Second-Quarter 2021 Summary

Horizon Therapeutics plc

August 4, 2021

Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to Horizon's full-year 2021 net sales and adjusted EBITDA 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, studies 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 2021 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 presentation as a result of new information.

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Expanding Supply Capacity

Acquired biologics drug product manufacturing facility in Waterford, Ireland

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Our Pipeline

Advancing Horizon's Profile as an Innovation-Driven Biotech

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TEPEZZA®

One of the Most Successful Rare Disease Medicine Launches

6

KRYSTEXXA®

Transformed This 11-Year-Old Biologic into a High-Growth Medicine

7

UPLIZNA®

First and Only FDA-Approved B-Cell-Depleting Therapeutic for the Treatment of NMOSD

Horizon: High-Growth Biotech with a Proven Track Record of Outperformance

We are a **high-growth, innovation-driven, profitable biotech**

Delivering **innovative therapies** to patients

With a **strong track record of execution**

Focused on generating **high returns** for shareholders

What Sets Horizon Apart

Excellence in Commercial Execution

We seek to accelerate the growth trajectory and maximize the potential of our medicines through best-in-class commercial execution

Proven & Disciplined Business Development

We acquire medicines through our strong in-house business development capability, focused on opportunities where we are uniquely positioned to drive value

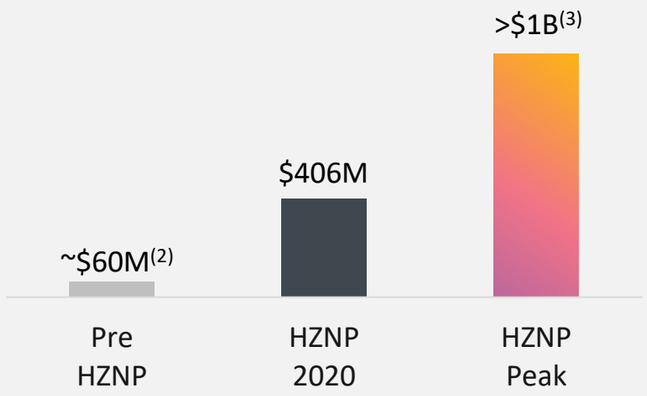
Strong Clinical Development Capability

We leverage deep drug development experience and an agile approach to continually innovate with our existing medicines and bring new ones to market

Examples of Our Proven Ability to Execute on All Three Fronts

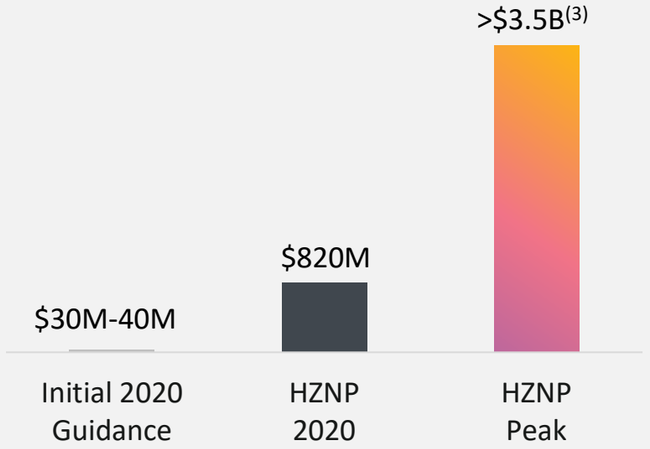
Excellence in Commercial Execution

KRYSTEXXA Annual Net Sales Pre- and Post-HZNP Ownership; Growth Has Been Volume Driven



Proven & Disciplined Business Development

TEPEZZA: Future Estimated Returns Far Exceed the Upfront Payment of ~$145M Plus Milestones(1)



Strong Clinical Development Capability

- **Expedited TEPEZZA approval through accelerated development program**
- **Developed and executing KRYSTEXXA immunomodulation strategy, doubling response rates (79%(4)+ vs. 42% in Phase 3)**
- **Achieved FDA approval for UPLIZNA in June 2020**

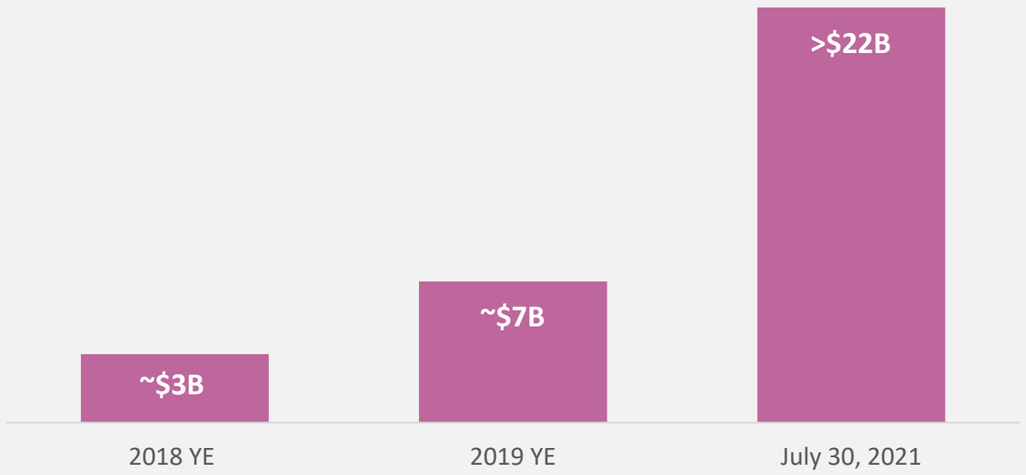
(1) Does not include royalties. (2) KRYSTEXXA net sales for FY15 recorded by Crealta Holdings LLC of ~$60M. (3) Horizon estimate of TEPEZZA and KRYSTEXXA peak U.S. annual net sales of >$3B and >$1B, respectively, and TEPEZZA ex-U.S. estimate of >$500M peak annual net sales. (4) Data from MIRROR open label trial (n=14). MIRROR randomized controlled trial on-going.

Horizon Has Delivered Significant Value Creation for Shareholders

Our Track Record of Execution Has Driven Transformational Growth; Significant Opportunity Exists

Transformed from small- to large-cap biotech in ~2 years
~7-fold market cap increase from 2018

Horizon Market Cap in $B[(1)]



Opportunity to take Horizon to the next level:

1. **Top-tier growth profile driven by TEPEZZA and KRYSTEXXA**
2. **Growing pipeline and business development to drive sustainable long-term growth**

(1) Market cap based on ordinary shares outstanding.
YE: Year end.

Second-Quarter 2021 and Recent Company Highlights

Outstanding Financial Results and Significant Progress Executing on Our Strategy

Financial Highlights

- **Record net sales of $832.5M,** up 80% driven by highly successful TEPEZZA relaunch; **adjusted EBITDA of $366.9M,** up 92%
- **Record TEPEZZA net sales of $453.3M** driven by strong demand and relaunch execution; **increasing full-year 2021 TEPEZZA net sales guidance to >$1.550B** and expect Q4 2021 year-over-year growth of >50%
- **Record KRYSTEXXA net sales of $130.3M,** up 73%; use with immunomodulation now >40%
- **Increasing full-year 2021 net sales guidance to $3.025B to $3.125B,** representing 40% growth at the midpoint; **increasing full-year 2021 adjusted EBITDA guidance to $1.26B to $1.30B,** representing 28% growth at the midpoint

Executing on Our Strategy

- Entered into **agreement with Arrowhead to develop a next-generation gout medicine** targeting XDH, a clinically validated target and primary source of serum uric acid
- **Acquired biologics drug product manufacturing facility** in Waterford, Ireland to support the growth of on-market medicines and development-stage biologics
- **Initiated enrollment in three trials:** KRYSTEXXA retreatment, HZN-7734 SLE and HZN-1116 autoimmune disease
- **New chronic TED data published** showing the benefit of treatment with TEPEZZA; adds to the growing body of evidence supporting the use of TEPEZZA in chronic TED patients
- **New UPLIZNA data presented** at medical meetings (AAN and EAN) **demonstrate long-term safety** and **efficacy in NMOSD**
- **Hosting Virtual R&D day on Sept. 29, 2021,** for investors and analysts

Note: Adjusted EBITDA is a non-GAAP measure; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.
XDH: Xanthine dehydrogenase. SLE: Systemic lupus erythematosus. TED: Thyroid Eye Disease. AAN: American Academy of Neurology. EAN: European Academy of Neurology. NMOSD: Neuromyelitis optica spectrum disorder.

