Third-Quarter 2022 Summary

Horizon Therapeutics plc

November 2, 2022

Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to Horizon's full-year 2022 net sales and adjusted EBITDA guidance; expected financial performance and operating results in future periods, including projected growth in net sales of certain of Horizon's medicines; estimates of peak annual net sales; development, manufacturing and commercialization plans; expected timing of clinical trials and, availability of clinical data; expected future milestones, pipeline expansions and regulatory approvals; potential market opportunities 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; impacts of the on-going war between Russia and Ukraine; changes in inflation, interest rates and general economic conditions; acquisitions, such as the risk that acquired businesses or products 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 related transactions will not occur; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; Horizon's ability to successfully implement its business strategies, including the risks that its TEPEZZA growth and global expansion initiatives and strategies may not be successful and that new challenges to TEPEZZA growth may arise in the future; 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 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 presentation as a result of new information.

Presentation At A Glance

1. Third-Quarter 2022 Results; Increased Full-Year 2022 Guidance and Peak Annual Net Sales Expectations
2. Our Pipeline
3. Our Key Growth Drivers: TEPEZZA®, KRYSTEXXA® and UPLIZNA®

Third-Quarter 2022 and Recent Company Highlights

Financial Highlights

- Third-quarter 2022 net sales of **$925.4M**; adjusted EBITDA of **$335.3M**
- Third-quarter 2022 **TEPEZZA** net sales of **$490.9M**; continue to expect full-year 2022 net sales percentage growth in the **high teens**
- Third-quarter 2022 **KRYSTEXXA** net sales of **$191.6M**; increasing full-year 2022 net sales growth expectations to **approximately 25%**
- Increasing full-year 2022 net sales guidance to **$3.59B to $3.61B** and adjusted EBITDA guidance to **$1.32B to $1.34B**
- Increasing **TEPEZZA ex-U.S. peak** annual net sales expectations to **>$1B**, bringing **global peak** annual net sales expectations to **>$4B**(1)
- Increasing **KRYSTEXXA U.S. peak** annual net sales expectations to **>$1.5B**(1)
- Announced **$500M** share repurchase program; **$250M** in ordinary shares repurchased to date
- Cash position of **$2.13B** and gross leverage ratio of **1.8 times**(2) at September 30, 2022

Executing on Our Strategy

- **Announced positive topline data from dazodalibep Sjögren's syndrome Phase 2 trial**; planning to initiate a Phase 3 program in 2023
- **Completed enrollment in TEPEZZA chronic/low CAS thyroid eye disease trial** with topline results expected in second-quarter 2023
- **First patient enrolled in ADX-914 Phase 2 trial** in collaboration with Q32 Bio
- **Continued global expansion for UPLIZNA and TEPEZZA:** UPLIZNA commercial launch underway in **Germany**, **Austria** and in **France** under early access program; **submitted regulatory filings** for UPLIZNA and TEPEZZA in **Brazil**
- **Published inaugural Sustainability Accounting Standards Board (SASB) Index** as part of the updated 2021 ESG Overview
- Continued to be recognized as a top workplace: **Fortune's "Best Workplaces in Biopharma 2022™"** for sixth consecutive year and ranked **first overall** for the third time

EBITDA: Earnings before interest, taxes, depreciation and amortization. Adjusted EBITDA is a non-GAAP measure; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures. | CAS: Clinical activity score.
(1) Horizon estimates of TEPEZZA and KRYSTEXXA peak U.S. annual net sales of >$3B and >$1.5B, respectively, and TEPEZZA ex-U.S. estimate of >$1B peak annual net sales.
(2) Gross Leverage Ratio: Principal amount of debt outstanding at September 30, 2022, to adjusted EBITDA over the preceding 12-month period. Principal amount of debt outstanding at September 30, 2022, was $2.6B.

Third-Quarter 2022 Financial Results

($M, except for per share amounts and percentages)	Q3 2022	Q3 2021	% Change	YTD 2022	YTD 2021	% Change
Net sales	**$925.4**	**$1,037.0**	**(11)**	**$2,687.0**	**$2,211.9**	**21**
Net Income	135.8	326.5	(58)	401.1	361.3	11
Non-GAAP net income	293.3	410.3	(29)	862.9	755.7	14
Adjusted EBITDA[1]	**335.3**	**505.0**	**(34)**	**1,013.1**	**868.3**	**17**
Earnings per share – diluted	0.58	1.38	(58)	1.70	1.54	10
Non-GAAP earnings per share – diluted	1.25	1.74	(28)	3.66	3.21	14
Cash and cash equivalents[2]				**$2,130.5**	**$1,068.5**	**99**

EBITDA: Earnings before interest, taxes, depreciation and amortization.| IPR&D: In-process research and development. (1) Third-quarter 2022 and 2021 adjusted EBITDA includes $19M and $4M, respectively, in acquired IPR&D and milestones expenses. Year-to-date 2022 and 2021 adjusted EBITDA includes $19M and $47M, respectively, in acquired IPR&D and milestones expenses. (2) Cash and cash equivalents at September 30, 2022, and September 30, 2021, respectively.
Note: Non-GAAP net income, adjusted EBITDA and non-GAAP earnings per share diluted are non-GAAP measures; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.

Third-Quarter 2022 Orphan Segment Results

($M)	Q3 2022	Q3 2021	% Change		YTD 2022	YTD 2021	% Change
TEPEZZA®(1)	$490.9	$616.4	(20)		$1,472.2	$1,071.7	37
KRYSTEXXA®	191.6	158.1	21		500.1	395.2	27
RAVICTI®	84.3	76.2	10		238.1	217.6	9
PROCYSBI®(2)	57.8	49.3	17		155.1	142.5	9
UPLIZNA®(3)	43.8	18.7	134		112.9	35.0	222
ACTIMMUNE®	34.4	30.1	15		95.8	86.6	11
BUPHENYL®	1.7	1.9	(8)		5.3	5.8	(9)
QUINSAIR™	0.2	0.3	(26)		0.9	0.7	16
Orphan Net Sales	**$904.7**	**$951.0**	**(5)**		**$2,580.4**	**$1,955.1**	**32**
Orphan Segment Operating Income	**$366.9**	**$476.2**	**(23)**		**$1,033.5**	**$798.5**	**29**

(1) TEPEZZA net sales in the third quarter of 2021 accounted for a larger share of full-year 2021 net sales due to a supply disruption caused by the U.S. government-mandated COVID-19 vaccine orders. (2) PROCYSBI net sales in the third quarter of 2022 benefitted from a $7.5M partial release in the pricing review liability recorded during the three months ended September 30, 2022, as a result of a decision made by the Patented Medicines Prices Review Board (PMPRB) in September relating to PROCYSBI pricing in Canada. (3) Third-quarter and year-to-date 2022 UPLIZNA net sales included $3.2M and $17.0M, respectively, in international net sales, related primarily to revenue and milestone payments from the Company's international partners.

Third-Quarter 2022 Inflammation Segment Results

($M)	Q3 2022	Q3 2021	% Change		YTD 2022	YTD 2021	% Change
RAYOS®	$10.6	$14.9	(29)		$35.1	$43.6	(19)
PENNSAID 2%®(1)	7.6	48.0	(84)		66.6	142.7	(53)
DUEXIS®(2)	2.0	20.9	(90)		3.2	62.5	(95)
VIMOVO®	0.5	2.2	(78)		1.7	8.1	(79)
Inflammation Net Sales	**$20.7**	**$86.0**	**(76)**		**$106.6**	**$256.9**	**(59)**
Inflammation Segment Operating (Loss) Income	**($10.8)**	**$34.1**	**NM**		**($2.0)**	**$123.6**	**NM**

NM: Not meaningful.
(1) On May 6, 2022, Apotex Inc. initiated an at-risk launch of generic PENNSAID 2% in the U.S. (2) On Aug. 4, 2021, Alkem Laboratories, Inc. initiated an at-risk launch of generic DUEXIS in the U.S.

