year ended December 31, 2021, we recognized a U.S. federal and state tax liability on U.S. taxable income generated from an intercompany transfer and license of intellectual property from a U.S. subsidiary to an Irish subsidiary which was partially offset by the recognition of a deferred tax asset in the Irish subsidiary, resulting in a non-GAAP tax adjustment of $28.3 million. We also recognized a reduction in the state tax rate expected to apply to the reversal of temporary differences between the book values and tax bases of certain assets acquired through the Viela acquisition. The reduction in state tax rate resulted in a reduction in the deferred tax liability relating to these assets and a non-GAAP tax adjustment of $49.1 million.

    During the year ended December 31, 2020, following the publication by the United States Department of Treasury and the Internal Revenue Service of the Final Regulations on the Anti-Hybrid Rules on April 8, 2020, we recorded a write-off of a deferred tax asset related to certain interest expense accrued to a foreign related party during the year ended December 31, 2019 and recognized a corresponding one-time tax provision, resulting in a non-GAAP tax adjustment of $15.2 million. We also recognized a U.S. federal tax liability on U.S. taxable income generated from an intercompany transfer of intellectual property from a U.S. subsidiary to an Irish subsidiary, which was partially offset by the recognition of a deferred tax asset in the Irish subsidiary, resulting in a non-GAAP tax adjustment of $5.3 million.

12. During the year ended December 31, 2021, we recorded a right-of-use asset impairment charge of $12.4 million as a result of vacating the leased Lake Forest office.

    During the year ended December 31, 2020, we recorded an impairment charge of $1.7 million related to the Novato, California office lease, which was assumed through an acquisition.

13. Gain on sale of assets during the year ended December 31, 2021, represents a $2.0 million contingent consideration payment related to the sale of MIGERGOT in 2019.

    During the year ended December 31, 2020, we completed the sale of rights to RAVICTI and BUPHENYL in Japan for cash proceeds of $5.4 million, and we recorded a gain of $4.9 million on the sale.

14. During the year ended December 31, 2016, we entered into a definitive agreement to acquire certain rights to interferon gamma-1b, marketed as IMUKIN in an estimated thirty countries primarily in Europe and the Middle East, or the IMUKIN purchase agreement. We already owned the rights to interferon gamma-1b marketed as ACTIMMUNE in the United States, Canada and Japan. In connection with the IMUKIN purchase agreement, we also committed to pay our contract manufacturer certain amounts related to the harmonization of the manufacturing

processes for ACTIMMUNE and IMUKIN drug substance, or the harmonization program. At the time we entered into the IMUKIN purchase agreement and the harmonization program commitment was made, we had anticipated achieving certain benefits should the Phase 3 clinical trial evaluating ACTIMMUNE for the treatment of Friedreich's ataxia, be successful. If the study had been successful and if U.S. marketing approval had subsequently been obtained, we had forecasted significant increases in demand for the medicine and the harmonization program would have resulted in significant benefits to us. Following our discontinuation of the Friedreich's ataxia program, we determined that certain assets, including an upfront payment related to the IMUKIN purchase agreement, were impaired, and the costs under the harmonization program would no longer have benefit to us and should be expensed as incurred.

15. We recorded $5.0 million of expense during the year ended December 31, 2021 for litigation settlements.

16. Represents arrangement and other fees relating to our refinancing activities.

17. During the year ended December 31, 2020, we recorded a loss on debt extinguishment of $31.9 million in the condensed consolidated statements of comprehensive income, which reflects the extinguishment of our Exchangeable Senior Notes.

18. Following consultation with the staff of the Division of Corporation Finance of the U.S. Securities and Exchange Commission, we no longer exclude upfront and milestone payments related to license and collaboration agreements from our non-GAAP financial measures and its line item components. Adjusted EBITDA and non-GAAP net income for the three months ended December 31, 2021 and 2020, includes $36.2 million and $30.0 million, respectively, of upfront and milestone payments related to license and collaboration agreements. Adjusted EBITDA and non-GAAP net income for the years ended December 31, 2021 and 2020, includes $89.7 million and $33.0 million, respectively, of upfront and milestone payments related to license and collaboration agreements. These amounts continue to be excluded from our segment operating income and from certain measures contained in our credit agreement that are relevant to, among other things, the calculation of the interest rate.