Second-Quarter 2021 Financial Results

Performance Driven by Rapid TEPEZZA Relaunch

($M, except for per share amounts and percentages)	Q2 2021	Q2 2020	% Change	YTD 2021	YTD 2020	% Change
Net sales	**$832.5**	**$462.8**	**80**	**$1,175.0**	**$818.7**	**44**
Net Income (Loss)	158.1	(80.0)	298	34.8	(93.6)	137
Non-GAAP net income	381.4	83.8	355	388.8	167.0	133
Adjusted EBITDA	**366.9**	**190.7**	**92**	**412.7**	**297.9**	**39**
Earnings (Loss) per share – diluted	0.67	(0.42)	261	0.15	(0.49)	131
Non-GAAP earnings per share – diluted	1.62	0.40	305	1.66	0.80	108

Note: Non-GAAP net income, adjusted EBITDA and non-GAAP earnings per share are non-GAAP measures; see reconciliations at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.

Second-Quarter 2021 Orphan Segment Results

Strong Growth of TEPEZZA, KRYSTEXXA and Other Rare Disease Medicines Generated 97 Percent YOY Net Sales Growth

($M)	Q2 2021	Q2 2020	% Change		YTD 2021	YTD 2020	% Change
TEPEZZA®	$453.3	$165.9	173		$455.3	$189.4	140
KRYSTEXXA®	130.3	75.2	73		237.1	168.5	41
RAVICTI®(1)	68.4	65.6	4		141.3	126.7	12
PROCYSBI®	49.8	41.4	20		93.1	79.7	17
ACTIMMUNE®	27.8	28.3	(2)		56.5	54.8	3
UPLIZNA®(2)	14.5	-	NM		16.3	-	NM
BUPHENYL®(1)	2.2	2.8	(24)		3.9	5.2	(24)
QUINSAIR™	0.2	0.1	280		0.5	0.3	58
Orphan Net Sales	**$746.5**	**$379.3**	**97**		**$1,004.0**	**$624.6**	**61**
Orphan Segment Operating Income	**$321.2**	**$151.5**	**112**		**$322.3**	**$205.9**	**57**

(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.
NM: Not meaningful.

Second-Quarter 2021 Inflammation Segment Results

Accelerating Operating Margins Provide Cash Flows to Invest in Growth Drivers and Pipeline Expansion

($M)	Q2 2021	Q2 2020	% Change		YTD 2021	YTD 2020	% Change
PENNSAID 2%®	$48.9	$35.0	40		$94.8	$76.6	24
DUEXIS®	22.1	27.8	(20)		41.6	59.1	(30)
RAYOS®	13.4	14.5	(7)		28.7	32.7	(12)
VIMOVO®(1)	1.6	6.2	(75)		5.9	25.7	(77)
Inflammation Net Sales	**$86.0**	**$83.5**	**3**		**$171.0**	**$194.1**	**(12)**
Inflammation Segment Operating Income	**$46.8**	**$38.1**	**23**		**$89.4**	**$90.0**	**(1)**

(1) On Feb. 27, 2020, Dr. Reddy's Laboratory initiated an at-risk launch of generic VIMOVO in the U.S.

Increasing Full-Year 2021 Guidance Driven by TEPEZZA

	Updated Guidance	Previous Guidance
Net Sales	**$3.025B to $3.125B**	$2.75B to $2.85B
Adjusted EBITDA	**$1.26B to $1.30B**	$1.02B to $1.06B

Key Highlights

- Net sales and adjusted EBITDA guidance midpoints represent **year-over-year growth** of **40%** and **28%**, respectively
- Higher **TEPEZZA** full-year 2021 net sales expectations of **>$1.550B** (previously >$1.275B); 4Q 2021 year-over-year growth expected to be >50%
- The Company continues to expect **KRYSTEXXA** full-year 2021 net sales of **>$500M**

Note: Adjusted EBITDA is a non-GAAP measure.

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

Expanding our pipeline for sustainable growth

Maximizing the value of our key growth drivers

Building a global presence

Progress and Expected Milestones in 2021

- ✓ Resumed TEPEZZA commercial supply
- ✓ Completed Viela acquisition
- Initiating eight trials; four already initiated
- Key trial readouts
  - KRYSTEXXA MIRROR RCT in Q4 2021
  - KRYSTEXXA PROTECT in Q4 2021
- ✓ Arrowhead agreement for next-generation gout medicine
- ✓ Acquired biologics drug product manufacturing facility in Waterford, Ireland
- Building out infrastructure to support potential Q1 2022 approval and launch of UPLIZNA for NMOSD in Europe
- Bringing on a second TEPEZZA drug product manufacturer by year-end

Significant Anticipated Milestones Beyond 2021

- Key trial readouts
  - TEPEZZA chronic TED and SC administration program
  - KRYSTEXXA retreatment, shorter infusion duration and monthly dosing
  - UPLIZNA MG and IgG4-related disease
  - HZN-825 diffuse cutaneous systemic sclerosis and IPF
  - HZN-4920 Sjögren's syndrome
  - HZN-7734 SLE
- Continue building out pipeline and in-house R&D capabilities
- Launch UPLIZNA in Europe; continue global expansion
- Initiate TEPEZZA Japan clinical program
- Manufacturing approval of first medicine at Waterford biologics drug product manufacturing facility
- Advance toward peak net sales expectations
  - TEPEZZA: >$3.5B[(1)]; KRYSTEXXA: >$1B[(1)]

MIRROR RCT: Registrational, randomized, placebo-controlled 145-patient trial evaluating the use of KRYSTEXXA in combination with methotrexate to increase the response rate. PROTECT: Clinical trial evaluating the effect of KRYSTEXXA on serum uric acid levels in kidney transplant patients with uncontrolled gout.
NMOSD: Neuromyelitis optica spectrum disorder. TED: Thyroid Eye Disease. SC: Subcutaneous. MG: Myasthenia gravis. IgG4-RD: Immunoglobulin G4-related disease. IPF: Idiopathic pulmonary fibrosis. SLE: Systemic lupus erythematosus.
(1) Horizon estimate of TEPEZZA and KRYSTEXXA peak U.S. annual net sales of >$3B and >$1B, respectively, and TEPEZZA ex-U.S. estimate of >$500M peak annual net sales.

Acquisition of Biologics Drug Product Manufacturing Facility Advances Our Transformation

Leverages Technical Expertise to Build a Robust and Effective Manufacturing Operation

- Adds to Horizon's **strong network of manufacturing operations**
- Enables us to meet **unmet needs of people impacted by rare disease** around the world
- Acquisition is an important step in our transformation and plays important role in **global expansion**
- Will be used to **support growth of on-market biologics** (TEPEZZA, KRYSTEXXA, UPLIZNA) and **development-stage biologics**
- Next Steps
  - Approval for release of first medicine anticipated in ~2 years

Pipeline Update

Advancing Horizon's Profile as an Innovation-Driven Biotech

Advancing Our Pipeline to Drive Long-Term Growth

22 Programs with Eight Trials Scheduled to Initiate in 2021; Four Already Initiated

Key Milestones:

Upcoming Key Trial Initiations:

- TEPEZZA chronic TED: in coming weeks
- TEPEZZA diffuse cutaneous systemic sclerosis: Q3 2021
- HZN-825 diffuse cutaneous systemic sclerosis: Q3 2021
- HZN-825 IPF: Q3 2021

Key Trial Readouts:

- KRYSTEXXA MIRROR RCT: Q4 2021
- KRYSTEXXA PROTECT: Q4 2021
- TEPEZZA in chronic TED: 2H 2022
- UPLIZNA in IgG4-RD: 2023
- UPLIZNA in MG: 2023
- HZN-4920 in Sjögren's: 2023
- HZN-7734 in SLE: 2023
- HZN-825 in diffuse cutaneous systemic sclerosis: 2024
- HZN-825 in IPF: 2024