Increased Full-Year 2022 Guidance

	Updated Guidance	Previous Guidance
Net Sales	**$3.59B to $3.61B**	$3.53B to $3.60B
Adjusted EBITDA	**$1.32B to $1.34B**	$1.268B to $1.318B

Key Highlights:

- Continue to expect **TEPEZZA** full-year 2022 net sales percentage growth in the **high teens**
- Increased **KRYSTEXXA** full-year 2022 net sales growth expectations to **approximately 25%**
- Expect inflammation segment fourth-quarter 2022 net sales of **less than $10M** due to market erosion caused by generic **PENNSAID 2%**(1) entrant

EBITDA: Earnings before interest, taxes, depreciation and amortization. Adjusted EBITDA is a non-GAAP measure. (1) On May 6, 2022, Apotex Inc. initiated an at-risk launch of generic PENNSAID 2% in the U.S.

Increased Peak Annual Net Sales Expectations for TEPEZZA and KRYSTEXXA[(1)]

	Updated Guidance	Previous Guidance
TEPEZZA (Global)	**>$4.0B**	>$3.5B
KRYSTEXXA (U.S.)	**>$1.5B**	>$1B

Key Highlights:

- Increased **TEPEZZA** ex-U.S. peak annual net sales expectations **to >$1B from >$500M** following further assessment of ex-U.S. market opportunity and now incorporating plans to launch TEPEZZA in Europe
- Increased **KRYSTEXXA** U.S. peak annual net sales expectations **to >$1.5B from >$1B** given the strong momentum across rheumatology and nephrology with continued growth in the use of KRYSTEXXA with immunomodulation following label expansion

(1) Horizon estimates.

Executing on Our Strategy Has Positioned Horizon as a Leading, High-Growth, Global Biotech

Progress and Achieved Milestones in 2022

- ✓ Launched KRYSTEXXA with methotrexate campaign following U.S. FDA approval of expanded label; sales force actively promoting its many benefits
- ✓ Completed enrollment of TEPEZZA chronic/low CAS TED clinical trial
- ✓ Met the primary endpoint in dazodalibep Sjögren's syndrome trial serving as additional validation of its mechanism of action
- ✓ Entered into collaboration and option agreement with Q32 Bio for its candidate ADX-914 in development for T-cell-driven autoimmune diseases; Phase 2 trial in atopic dermatitis initiated in October
- ✓ Initiated three clinical trials to date
- ✓ Announced positive topline data in dazodalibep rheumatoid arthritis trial
- ✓ Received European Commission approval for UPLIZNA in NMOSD; commercial launch underway in Germany, Austria, and in France under early access program
- ✓ Submitted regulatory filings in Brazil for TEPEZZA and UPLIZNA and continued build-out of infrastructure
- ✓ Announced planned expansion of Waterford facility to add new drug substance biologics development and manufacturing capabilities

Expected Milestones in 2023 and Beyond

- Expect several important data readouts for TEPEZZA (chronic/low CAS TED), UPLIZNA (MG and IgG4-RD) and daxdilimab (AA and SLE)
- Initiate a Phase 3 program for dazodalibep in Sjögren's syndrome
- Launch UPLIZNA in other targeted international markets, including Brazil(1)
- Complete TEPEZZA OPTIC-J trial for potential approval in Japan; prepare for potential launch in Japan, Europe, Brazil and other targeted international markets(1)
- Obtain regulatory approval for Waterford biologics drug product manufacturing facility and complete expansion of drug substance facility
- Advance toward aggregate global peak annual net sales expectations for our three key growth drivers of >$6.5B(2):
  - TEPEZZA: >$4B(2)
  - KRYSTEXXA: >$1.5B(2)
  - UPLIZNA: >$1B(2)

Executing on Our Strategy

- **Expanding our pipeline for sustainable growth**
- **Maximizing the value of our key growth drivers**
- **Building a global presence**

CAS: Clinical activity score. | TED: Thyroid eye disease. | NMOSD: Neuromyelitis optica spectrum disorder. | MG: Myasthenia gravis. | IgG4-RD: Immunoglobulin G4-related disease. | AA: Alopecia areata. | SLE: Systemic lupus erythematosus.
(1) Assuming marketing approval in applicable jurisdictions. (2) Horizon estimates of TEPEZZA and KRYSTEXXA peak U.S. annual net sales of >$3B and >$1.5B, respectively, and TEPEZZA ex-U.S. estimate of >$1B peak annual net sales. Horizon estimate of UPLIZNA global peak annual net sales of >$1B assumes three global indications in NMOSD, MG and IgG4-RD. UPLIZNA is currently approved for NMOSD in the U.S., EU member states, Japan & China.

Driving Long-Term Value Through Strategic Capital Allocation

Strong Balance Sheet and Cash Flow Generation

$2.1B
in cash and cash equivalents as of 9/30

>$1B
in cash flow from operations in LTM

1.8x
gross leverage ratio as of 9/30[(1)]

0.3x
net leverage ratio as of 9/30[(2)]

Top Priority: Business Development

Maintaining strong focus in rare diseases with significant unmet need

Deepening our presence in autoimmune and severe inflammatory diseases

Balancing the pipeline across early-to-late-stage programs

Increasing research-based partnerships and collaborations

Additional Priorities: Share Repurchase and CapEx

Announced $500M share repurchase program

To date, 3.9M shares repurchased at a value of $250M

Planned expansion of biologics manufacturing facility in Waterford, Ireland

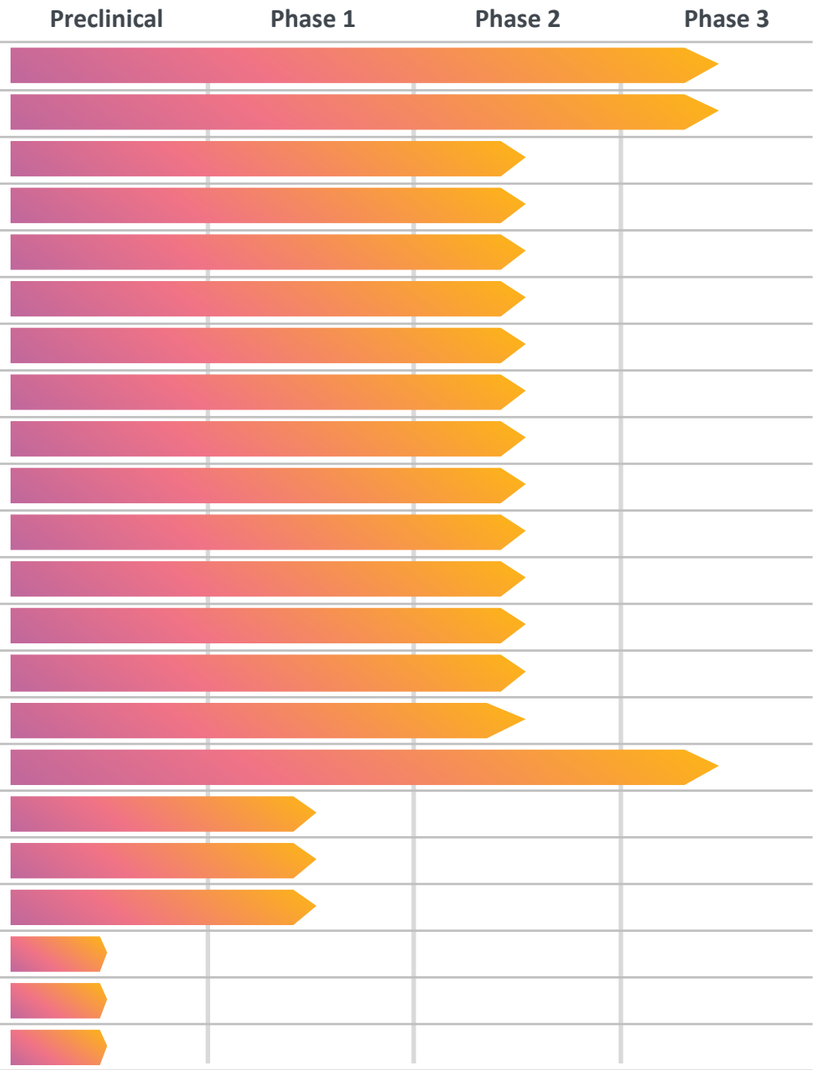
LTM: Last twelve months ending September 30, 2022. | CapEx: Capital expenditures. | EBITDA: Earnings before interest, taxes, depreciation and amortization. Adjusted EBITDA and net debt are non-GAAP measures; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.
(1) Gross Leverage Ratio: Principal amount of debt outstanding at September 30, 2022, to adjusted EBITDA over the preceding 12-month period. (2) Net Leverage Ratio: Net debt at September 30, 2022, to adjusted EBITDA over the preceding 12-month period.