Program	Potential Indication	Preclinical	Phase 1	Phase 2	Phase 3
KRYSTEXXA	Combination with Immunomodulation in Uncontrolled Gout(1)				
UPLIZNA	Myasthenia Gravis				
	IgG4-Related Disease				
	Kidney Transplant Desensitization				
HZN-825	Diffuse Cutaneous Systemic Sclerosis				
	Idiopathic Pulmonary Fibrosis				
HZN-4920	Sjögren's Syndrome				
	Rheumatoid Arthritis				
	Kidney Transplant Rejection				
HZN-7734	Systemic Lupus Erythematosus				
TEPEZZA	Subcutaneous Administration				
	Diffuse Cutaneous Systemic Sclerosis				
HZN-1116	Autoimmune Diseases				
Arrowhead	Next-Gen Uncontrolled Gout				
HZN-003					
HZN-007					
HemoShear	Novel Gout Targets				

Horizon is exploring the potential of its on-market medicines to identify paths for new treatment methods and improve patient outcomes

- Evaluating efficacy and safety of **KRYSTEXXA** in broader patient populations – **PROTECT (nephrology)** and retreatment **(ADVANCE)**
- Exploring the patient experience with **KRYSTEXXA** – monthly dosing **(FORWARD)** and shorter infusion durations **(AGILE)**
- Quantifying the impact of **TEPEZZA** for patients with **chronic Thyroid Eye Disease**

TED: Thyroid Eye Disease. IPF: Idiopathic pulmonary fibrosis. RCT: Randomized controlled trial. IgG4-RD: Immunoglobulin G4-Related Disease MG: Myasthenia gravis. SLE: Systemic lupus erythematosus.
(1) Phase 4.

Entered into Agreement with Arrowhead to Develop Next-Generation Gout Medicine

Expanding Our Position as the Leader in Uncontrolled Gout

Transaction Overview

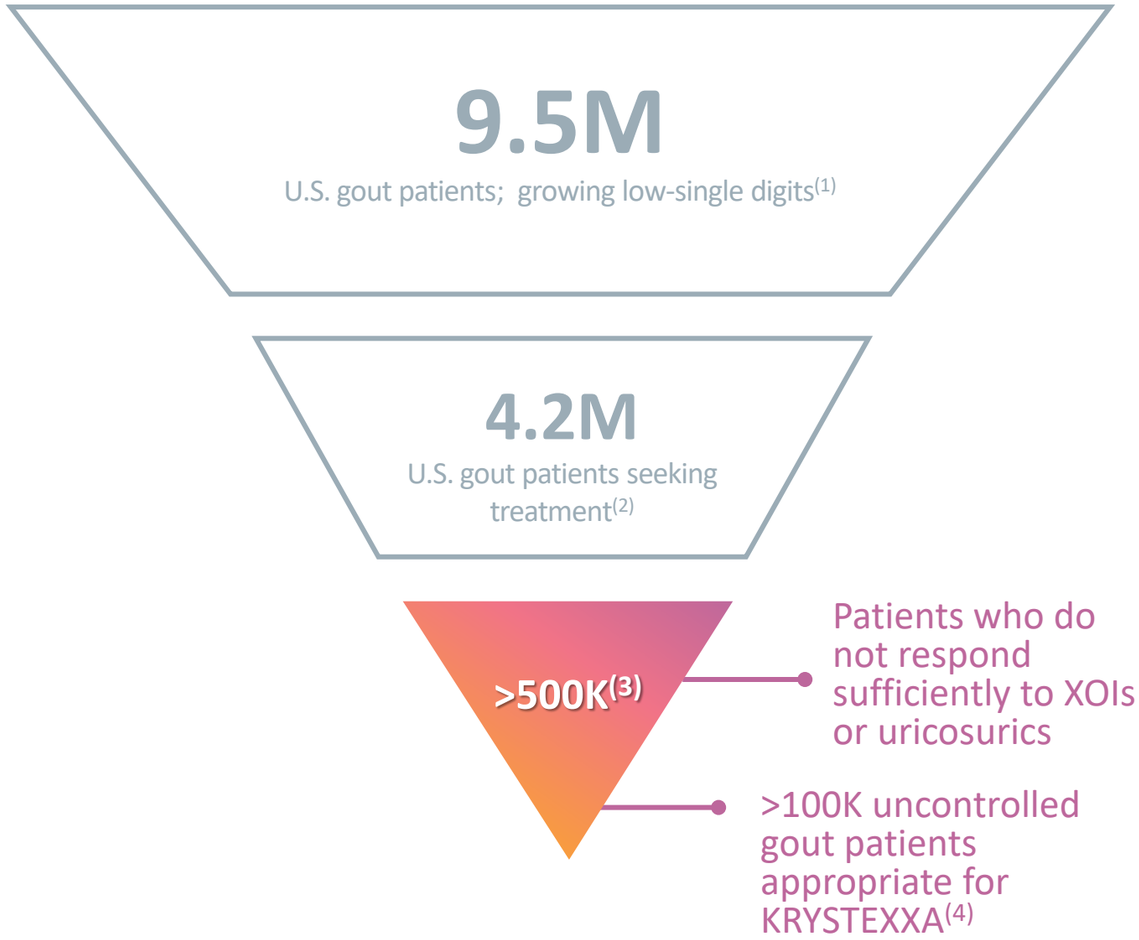
- Horizon and Arrowhead Pharmaceuticals Inc. entered into an agreement for a discovery-stage investigational RNAi therapeutic targeting XDH as a potential treatment for people with uncontrolled gout
- Upfront payment of $40M plus additional development, regulatory and commercial milestones and royalties

Strategic Rationale

- Hundreds of thousands of patients are treated with urate-lowering therapies and do not respond sufficiently
- Combines a validated target that is the primary source of serum uric acid (XDH) with a clinically validated modality (liver-specific GalNAc)
- As the leader in gout, Horizon is uniquely positioned to successfully develop and commercialize the candidate that comes out of this program

Development Plan

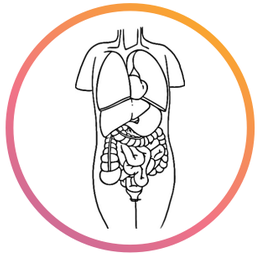
- Plan to start Phase 1 study within 2 years
- Potential approval in late 2020s



(1) Prevalence of gout and hyperuricemia in the U.S. general population: The National Health and Nutrition Examination Survey (NHANES) 2007-2016. Arthritis Rheum. 2019 Jun;71(6):991-999. (2) Horizon estimate based on analysis of IMS and IQVIA data.
(3) Approximate number of patients in addressable target market; Horizon estimates. (4) Approximate number of patients in our annual addressable target market in rheumatology and nephrology; Horizon estimate.
RNAi: RNA interference. XDH: Xanthine dehydrogenase. XOIs: Xanthine oxidase inhibitors.

UPLIZNA Being Pursued in Three Additional Indications, Representing a Large Opportunity

UPLIZNA: Next-Generation Anti-CD19 Humanized Monoclonal Antibody Engineered for Efficient, Targeted B-Cell Depletion



	Myasthenia Gravis (MG)	IgG4-Related Disease (IgG4-RD)	Kidney Transplant Desensitization
Indication & Trial Phase	• A chronic, rare autoimmune neuromuscular disorder • Symptoms include weakness in voluntary skeletal muscles, especially those that control the eyes, mouth, throat and limbs • Phase 3 randomized placebo-controlled trial **underway**	• A group of disorders marked by tumor-like swelling and fibrosis of affected organs, such as the pancreas, salivary glands and kidneys • Phase 3 randomized placebo-controlled trial **underway**	• Desensitization is aimed at reducing alloantibodies that often preclude patients with ESRD from finding a matching organ and also result in poor post-transplant outcomes through antibody mediated graft rejection • Phase 2 open-label trial **underway**

CD: Cluster of differentiation. ESRD: End-stage renal disease.

HZN-825 Advancing in Two Phase 2b Pivotal Trials

HZN-825 is an Oral LPAR$_1$ Antagonist that Selectively Targets the Area Which Is Believed to Drive Fibrosis

Indication & Trial Phase	Diffuse Cutaneous Systemic Sclerosis	Interstitial Lung Diseases (ILD)
	• Rare, chronic autoimmune disease that can progress to internal organ damage; high mortality rate(1) • Primarily managed by rheumatologists • Phase 2b pivotal trial **expected** to initiate Q3 2021	• Initiating our ILD program with a trial in the IPF indication. IPF is a rare progressive lung disease with a median survival of <5 years, and is the most common ILD • Managed by rheumatologists and pulmonologists • Phase 2b pivotal trial **expected** to initiate Q3 2021

- >80% of patients with diffuse cutaneous systemic sclerosis develop ILD(2)
- Primary endpoint in both trials will be Forced Vital Capacity (FVC)

(1) Nikpour M, Baron M. *Curr Opin Rheumatol.* 2014 Mar;26(2):131-7. (2) Hoffmann-Vold et al, 2015.
LPAR$_1$: Lysophosphatidic acid receptor 1. IPF: Idiopathic pulmonary fibrosis. Forced vital capacity is a measure of lung capacity used to assess the progression of lung disease and the effectiveness of treatment.

HZN-4920 in Phase 2 Trials for Three Indications, Each Addressing Immune Overactivation

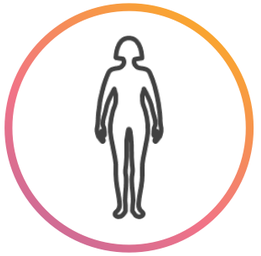
HZN-4920 is a CD40 Ligand Antagonist Designed to Block a Central Pathway Involved in Many Autoimmune Diseases

Indication & Trial Phase	Sjögren's Syndrome	Rheumatoid Arthritis	Kidney Transplant Rejection
	• An autoimmune disease attacking the salivary and tear glands, with severe cases affecting multiple organs • Symptoms include dry eyes, dry mouth, arthritis, kidney and lung or liver dysfunction • Phase 2b trial **underway**	• A chronic inflammatory disorder characterized by progressive destruction of joints • Phase 2 trial **underway**; dose-ranging	• Occurs when the immune system detects an organ transplant as a threat and attacks it • Results in organ rejection • Phase 2 open-label trial **underway**

CD: Cluster of differentiation.

HZN-7734 Phase 2 Trial Initiated; HZN-1116 Phase 1 Trial Initiated

HZN-7734 is a pDC Depleter and Anti-ILT7 Human Monoclonal Antibody; HZN-1116 is a Monoclonal Antibody



Indication & Trial Phase	Systemic Lupus Erythematosus (SLE)	Autoimmune Diseases
	HZN-7734	HZN-1116
	• Inflammatory disease in which the immune system can attack any organ system; in particular, affects the skin, joints, kidneys, blood cells, heart and lungs • Symptoms include skin rash, arthritis, kidney disease, inflammation of the heart and lungs • Phase 2 trial **initiated** June 2021	• Phase 1 trial **initiated** in July 2021

ILT: Immunoglobulin-like transcripts. pDCs: Plasmacytoid dendritic cells.

Maximizing the Long-Term Potential of TEPEZZA

Advancing Three R&D Programs

Thyroid Eye Disease (TED) Programs

Maximizing the Future and Long-Term Potential of TEPEZZA for TED Patients

Chronic Disease

- Randomized, placebo-controlled trial of TEPEZZA planned in chronic TED patients
- Objective is to generate data supporting TEPEZZA adoption in the already indicated chronic TED patient population
- **Expect** to initiate in coming weeks

Subcutaneous Administration

- Pharmacokinetic trial **underway** to explore subcutaneous TEPEZZA dosing
- Objective is to assess the potential for additional administration options for TEPEZZA
- Partnered with Halozyme to leverage proprietary ENHANZE® drug delivery technology

Potential Additional Indication

High Unmet Need in a Rare, Chronic Autoimmune Disease; Core Therapeutic Area

Diffuse Cutaneous Systemic Sclerosis

- Exploratory study to investigate the safety, tolerability and effect on IGF-1/IGF-1R inflammatory/fibrotic biomarkers
- Similar underlying pathologies of TED and diffuse cutaneous systemic sclerosis
- Preclinical data implicate IGF-1/IGF-1R signaling in diffuse cutaneous systemic sclerosis pathology
- **Expect** to initiate Phase 1 trial in Q3 2021

IGF-1R: Insulin-like growth factor 1 receptor.

KRYSTEXXA Development Programs

Five Trials Underway to Maximize the Value of KRYSTEXXA

Improve Response Rate

MIRROR RCT: Randomized, placebo-controlled trial **underway** evaluating KRYSTEXXA plus immunomodulator MTX

- Primary and secondary endpoint results after trial completes, expected Q4 2021

Demonstrate Benefit in Broader Populations

PROTECT: Open-label trial **underway** evaluating KRYSTEXXA for uncontrolled gout in kidney transplant patients (most severe)

Retreatment (ADVANCE): Open-label trial **initiated** May 2021 to evaluate KRYSTEXXA plus MTX in patients who have previously failed KRYSTEXXA alone

Improve Patient Experience

Shorter infusion duration (AGILE): Open-label trial **underway** evaluating KRYSTEXXA plus MTX at shorter durations (current duration is 2+ hours)

Monthly dosing (FORWARD): Open-label trial **underway** to assess impact of dosing two KRYSTEXXA plus MTX vials 1x/month (current dosing is one vial 2x/month)

MTX: Methotrexate.

TEPEZZA

One of the Most Successful Rare Disease Medicine Launches

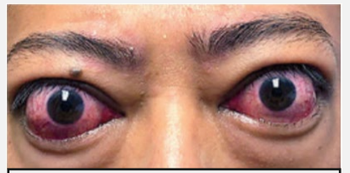
TEPEZZA is the First and Only Medicine Approved for Thyroid Eye Disease

Thyroid Eye Disease (TED)

- Rare, serious, progressive and vision-threatening autoimmune disease
  - Causes proptosis (eye bulging); associated with diplopia (double-vision); painful and disfiguring
- **15K-20K:** Estimated U.S. annual patient incidence of acute TED (lasts 1-3 years)(1)
- **>70K:** Estimated U.S. prevalence of chronic TED(1)
  - Symptoms no longer changing but persisting; typically includes patients who have had chronic TED for 5 years or less
- Comparable disease incidence/prevalence and burden in many other countries outside the U.S.

How TEPEZZA Works

- TEPEZZA is a targeted therapy that **significantly reduces proptosis**



Before

- TEPEZZA **blocks IGF-1R** and turns off signaling complex at the source of the disease