Pipeline Update

Enhancing Horizon's Profile as an Innovation-Driven Biotech

Expanding Our Pipeline to Drive Long-Term Growth

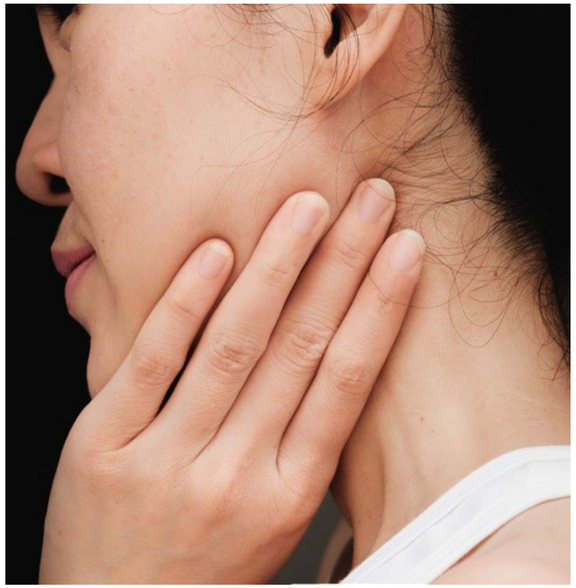
Medicine/Candidate	Program/Potential Indication
UPLIZNA	Myasthenia Gravis (MG)
	IgG4-Related Disease (IgG4-RD)
Daxdilimab	Systemic Lupus Erythematosus (SLE)
	Alopecia Areata (AA)
	Discoid Lupus Erythematosus (DLE)(1)
	Lupus Nephritis (LN)(1)
	Dermatomyositis (DM)(1)
Dazodalibep	Sjögren's Syndrome(2)
	Rheumatoid Arthritis(3)
	Kidney Transplant Rejection
	Focal Segmental Glomerulosclerosis (FSGS)(1)
HZN-825	Diffuse Cutaneous Systemic Sclerosis (dcSSc)
	Idiopathic Pulmonary Fibrosis (IPF)
ADX-914	Atopic Dermatitis(4)
	Additional Autoimmune Disease(1,4)
TEPEZZA	TED in Japan (OPTIC-J)
	Subcutaneous Administration
	Diffuse Cutaneous Systemic Sclerosis (dcSSc)
HZN-1116	Autoimmune Diseases
Alpine	Autoimmune Diseases(5)
ARO-XDH	Next-Gen Uncontrolled Gout(5)
HemoShear	Novel Gout Targets(5)

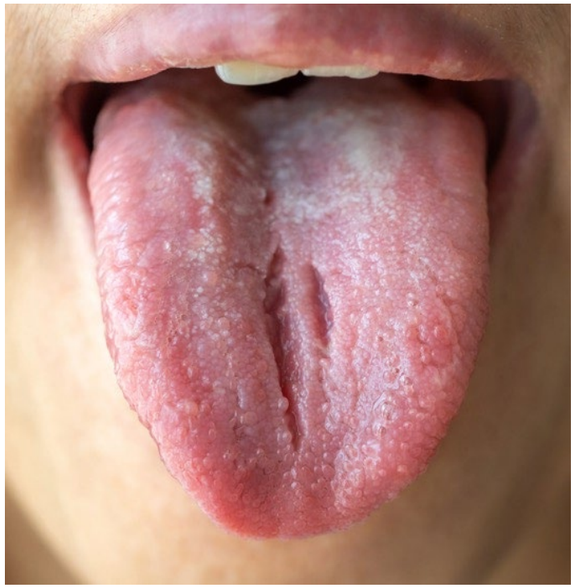


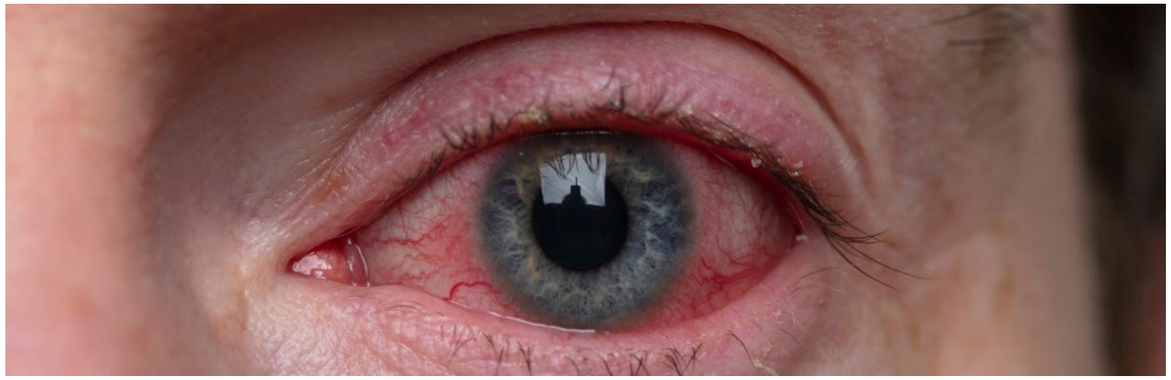
- **>20 programs**
- **Initiated 3 clinical trials** year-to-date
- **10 potential approvals** in the second half of the decade
- **3 additional Phase 4 programs:**
  - TEPEZZA chronic/low CAS TED
  - KRYSTEXXA shorter infusion duration
  - KRYSTEXXA monthly dosing

IgG4: Immunoglobulin G4. | TED: Thyroid eye disease.
CAS: Clinical activity score.
(1) Planned programs; not yet initiated.
(2) Announced positive topline results for patients with moderate-to-severe systemic disease activity on September 12, 2022. The trial met the primary endpoint and was well tolerated. Patient population with localized symptoms is fully enrolled and trial continues to progress.
(3) Trial complete. Announced positive topline results on May 3, 2022. The trial met the primary endpoint across all doses and was well tolerated.
(4) Horizon has an option to acquire ADX-914 from Q32 Bio on pre-negotiated terms through the completion of Phase 2 clinical trials. Phase 2 trials to be conducted by Q32.
(5) External collaborations.

Sjögren's Syndrome is an Autoimmune Disease Involving Overexpression of CD40/CD40L







Sjögren's Syndrome

- Chronic, systemic autoimmune disease attacking the salivary and tear (exocrine) glands, with severe cases affecting multiple organs
- Disease manifestations include dry eyes, dry mouth, arthritis and kidney or lung dysfunction
- Overexpression of CD40/CD40L observed at site of inflammation and in circulation
- ~250K-350K patients with Sjögren's syndrome in the U.S., of which ~50K have moderate-to-severe systemic disease activity and are also appropriate for novel therapies including biologics(1)

Unmet Need

- No FDA-approved disease modifying treatments
- Current treatments: palliative care (artificial tears, medicines for dry mouth); topical cyclosporine; steroids/immunosuppressants used off-label as needed to manage systemic symptoms

CD40: Cluster of differentiation 40. | CD40L: Cluster of differentiation 40 ligand.
(1) Horizon estimate.