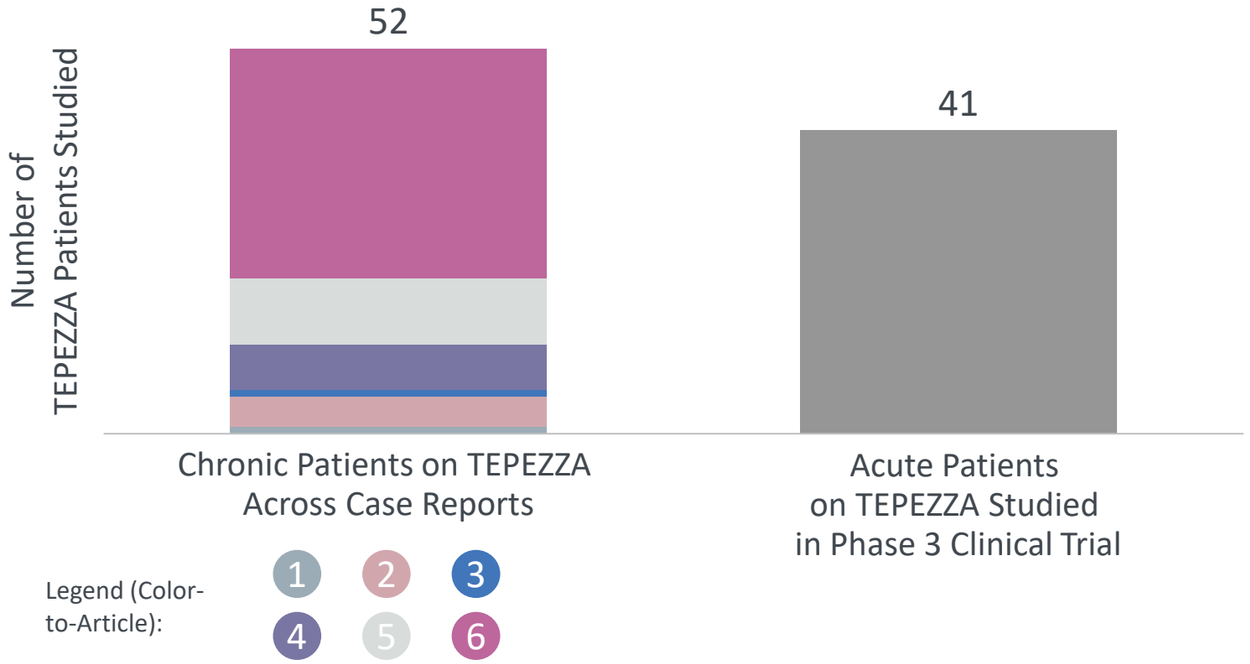
After

IGF-1R: Insulin-like growth factor 1 receptor.
(1) Horizon estimate.

Growing Body of Evidence Continues to Support the Use of TEPEZZA in Chronic TED

Case Study*	Patients	Key Results
1) Ozzello – AJO – 2020	1	Proptosis reduction of 5 mm and 6 mm in the right and left eye respectively after 3 infusions
2) Ugradar – Eye – 2020	4	4 non-inflammatory TED patients experienced mean proptosis reduction of 2.6 mm
3) Davis – NANOS – 2021 (Poster)	1	Proptosis reduction of 5-6 mm from baseline after completing treatment
4) Diniz – OPRS – 2021	6	71% overall proptosis response rate (proptosis reduction ≥2 mm)
5) Ozzello – Orbit – 2021	9	78% of study participants experienced proptosis reduction of ≥2 mm in at least one eye
6) Ugradar – Eye – 2021	31	90% of study participants experienced clinically significant improvement (≥2 mm) in proptosis

Total Number of Chronic TED Patients Across Case Studies Compared to Number of Acute Patients on TEPEZZA from Phase 3 Clinical Trial



* Studies ordered chronologically

(1) Ozzello DJ, et al. *Am J Ophthalmol Case Rep*. 2020 May 15;19:100744. doi: 10.1016/j.ajoc.2020.100744
(2) Ugradar S, et al. *Eye (Lond).* 2020 Nov 21. doi: 10.1038/s41433-020-01297-w
(3) Davis R, et al. NANOS 2021 Feb annual meeting abstract. https://collections.lib.utah.edu/ark:/87278/s6gz077j
(4) Diniz SB, et al. *Ophthalmic Plast Reconstr Surg*. 2021 Mar 8. doi: 10.1097/IOP.0000000000001959
(5) Ozzello DJ, et al. *Orbit*. 2021 Jun 1:1-8. doi: 10.1080/01676830.2021.1933081
(6) Ugradar S, et al. *Eye (Lond).* 2021 Jul 9. doi: 10.1038/s41433-021-01593-z

AJO: American Journal of Ophthalmology. OPRS: Ophthalmic Plastic and Reconstructive Surgery. NANOS: North American Neuro-Ophthalmology Society. TRCO: The Royal College of Ophthalmologists.
Note: Data from separate clinical trials may not be directly comparable due to differences in trial protocols, endpoints, conditions and patient populations.

We Are Investing to Drive the Continued Strong Growth of TEPEZZA

Supply Capacity

- **Resumed TEPEZZA supply** in April following U.S. FDA approval of increased scale of production process for TEPEZZA
- On track to add second **drug product manufacturer** by end of 2021, as well as working to add two additional **drug substance manufacturing** sites
- Acquired biologics drug product manufacturing facility for TEPEZZA and other medicines

Commercial Execution

- **Doubled** commercial and field-based organization to **~200 employees**
- **Expanding marketing strategies** to drive increased awareness of TED
- Significant investment in national branded and unbranded television (DTC) campaigns

Global Expansion

- Pursuing global strategy for TEPEZZA to **drive access in other parts of the world**
- Planning to enter a broad range of markets across multiple geographies, including Japan

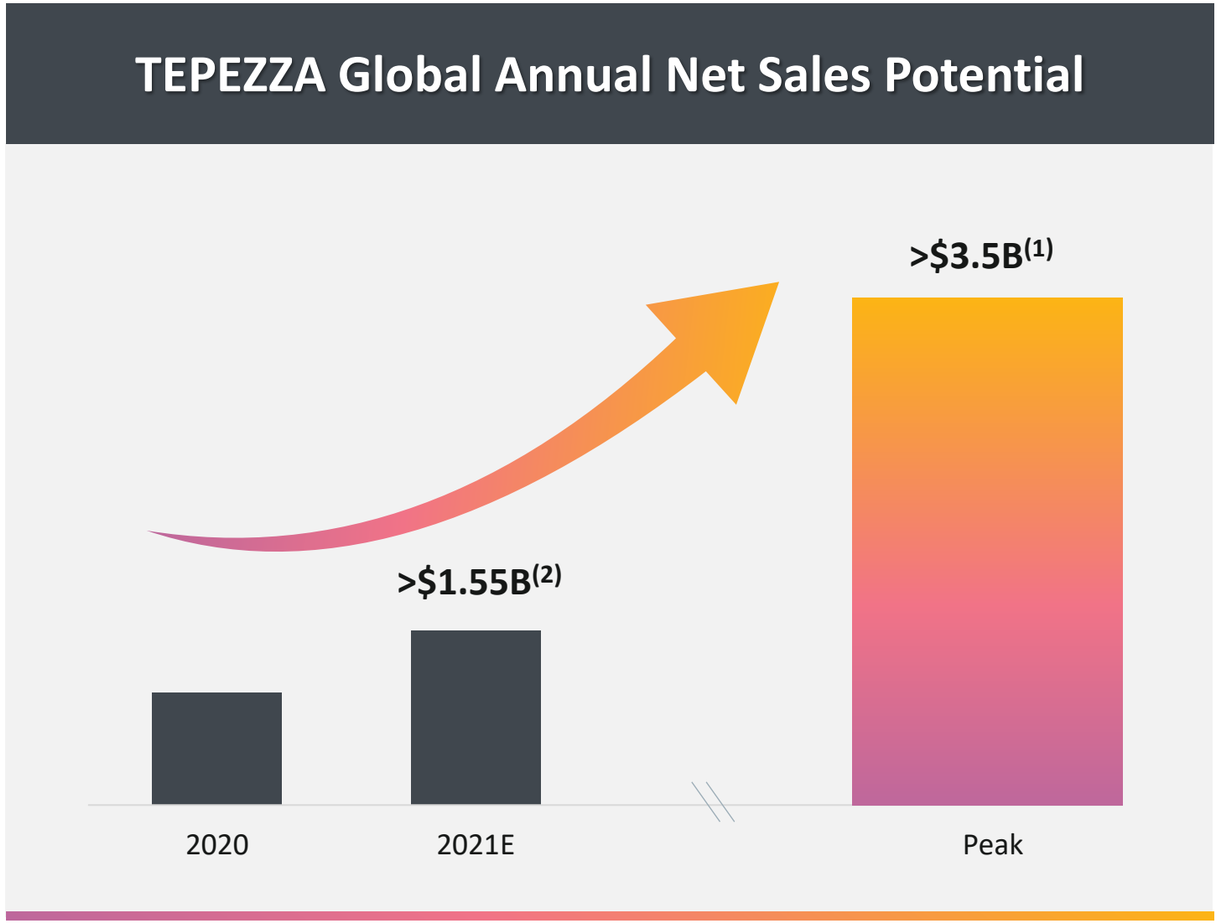
TED: Thyroid Eye Disease. DTC: Direct-to-consumer.

Exceptional Launch and Increased Net Sales Opportunity

Peak Annual Net Sales Estimate >$3.5B[(1)]

Growth Drivers

1. **Pre-launch, launch and new expansion efforts to drive strong awareness and high demand**
2. **Severity of disease a motivating factor for patients to seek treatment**
3. **Broad label allows for adoption in acute and chronic patients**



(1) Horizon estimate of TEPEZZA peak U.S. annual net sales of >$3B and TEPEZZA ex-U.S. estimate of >$500M peak annual net sales. (2) Horizon 2021 guidance.

KRYSTEXXA

Transformed a 11-Year-Old Biologic into a High-Growth Medicine

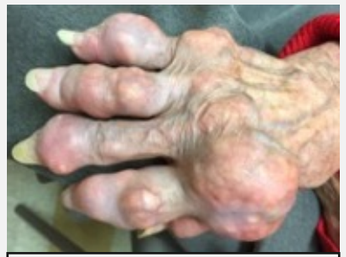
KRYSTEXXA is the Only Medicine Approved For Uncontrolled Gout

Uncontrolled Gout

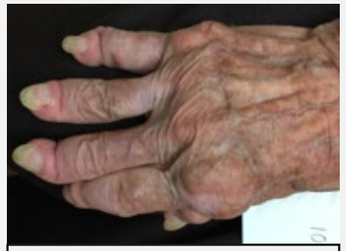
- Gout is the most common inflammatory arthritis; systemic disease with multiple co-morbidities
- **9.5 million estimated U.S. gout patients** growing at low-single digits per year(1)
- **>100K uncontrolled gout patients** appropriate for KRYSTEXXA in the U.S., growing in line with gout population(2)
- Opportunity for KRYSTEXXA to help **significantly more patients**

How KRYSTEXXA Works

- KRYSTEXXA **rapidly reverses** disease progression(3)
- **Converts urate**, the source of uric acid crystals, **into a water-soluble substance**, allantoin



Before



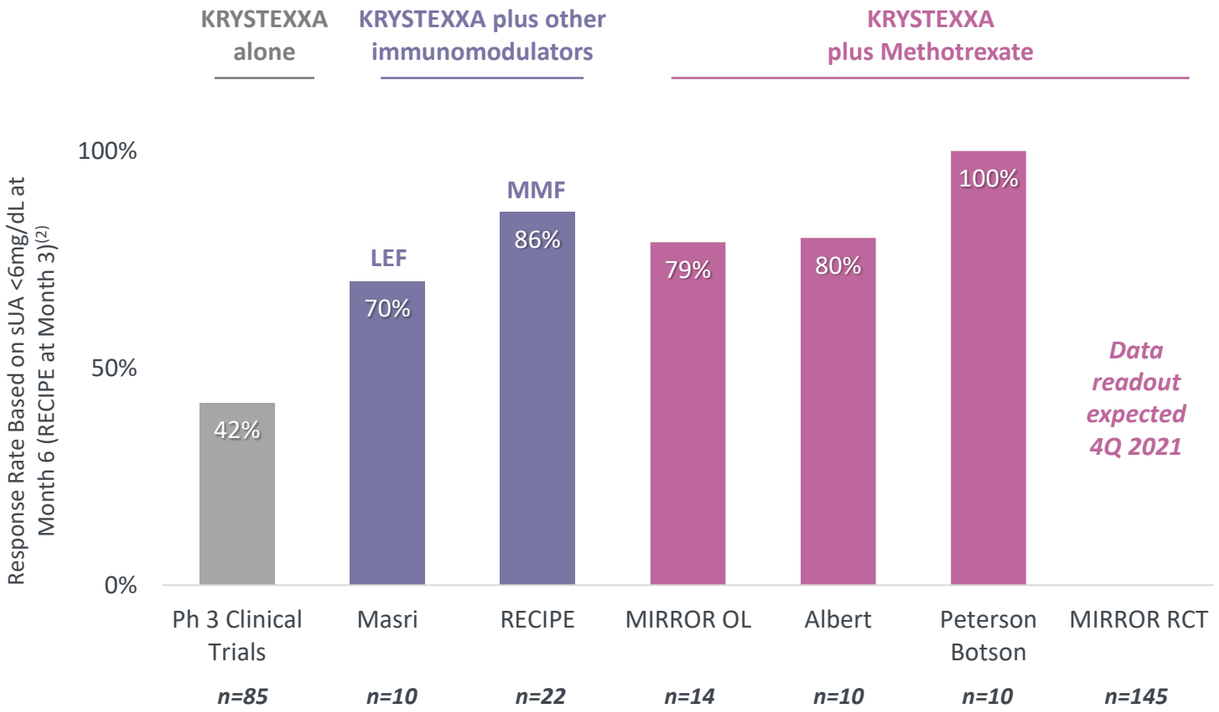
After

(1) Prevalence of gout and hyperuricemia in the U.S. general population: *The National Health and Nutrition Examination Survey* (NHANES) 2007-2016. Arthritis Rheum. 2019 Jun;71(6):991-999.
(2) Approximate number of patients in our annual addressable target market in rheumatology and nephrology; Horizon estimate.
(3) Sundy JS, Baraf HSB, Yood RA, et al. Efficacy and Tolerability of Pegloticase for the Treatment of Chronic Gout in Patients.
Uncontrolled gout: Chronic gout refractory (unresponsive) to conventional therapies

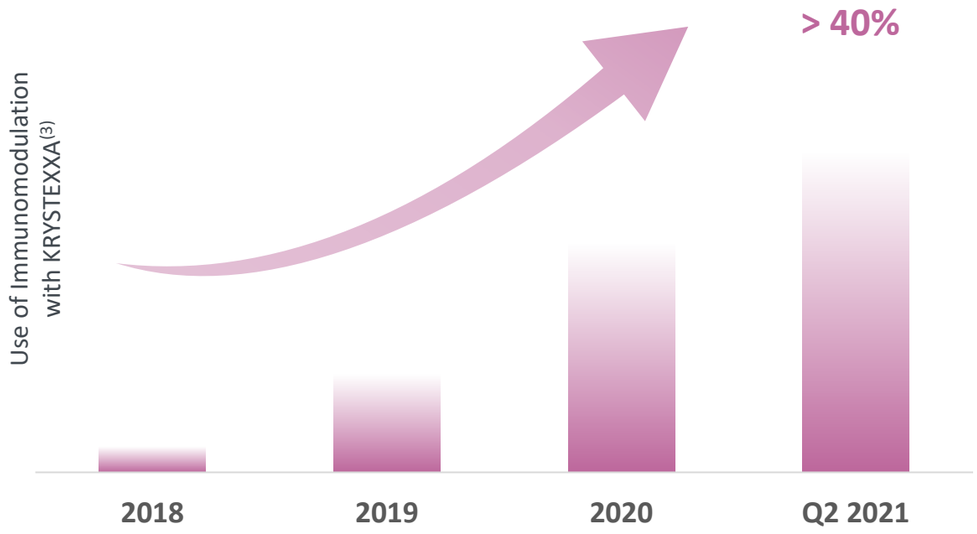
KRYSTEXXA Immunomodulation Strategy is Resonating with Physicians

Aiming to Maximize the Number of Patients That Benefit from KRYSTEXXA

Response Rate of KRYSTEXXA plus Immunomodulators Significantly Higher Than KRYSTEXXA Alone(1)