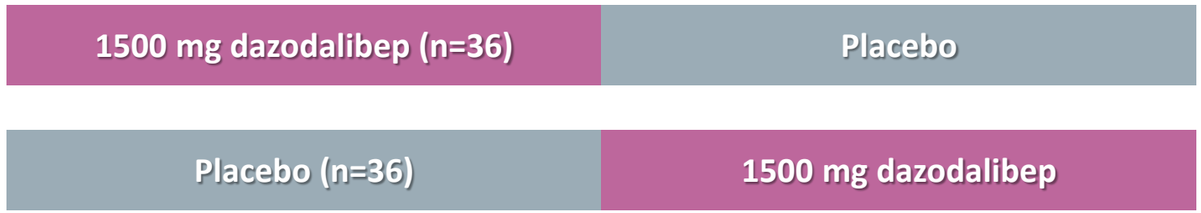
Phase 2 Trial Evaluating the Safety and Efficacy of Dazodalibep in Sjögren's Syndrome

Topline Results Announced in Patients with Moderate-to-Severe Systemic Disease Activity

Moderate-to-Severe Systemic Disease Activity (n=72)

- Subjects with ESSDAI ≥ 5
- Primary endpoint: change from baseline in ESSDAI at Day 169

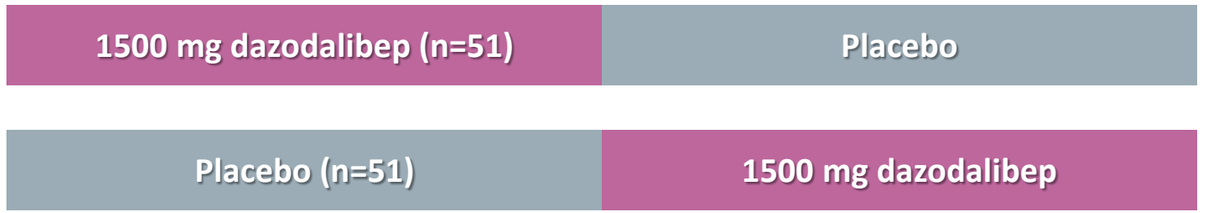
Topline results announced at this timepoint



Induction followed by monthly IV dosing

Moderate-to-Severe Localized Symptoms (n=102)

- Subjects with ESSPRI score ≥ 5 and residual stimulated salivary flow but with mild systemic disease activity defined by ESSDAI score < 5
- Primary endpoint: change from baseline in ESSPRI at Day 169



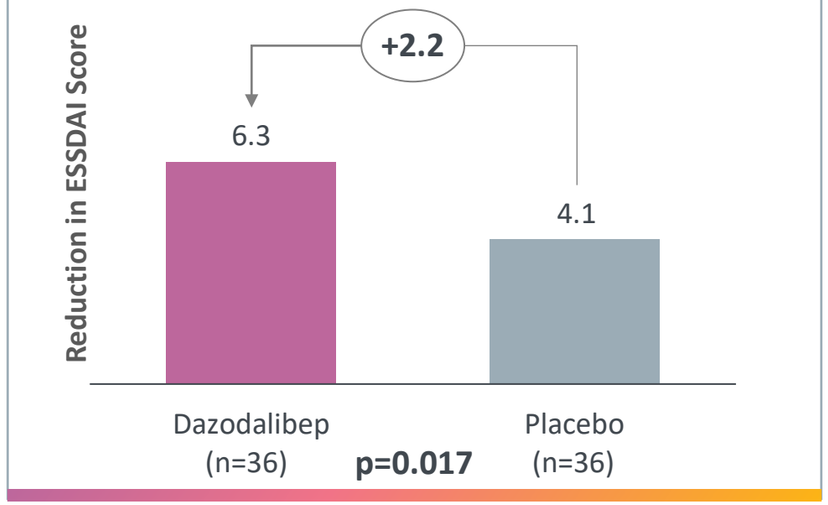
Induction followed by monthly IV dosing

Secondary endpoints: change from baseline in ESSPRI at Day 169 (systemic disease patients only), change from baseline in FACIT-Fatigue score at Day 169, change from baseline in PGIS at Day 169, safety and tolerability of multiple IV doses of dazodalibep and anti-drug antibodies until the study completion

EULAR: European League Against Rheumatism | ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index: A Sjögren's specific disease activity index composed of 12 system domains. | ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index: Patient reported index composed of three questions assessing dryness, fatigue and pain. | IV: Intravenous. | FACIT: Functional Assessment of Chronic Illness Therapy. | PGIS: Patient's Global Impression of Severity.

Phase 2 Trial Evaluating Dazodalibep for the Treatment of Sjögren's Syndrome Met the Primary Endpoint in Patients with Moderate-to-Severe Systemic Disease Activity

Phase 2 Trial Results



Next Steps:

- Phase 2 trial continues to progress with fully enrolled moderate-to-severe localized symptom patient population
- Working with regulators to design Phase 3 program, which is planned to initiate in 2023

Primary Endpoint

- Met primary endpoint in patients with moderate-to-severe systemic disease activity as defined by ESSDAI as a score of ≥ 5
- At Week 24, patients treated with dazodalibep achieved a 6.3-point reduction in ESSDAI score compared to patients treated with placebo who achieved a 4.1-point reduction, resulting in a statistically significant least squares mean difference of 2.2 points (p=0.017)
- Dazodalibep was well tolerated through Week 24; the most common adverse events were COVID-19 infection, diarrhea, dizziness, ligament sprain and upper respiratory infections

Key Secondary, Exploratory and Post-Hoc Analyses[1]

- Numerical improvement in dryness, an important symptom of Sjögren's syndrome as it impacts chewing, swallowing and dentition[2]
- Numerical improvement in fatigue as measured by FACIT-F and physical functioning measured by SF-36
- Numerical improvements in the number of tender and swollen joints
- Post-hoc responder analysis of patients achieving high levels of improvement on ESSDAI favored dazodalibep over placebo

EULAR: European League Against Rheumatism. | ESSDAI: EULAR Sjögren's Syndrome Disease Activity Index: A Sjögren's specific disease activity index composed of 12 system domains. | FACIT-F: Functional Assessment of Chronic Illness Therapy – Fatigue. SF-36 = Short Form Health Survey. (1) The trial was only powered for statistical significance on the primary endpoint. (2) Dryness was defined by ESSPRI: EULAR Sjögren's Syndrome Patient Reported Index: Patient reported index composed of three questions assessing dryness, fatigue and pain.

Entered into Collaboration and Option Agreement with Q32 Bio to Develop ADX-914, an IL-7Rα Antibody Inhibitor That Blocks Signaling by Two Key Immune Pathways

Transaction Overview	• Entered into a collaboration and option agreement in August 2022 for Q32's pipeline candidate ADX-914 in development for autoimmune diseases • Q32 is a clinical-stage biotechnology company developing biologic therapeutics to rebalance immunity in severe autoimmune and inflammatory diseases • Upfront option fee and staged development funding of $55M across 2022-2023, including $32.5M in the second half of 2022 • Horizon has an option to acquire ADX-914 through the data readouts of two Phase 2 trials
Strategic Rationale	• Complements our existing pipeline in autoimmune diseases • ADX-914 is a potential best-in-class, fully human anti-IL7Rα antibody designed to block signaling of two key immune pathways (IL-7 and TSLP) • The IL-7 and TSLP pathways are biologically and genetically implicated as central mediators of T-cell-mediated pathologies(1) • Q32 recently completed a biomarker-enabled Phase 1 study that demonstrated pharmacological effect on T cells in healthy volunteers
Development Plan	• Two Phase 2 trials: one in atopic dermatitis initiated in October 2022 and another in a second autoimmune disease in 2023

ADX-914 Delivers Unique MOA that is Complementary to our Expanding Pipeline

Blockade of TSLP inhibits:

1) Polarization of dendritic cells
2) B-cell expansion and differentiation
3) Activation of mast cells

ADX-914

Blockade of IL-7 inhibits:

1) Survival and proliferation of T cells
2) T-cell-driven antibody responses

IL-7Rα: Interleukin-7 receptor subunit alpha. | TSLP: Thymic stromal lymphopoietin. | MOA: Mechanism of action.