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



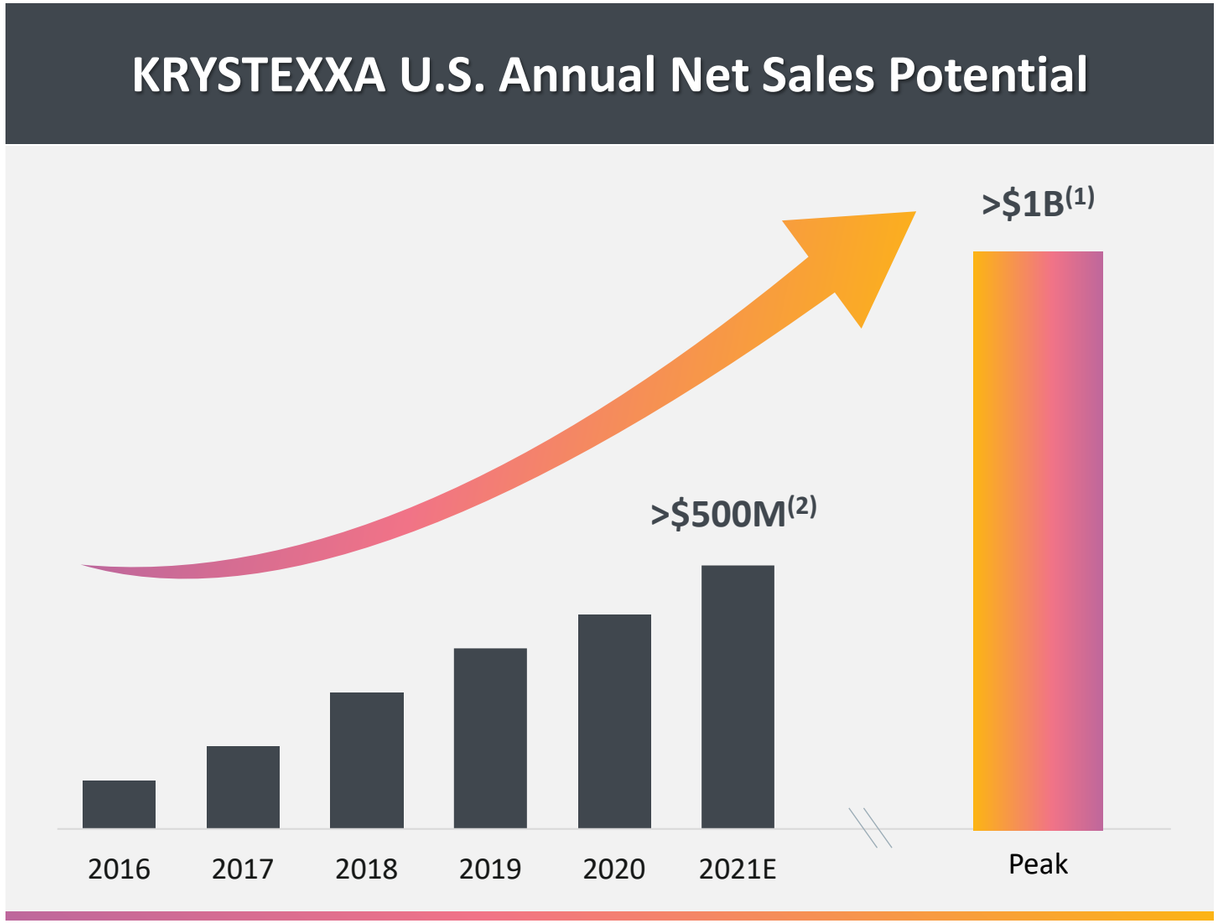
(1) Reflects KRYSTEXXA plus immunomodulation results. (2) Albert and Masri based on patient receiving ≥12 infusions. (3) Horizon analysis of Hub and claims data of KRYSTEXXA-treated patients also receiving immunomodulators.
RECIPE is an investigator-initiated randomized (3:1) placebo-controlled trial with 32 patients. 86% (19 of 22 patients) of KRYSTEXXA with MMF patients achieved the primary endpoint at Week 12 vs. 40% (4 of 10) in the placebo arm. At Week 24, when all patients were on KRYSTEXXA therapy alone for 12 weeks, sUA response was sustained in 68% of the MMF arm vs. 30% in the placebo arm. KRYSTEXXA Phase 3 Clinical Trials (blinded, placebo-controlled): 36 out of 85 patients achieved a complete response. MIRROR OL (open-label): 11 out of 14 patients enrolled achieved a complete response.
Albert Case Series (open-label): 8 out of 10 patients achieved a complete response. *Arthritis & Rheumatology,* 2019;71(S10): Abstract 1236. Peterson Botson Case Series (open-label): 10 out of 10 patients achieved a complete response. *Annals of the Rheumatic Diseases,* 2019;78(2):SAT0404.
Masri Case Series (open-label): 7 out of 10 patients achieved a complete response. LEF: Leflunomide. MMF: Mycophenolate mofetil. MTX: methotrexate. RCT: Randomized controlled trial. Note: Data from separate clinical trials may not be directly comparable due to differences in trial protocols, endpoints, conditions and patient populations.

KRYSTEXXA Commercial Strategy Has Accelerated Volume Growth

Peak U.S. Annual Net Sales Expectations of >$1B[(1)]

Growth Drivers

1. **Growth in use of KRYSTEXXA plus Immunomodulation**
2. **Growth in New and Existing Accounts**
3. **Accelerating Nephrology Growth**



(1) Horizon estimate. (2) Horizon 2021 guidance.

UPLIZNA

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

UPLIZNA U.S. Relaunch Strategy and Global Expansion

Expect to Complete Field Expansion by End of Q3 2021; Added Significant Neurology Talent to Date

OPTIMIZE
UPLIZNA through Focused Commercial Execution

- **Invest** in sales and marketing organization to expand reach and share of voice
- **Establish best-in-class** patient services, site of care and payer support
- **Raise awareness** of the benefits of UPLIZNA vs. other therapies

MAXIMIZE
the Value of UPLIZNA through Collaborative and Clinical Research

- **Invest** in medical and scientific engagement; **establish scientific leadership**
- **Conduct further analysis** of UPLIZNA NMOSD data to expand understanding of differentiation
- **Continue to build base** of compelling real-world evidence

GLOBALIZE
UPLIZNA Beginning with Europe

- **Preparing to build out European infrastructure** to support the launch of UPLIZNA for NMOSD as well as evaluating other markets in connection with our **global expansion strategy**
- **Adding key capabilities** to support the potential near-term launch of UPLIZNA as well as the potential launch of additional medicines

NMOSD: Neuromyelitis optica spectrum disorder.

Building a Robust Commercial Infrastructure to Support the UPLIZNA Patient Journey

Applying Key Learnings from TEPEZZA and KRYSTEXXA to the Relaunch of UPLIZNA for Treatment of NMOSD

Physicians

Expanding the sales force with deep physician relationships and buy-and-bill experience; adding field-based KOL liaisons

- Disease and treatment education
- Education on the benefits of UPLIZNA vs. other therapies
- Referral facilitation
- Reimbursement support

Patient Education & Support

Leveraging Horizon's leading patient services capabilities and dedicated marketing efforts

- 1-to-1 patient support from diagnosis through treatment
- Disease and treatment education
- Grassroots advocacy efforts

Site of Care (Infusion Centers)

National and regional teams supporting infusion centers

- Logistical support
- Referral network build out
- Site-of-care identification and segmentation
- Disease and treatment education
- Reimbursement education

Payers

Reimbursement team supporting access

- Disease and treatment education
- Value proposition education to ensure optimal patient access

NMOSD: Neuromyelitis optica spectrum disorder.

Impressive Clinical Trial Results Support UPLIZNA as a Safe and Effective Long-Term Treatment for NMOSD

New UPLIZNA Data from Phase 2/3 Trial Presented at Premier Medical Meetings

American Academy of Neurology (AAN) and European Academy of Neurology (EAN)

AAN 2021 Virtual Annual Meeting

ean the home of neurology

Key Findings Support Safe and Effective Long-Term Use

- **Long-term UPLIZNA** treatment provided a **sustained reduction** in **NMOSD attack risk** from baseline
- **87.7%** of original RCP UPLIZNA patients (n=165) and **83.4%** percent of original RCP placebo patients (n=51) **remained attack-free** during OLP **for at least four years**

Americas Committee for Treatment and Research in Multiple Sclerosis (ACTRIMS)

actrims 2021 FORUM VIRTUAL February 25-27

Key Findings Support Durable Effect of UPLIZNA, Including Patient Switches from Rituximab

- **Safety** and **efficacy** of UPLIZNA **demonstrated** in patients with **previous rituximab exposure** (n=17)
- **Similar annual relapse rate** between the groups:
  - **Prior** rituximab exposure patients: **0.083**
  - **No prior** rituximab exposure patients: **0.102**

NMOSD: Neuromyelitis optica spectrum disorder. OLP: Open-label period. RCP: Randomized controlled period.