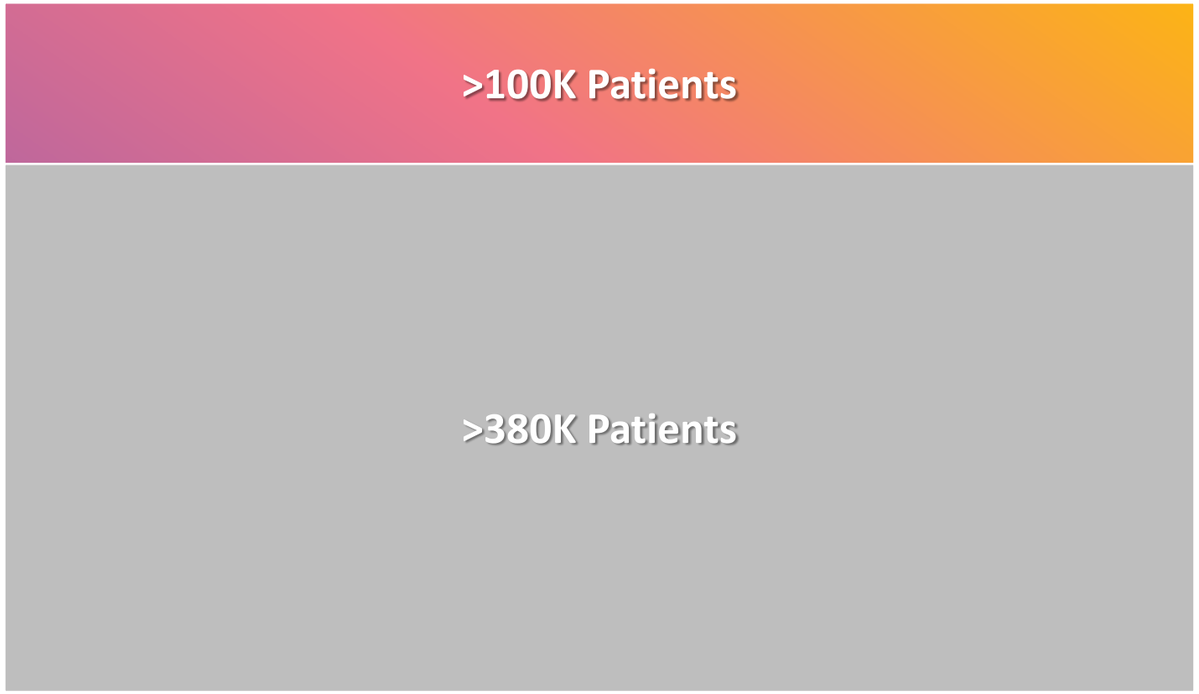
(1) Marković I, Savvides SN. Modulation of Signaling Mediated by TSLP and IL-7 in Inflammation, Autoimmune Diseases and Cancer. Front Immunol. 2020 Jul 21;11:1557.

TEPEZZA

The First and Only Medicine Approved for Thyroid Eye Disease

Extensive Market Research Completed Supports >100K Patients Appropriate for TEPEZZA[(1)]

Thyroid Eye Disease (TED) Market[(1)]



Moderate-to-severe addressable population

Mild TED patients and patients not currently seeing a TED-treating physician

Extensive Market Research and Segmentation

- ☑ Completed two large-scale claims analyses dating back 10 years covering several hundred thousand data points
- ☑ Identified and categorized patients with thyroid eye disease or Graves' disease patients with eye symptoms to determine the incidence of moderate-to-severe patients
- ☑ Commissioned wide-ranging physician and patient market research
- ☑ Conducted top-down review of Graves' disease literature
- ☑ Analyzed patient chart audits; segmented moderate-to-severe patients based on signs and symptoms
- ☑ Engaged with experts for qualitative research regarding the patient journey, referral and treatment patterns

(1) Horizon estimates. | Source: HCP chart survey and claims analysis.

U.S. Moderate-to-Severe TED Market: >100K Patients Appropriate for TEPEZZA[1]

Patients' Symptoms, Not Time Since Diagnosis, Drive Treatment of TED

>100K U.S. TED Patient Market Segmentation[1]

High Proptosis and/or Diplopia with High CAS

>20K Moderate-to-Severe Patients

Primarily Seen by Ocular Specialists

< 20% Penetration in LTM[2]

High Proptosis and/or Diplopia with Low CAS

>80K Moderate-to-Severe Patients

Primarily Seen by Ophthalmologists and Endocrinologists

< 3% Penetration in LTM[2]

~15-20K newly diagnosed moderate-to-severe TED patients each year[1]

Key Takeaways:

1. Segmented the market based on symptoms and disease activity
2. Patients' symptoms, not time since diagnosis, drive treatment of TED
3. Taking actions to drive increased penetration in both patient segments

TED: Thyroid eye disease. | CAS: Clinical activity score. | LTM: Last twelve months.
(1) Horizon estimates. (2) Last twelve months as of August 3, 2022. | Source: HCP chart survey and claims analysis. High CAS and high proptosis are defined as CAS ≥ 3 and proptosis ≥ 3mm, respectively.

Actions We Are Taking to Drive Growth Across Key Market Segments

	Ocular Specialists ~2,000 Physician Targets Seeing ~1/3 of the Addressable Patients(1)	Ophthalmologists/Endocrinologists ~10,000 Physician Targets Seeing ~2/3 of the Addressable Patients(1)
High Proptosis and/or Diplopia with High CAS	☑ Achieved rapid adoption among early prescribers ☑ Driving commercial execution ☑ Improving patient services model to better support patient access ☑ Increasing education on medical co-management	☑ Educating ophthalmologists and endocrinologists about thyroid eye disease (TED) and TEPEZZA ☑ Expanding reach to physician targets through field force expansion ☐ Increase the breadth of prescribers alongside the urgency to diagnosis and refer to a current prescriber
High Proptosis and/or Diplopia with Low CAS	☑ Experienced early traction following case report data ☐ Generate clinical evidence in low CAS patients to drive adoption; topline data expected 2Q23(2)	

Significantly investing in DTC to motivate patients to seek treatment

CAS: Clinical activity score. | DTC: Direct to consumer. (1) Horizon estimates. (2) Chronic/Low CAS Phase 4 trial: A Study Evaluating TEPEZZA Treatment in Patients With Chronic (Inactive) Thyroid Eye Disease.
Source: HCP chart survey and claims analysis. High CAS and high proptosis are defined as CAS ≥ 3 and proptosis ≥ 3mm, respectively.

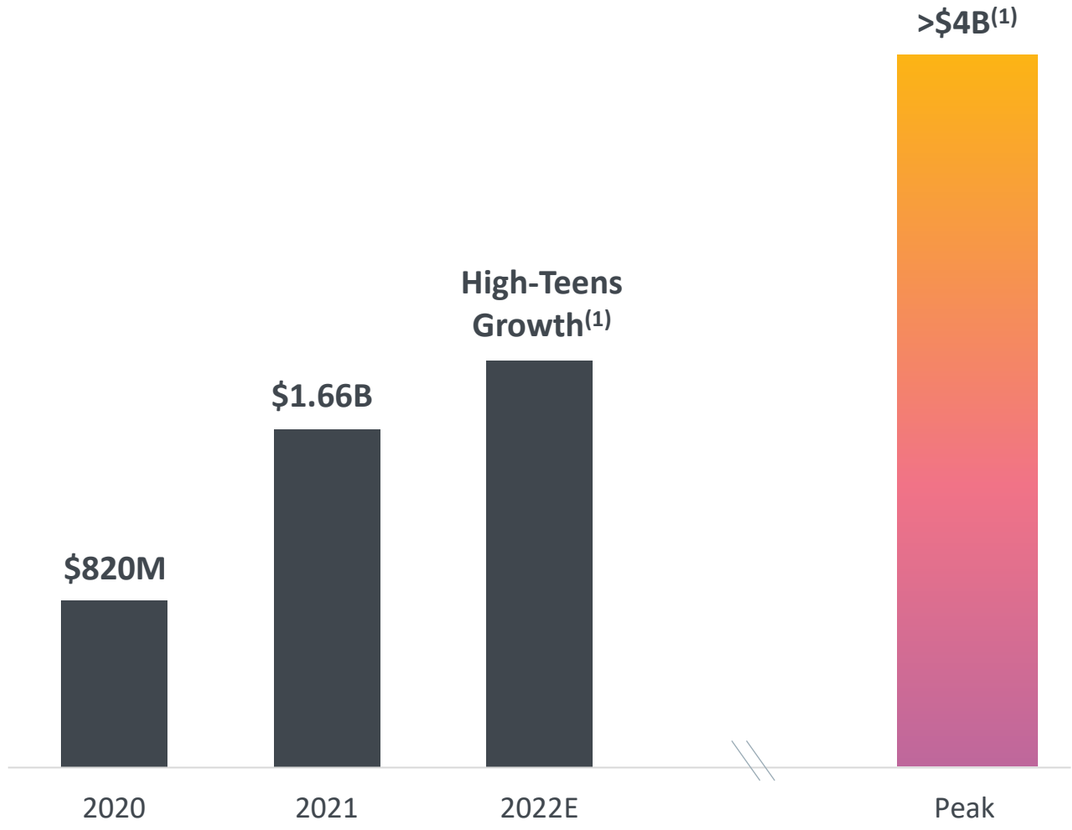
TEPEZZA: Confident in Global Peak Annual Net Sales Expectations and Path to Get There

Increasing Ex-U.S. Peak Annual Net Sales Expectations to >$1B Driven by Greater Opportunity in International Markets[(1)]

Growth Strategy: Continued Strong Uptake and Expand TEPEZZA to More Patients

1. Increase support to ocular specialists; drive urgency to diagnose and refer/treat among ophthalmologists and endocrinologists
2. Increase penetration in low CAS patients through clinical data generation
3. Maximize the potential of TEPEZZA through global expansion

TEPEZZA Has a Significant Opportunity to Achieve Global Peak Annual Net Sales



CAS: Clinical activity score. (1) Horizon estimates of TEPEZZA growth and peak U.S. annual net sales of >$3B and TEPEZZA ex-U.S. estimate of >$1B peak annual net sales.

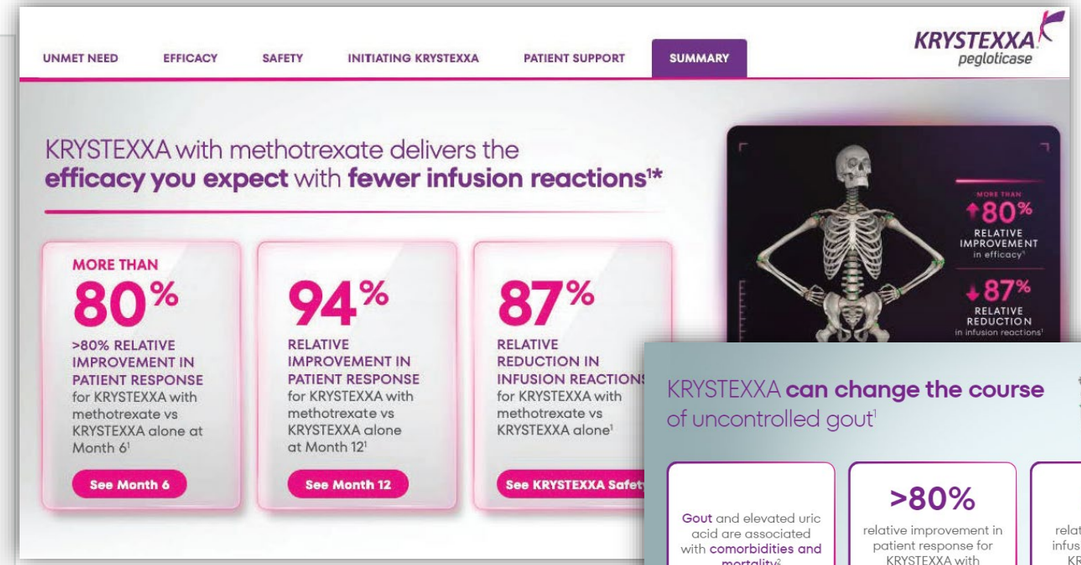
KRYSTEXXA

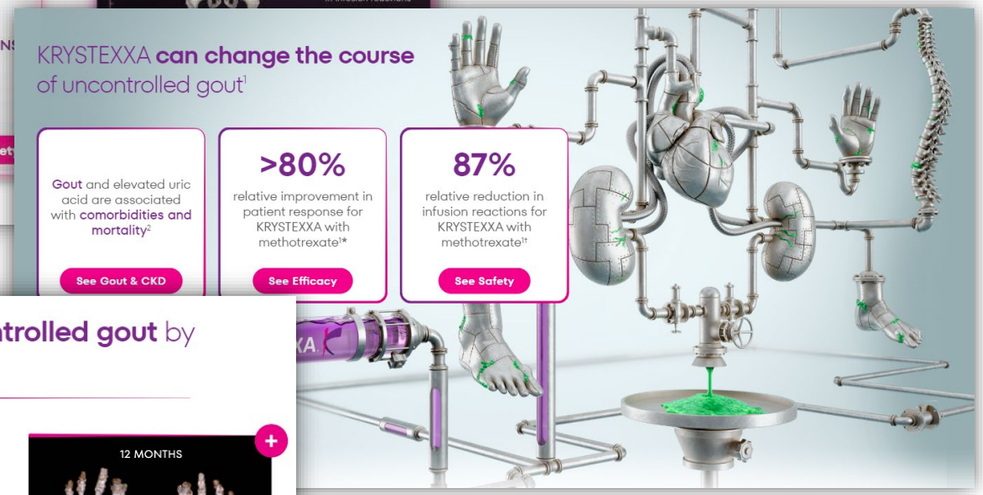
The First and Only Medicine Approved For Uncontrolled Gout

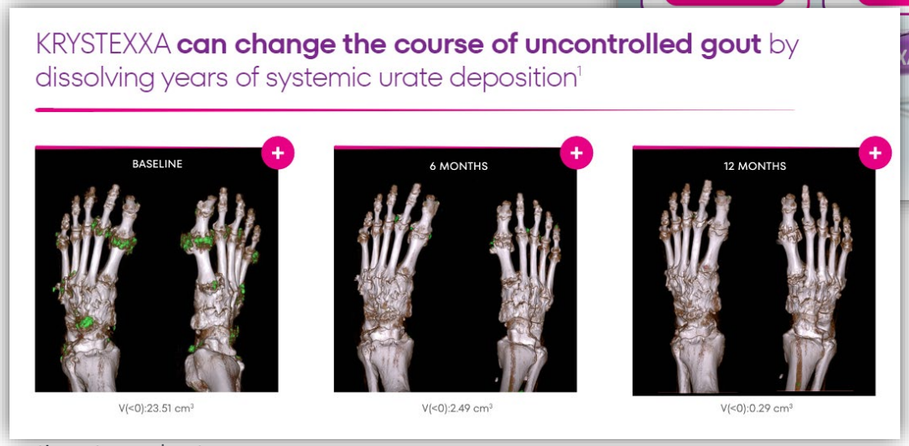
After FDA Approval, Our Team Launched a New Promotional Campaign

KRYSTEXXA with Methotrexate Launch

- ☑ Fully Trained Field Force and Speaker Bureau
- ☑ New Marketing Material
- ☑ 750+ Attendees at the National Launch Broadcast for Physicians
- ☐ Share Additional Results of MIRROR Trial at Future Medical Meetings and in Key Publications







(1) Please see Important Safety Information, including Boxed Warning and full Prescribing Information, at www.krystexxa.com

KRYSTEXXA with Immunomodulation is a Core Element of Horizon's Strategy

Immunomodulation Use Now Exceeding 60% Following Label Expansion

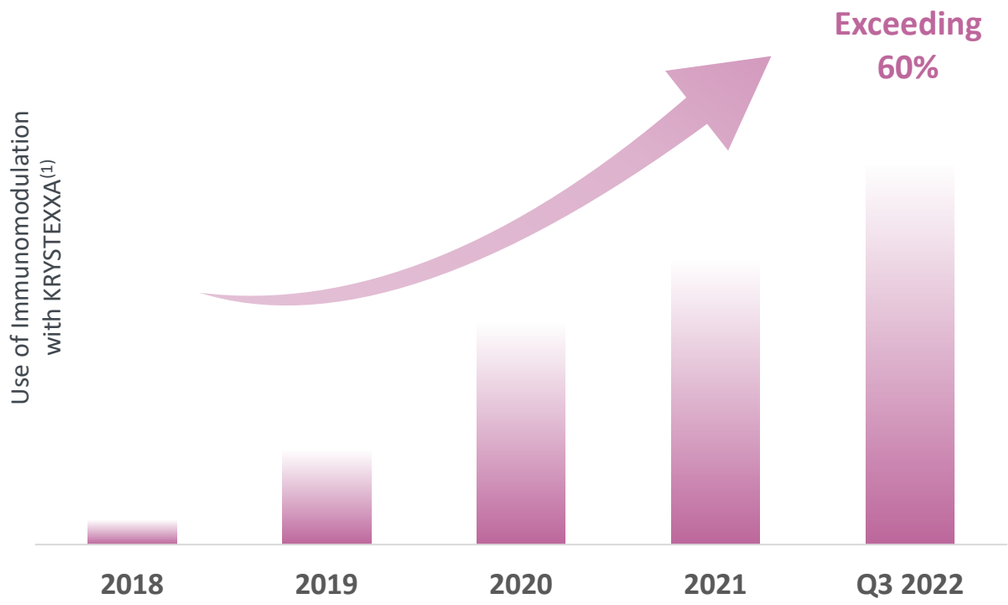
Real-World Feedback From Physicians

> *Seeing infusion reactions drop has changed my thought process, these data makes me comfortable enough to not only start considering patients, but to infuse them in our office.*

> *The FDA approval of combination therapy was the little nudge I needed to prescribe.*

> *I am very interested in the new information; this is a game changer for our practice.*

Immunomodulation Use Has Significantly Increased Since First Case Series Presented in 2018



(1) Horizon analysis of Hub and claims data of KRYSTEXXA-treated patients also receiving immunomodulators.

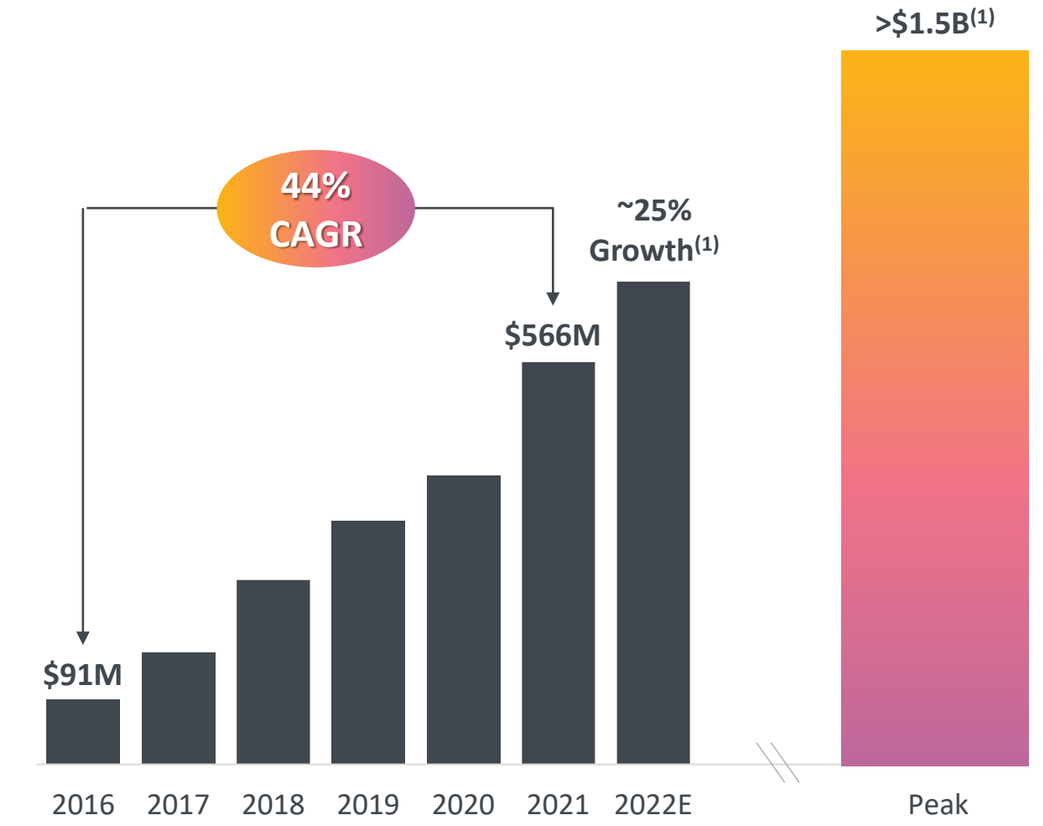
KRYSTEXXA: Increasing U.S. Peak Annual Net Sales Expectations to >$1.5B[(1)]

Strong Momentum and Continued Growth in the Use of KRYSTEXXA with Immunomodulation Following Label Expansion

Growth Drivers: Increase Total Patients and Vials Per Patient

1. **Redefine KRYSTEXXA with methotrexate as the standard of care**
2. **Expand utilization in core specialty areas through field force expansion; elevate urgency to treat**
3. **Invest to improve the patient experience**

Continued Strong Growth and Significant Peak Annual Net Sales Opportunity



CAGR: Compound annual growth rate.
(1) Horizon estimates of KRYSTEXXA growth and U.S. peak annual net sales of >$1.5B.

UPLIZNA

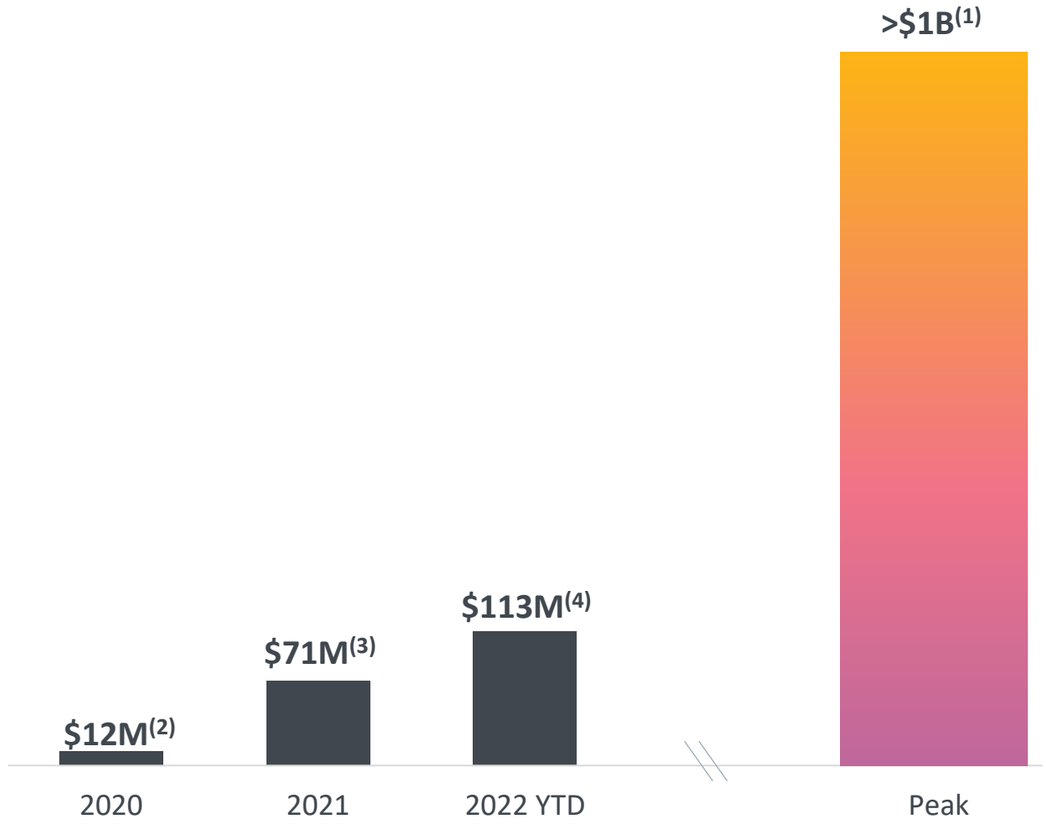
First and Only FDA-Approved B-Cell Depleting Therapeutic for the Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD)

UPLIZNA: Significant Opportunity Exists to Exceed $1B in Global Peak Annual Net Sales[(1)]

Growth Drivers: Transition Existing Patients and Drive Uptake in New Patients

1. **Drive awareness and understanding of the full range of benefits and differentiated clinical profile**
2. **Drive patient initiation and adherence; cultivate a positive patient experience**
3. **Maximize the potential of UPLIZNA through additional indications and global expansion**

UPLIZNA Global Peak Annual Net Sales Opportunity



(1) Horizon estimate of UPLIZNA global peak annual net sales of >$1B. Assumes three global indications in neuromyelitis optica spectrum disorder (NMOSD), myasthenia gravis (MG) and immunoglobulin G4-related disease (IgG4-RD). UPLIZNA is currently approved for NMOSD in the U.S., EU member states, Japan and China. (2) Viela sales. (3) UPLIZNA was acquired on March 15, 2021. Includes $10.6M that Viela reported prior to acquisition. (4) Through September 30, 2022, year-to-date UPLIZNA net sales included $17.0M in international net sales related primarily to revenue and milestone payments from the Company's international partners.

Reconciliations of GAAP to Non-GAAP Measures

Note Regarding Use of Non-GAAP Financial Measures

Horizon provides certain non-GAAP financial measures, including EBITDA, or earnings before interest, taxes, depreciation and amortization, adjusted EBITDA, 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 (expense) and tax rate, non-GAAP operating cash flow and certain other non-GAAP income statement line items, 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 Horizon's GAAP figures exclude, as applicable, acquisition and/or divestiture-related costs, manufacturing facility start-up costs, restructuring and realignment costs, as well as non-cash items such as share-based compensation, inventory step-up expense, depreciation and amortization, non-cash interest expense, goodwill and long-lived assets impairment charges, gain (loss) on equity security investments and sales of assets, and other non-cash adjustments. Certain other special items or substantive events may also be included in the non-GAAP adjustments periodically when their magnitude is significant within the periods incurred. 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 guidance to expected GAAP net income (loss) guidance because certain items such as acquisition/divestiture-related expenses and share-based compensation that are components of net income (loss) cannot be reasonably projected due to the significant impact of changes in Horizon's share price, the variability associated with the size and/or timing of acquisitions/divestitures, and other factors. These components of net income (loss) could significantly impact Horizon's GAAP net income (loss).

GAAP to Non-GAAP Reconciliation

EBITDA and Adjusted EBITDA – Three and Nine Months Ended September 30, Twelve Months Ended December 31, 2021

$ in thousands	Three Months Ended September 30,		Nine Months Ended September 30,		Twelve Months Ended December 31,
	2022	2021	2022	2021	2021
GAAP net income	**$ 135,839**	**$ 326,543**	**$ 401,074**	**$ 361,309**	**$ 534,491**
Depreciation	6,130	4,112	18,073	11,956	17,475
Amortization and step-up:					
Intangible amortization expense	92,951	90,368	273,546	245,260	336,277
Inventory step-up expense	21,779	8,912	66,342	16,914	27,572
Interest expense, net (including amortization of debt discount and deferred financing costs)	22,480	22,977	65,145	59,018	81,063
Benefit for income taxes	(758)	(19,302)	(28,467)	(109,537)	(71,664)
EBITDA	**$ 278,421**	**$ 433,610**	**$ 795,713**	**$ 584,920**	**$ 925,214**
Other non-GAAP adjustments:					
Acquisition/divestiture-related costs	825	9,228	3,437	88,166	95,929
Loss (Gain) on equity security investments	1,247	-	6,331	-	(1,257)
Restructuring and realignment costs	7,731	680	9,521	7,703	26,309
Manufacturing facility start-up costs	2,024	1,712	4,413	1,712	3,622
Impairment of goodwill	-	-	56,171	-	-
Impairment of long-lived assets	-	-	-	12,371	12,371
Gain on sale of assets	-	-	-	(2,000)	(2,000)
Share-based compensation	45,066	54,804	137,515	170,394	219,086
Litigation settlement	-	5,000	-	5,000	5,000
Total of other non-GAAP adjustments	**56,893**	**71,424**	**217,388**	**283,346**	**359,060**
Adjusted EBITDA	**$ 335,314**	**$ 505,034**	**$ 1,013,101**	**$ 868,266**	**$ 1,284,274**

GAAP to Non-GAAP Reconciliation

Operating Income – Three and Nine Months Ended September 30

$ in thousands	Three Months Ended September 30, 2022	Three Months Ended September 30, 2021	Nine Months Ended September 30, 2022	Nine Months Ended September 30, 2021
GAAP operating income	**$ 160,606**	**$ 331,543**	**$ 443,480**	**$ 310,040**
Non-GAAP adjustments:				
Acquisition/divestiture-related costs	825	9,224	3,437	89,241
Restructuring and realignment costs	7,731	680	9,521	7,703
Manufacturing facility start-up costs	2,024	1,712	4,413	1,712
Amortization and step-up:				
Intangible amortization expense	92,951	90,368	273,546	245,260
Inventory step-up expense	21,779	8,912	66,342	16,914
Impairment of long-lived asset	-	-	-	12,371
Impairment of goodwill	-	-	56,171	-
Gain on sale of asset	-	-	-	(2,000)
Share-based compensation	45,066	54,804	137,515	170,394
Depreciation	6,130	4,111	18,073	11,955
Litigation settlement	-	5,000	-	5,000
Total of non-GAAP adjustments	**176,506**	**174,811**	**569,018**	**558,550**
Non-GAAP operating income	**$ 337,112**	**$ 506,354**	**$ 1,012,498**	**$ 868,590**
Foreign exchange loss	(768)	(476)	(320)	(1,363)
Other (expense) income, net	(1,030)	(844)	923	1,039
Adjusted EBITDA	**$ 335,314**	**$ 505,034**	**$ 1,013,101**	**$ 868,266**

GAAP to Non-GAAP Reconciliation

Non-GAAP Net Income – Three and Nine Months Ended September 30

$ in thousands	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
GAAP net income	**$ 135,839**	**$ 326,543**	**$ 401,074**	**$ 361,309**
Non-GAAP adjustments:				
Acquisition/divestiture-related costs	825	9,228	3,437	88,166
Loss on equity security investments	1,247	-	6,331	-
Restructuring and realignment costs	7,731	680	9,521	7,703
Manufacturing facility start-up costs	2,024	1,712	4,413	1,712
Amortization and step-up:				
Intangible amortization expense	92,951	90,368	273,546	245,260
Inventory step-up expense	21,779	8,912	66,342	16,914
Amortization of debt discount and deferred financing costs	2,232	1,500	6,136	3,740
Impairment of long-lived asset	-	-	-	12,371
Impairment of goodwill	-	-	56,171	-
Gain on sale of asset	-	-	-	(2,000)
Share-based compensation	45,066	54,804	137,515	170,394
Depreciation	6,130	4,112	18,073	11,956
Litigation settlement	-	5,000	-	5,000
Total of pre-tax non-GAAP adjustments	**179,985**	**176,316**	**581,485**	**561,216**
Income tax effect of pre-tax non-GAAP adjustments	(24,623)	(36,602)	(121,754)	(141,665)
Other non-GAAP income tax adjustments	2,079	(56,007)	2,079	(25,126)
Total of non-GAAP adjustments	**157,441**	**83,707**	**461,810**	**394,425**
Non-GAAP net income	**$ 293,280**	**$ 410,250**	**$ 862,884**	**$ 755,734**

GAAP to Non-GAAP Reconciliation

Non-GAAP Earnings Per Share – Basic and Diluted – Three and Nine Months Ended September 30

	Three Months Ended September 30,		Nine Months Ended September 30,	
	2022	2021	2022	2021
Non-GAAP Earnings Per Share:				
Weighted average ordinary shares - Basic	**230,333,287**	**226,096,747**	**229,820,406**	**225,053,704**
Non-GAAP Earnings Per Share - Basic:				
GAAP earnings per share - Basic	**$ 0.59**	**$ 1.44**	**$ 1.75**	**$ 1.61**
Non-GAAP adjustments	0.68	0.37	2.00	1.75
Non-GAAP earnings per share - Basic	**$ 1.27**	**$ 1.81**	**$ 3.75**	**$ 3.36**
Weighted average ordinary shares - Diluted				
Weighted average ordinary shares - Basic	230,333,287	226,096,747	229,820,406	225,053,704
Ordinary share equivalents	5,052,283	10,102,042	6,102,624	10,202,720
Weighted average ordinary shares - Diluted	**235,385,570**	**236,198,789**	**235,923,030**	**235,256,424**
Non-GAAP Earnings Per Share - Diluted				
GAAP earnings per share - Diluted	**$ 0.58**	**$ 1.38**	**$ 1.70**	**$ 1.54**
Non-GAAP adjustments	0.67	0.36	1.96	1.67
Non-GAAP earnings per share - Diluted	**$ 1.25**	**$ 1.74**	**$ 3.66**	**$ 3.21**

GAAP to Non-GAAP Reconciliation

Net Debt – As of September 30, 2022

$ in thousands	As of September 30, 2022
Long-term debt-current maturities	$ 16,000
Long-term debt, net of current maturities	2,549,140
Total Debt	**2,565,140**
Debt discount	10,178
Deferred financing fees	18,708
Total Principal Amount of Debt	**2,594,026**
Less: cash and cash equivalents	2,130,527
Net Debt	**$ 463,499**