Reconciliations of GAAP to Non-GAAP Measures

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 operating expenses and non-GAAP operating income, 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 as well as EBITDA exclude acquisition and/or divestiture-related expenses, gain or loss from divestiture, gain or loss from sale of assets, upfront, progress and milestone payments related to license and collaboration agreements, litigation settlements, loss on debt extinguishment, costs of debt refinancing, drug manufacturing harmonization costs, restructuring and realignment costs, the income tax effect on pre-tax non-GAAP adjustments and other non-GAAP income tax adjustments, as well as non-cash items such as share-based compensation, depreciation and amortization, non-cash interest expense, long-lived asset impairment charges 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 2021 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. For example, adjusted EBITDA is used by Horizon as one measure of management performance under certain incentive compensation arrangements. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, financial measures calculated in accordance with GAAP. The non-GAAP financial measures used by 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 2021 adjusted EBITDA 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).

GAAP to Non-GAAP Reconciliation

EBITDA and Adjusted EBITDA – Three and Six Months Ended June 30

$ in thousands	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
GAAP net income (loss)	**$ 158,117**	**$ (80,010)**	**$ 34,766**	**$ (93,601)**
Depreciation	3,393	6,907	7,844	14,072
Amortization and step-up:				
Intangible amortization expense	88,523	66,749	154,892	125,324
Inventory step-up expense	7,091	-	8,002	-
Interest expense, net (including amortization of debt discount and deferred financing costs)	22,581	18,571	36,041	35,915
(Benefit) expense for income taxes	(42,484)	82,964	(90,235)	63,938
EBITDA	**$ 237,221**	**$ 95,181**	**$ 151,310**	**$ 145,648**
Other non-GAAP adjustments:				
Acquisition/divestiture-related costs	29,830	47,103	78,938	47,097
Restructuring and realignment costs	930	-	7,023	-
Impairment of long-lived assets	-	1,072	12,371	1,072
Gain on sale of asset	(2,000)	-	(2,000)	-
Share-based compensation	54,424	27,057	115,590	83,478
Upfront, progress and milestone payments related to license and collaboration agreements	46,500	3,000	49,500	3,000
Fees related to refinancing activities	-	-	-	54
Loss on debt extinguishment	-	17,254	-	17,254
Drug substance harmonization costs	-	-	-	290
Total of other non-GAAP adjustments	**129,684**	**95,486**	**261,422**	**152,245**
Adjusted EBITDA	**$ 366,905**	**$ 190,667**	**$ 412,732**	**$ 297,893**

GAAP to Non-GAAP Reconciliation

Operating Income – Three and Six Months Ended June 30

$ in thousands	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
GAAP operating income (loss)	**$ 138,515**	**$ 37,864**	**$ (21,503)**	**$ 21,373**
Non-GAAP adjustments:				
Acquisition/divestiture-related costs	30,626	46,988	80,017	47,272
Restructuring and realignment costs	930	-	7,023	-
Amortization and step-up:				
Intangible amortization expense	88,523	66,749	154,892	125,324
Inventory step-up expense	7,091	-	8,002	-
Impairment of long-lived assets	-	1,072	12,371	1,072
Gain on sale of asset	(2,000)		(2,000)	
Share-based compensation	54,424	27,057	115,590	83,478
Depreciation	3,393	6,907	7,844	14,072
Upfront, progress and milestone payments related to license and collaboration agreements	46,500	3,000	49,500	3,000
Fees related to refinancing activities	-	-	-	54
Drug substance harmonization costs	-	-	-	290
Total of non-GAAP adjustments	**229,487**	**151,773**	**433,239**	**274,562**
Non-GAAP operating income	**$ 368,002**	**$ 189,637**	**$ 411,736**	**$ 295,935**
Orphan segment operating income	321,235	151,541	322,289	205,897
Inflammation segment operating income	46,767	38,096	89,447	90,038
Total segment operating income	**$ 368,002**	**$ 189,637**	**$ 411,736**	**$ 295,935**
Foreign exchange (loss) gain	(39)	283	(887)	1,059
Other (expense) income, net	(1,058)	747	1,883	899
Adjusted EBITDA	**$ 366,905**	**$ 190,667**	**$ 412,732**	**$ 297,893**

GAAP to Non-GAAP Reconciliation

Non-GAAP Net Income – Three and Six Months Ended June 30

$ in thousands	Three Months Ended June 30, 2021	Three Months Ended June 30, 2020	Six Months Ended June 30, 2021	Six Months Ended June 30, 2020
GAAP net income (loss)	**$ 158,117**	**$ (80,010)**	**$ 34,766**	**$ (93,601)**
Non-GAAP adjustments:				
Acquisition/divestiture-related costs	29,830	47,103	78,938	47,097
Restructuring and realignment costs	930	-	7,023	-
Amortization and step-up:				
Intangible amortization expense	88,523	66,749	154,892	125,324
Inventory step-up expense	7,091	-	8,002	-
Amortization of debt discount and deferred financing costs	1,467	5,248	2,240	10,817
Impairment of long-lived assets	-	1,072	12,371	1,072
Gain on sale of asset	(2,000)	-	(2,000)	-
Share-based compensation	54,424	27,057	115,590	83,478
Depreciation	3,393	6,907	7,844	14,072
Upfront, progress and milestone payments related to license and collaboration agreements	46,500	3,000	49,500	3,000
Fees related to refinancing activities	-	-	-	54
Loss on debt extinguishment	-	17,254	-	17,254
Drug substance harmonization costs	-	-	-	290
Total of pre-tax non-GAAP adjustments	**230,158**	**174,390**	**434,400**	**302,458**
Income tax effect of pre-tax non-GAAP adjustments	(37,747)	(25,797)	(111,251)	(57,059)
Other non-GAAP income tax adjustments	30,881	15,210	30,881	15,210
Total of non-GAAP adjustments	**223,292**	**163,803**	**354,030**	**260,609**
Non-GAAP net income	**$ 381,409**	**$ 83,793**	**$ 388,796**	**$ 167,008**

GAAP to Non-GAAP Reconciliation

Non-GAAP Earnings (Loss) Per Share – Basic and Diluted – Three and Six Months Ended June 30

$ in thousands except share and per share data	Three Months Ended June 30,		Six Months Ended June 30,	
	2021	2020	2021	2020
Non-GAAP Earnings Per Share:				
Weighted average ordinary shares - Basic	**225,119,684**	**192,705,535**	**224,523,538**	**191,426,864**
Non-GAAP Earnings Per Share - Basic:				
GAAP earnings (loss) per share - Basic	**$ 0.70**	**$ (0.42)**	**$ 0.15**	**$ (0.49)**
Non-GAAP adjustments	0.99	0.85	1.58	1.36
Non-GAAP earnings per share - Basic	**$ 1.69**	**$ 0.43**	**$ 1.73**	**$ 0.87**
Non-GAAP Net Income	**$ 381,409**	**$ 83,793**	**$ 388,796**	**$ 167,008**
Effect of assumed exchange of Exchangeable Senior Notes, net of tax	-	1,692	-	3,567
Numerator - non-GAAP net income	**$ 381,409**	**$ 85,485**	**$ 388,796**	**$ 170,575**
Weighted average ordinary shares - Diluted				
Weighted average ordinary shares - Basic	225,119,684	192,705,535	224,523,538	191,426,864
Ordinary share equivalents	10,072,176	21,838,670	10,196,292	22,084,476
Denominator - weighted average ordinary shares – Diluted	**235,191,860**	**214,544,205**	**234,719,830**	**213,511,340**
Non-GAAP Earnings Per Share - Diluted				
GAAP earnings (loss) per share - Diluted	**$ 0.67**	**$ (0.42)**	**$ 0.15**	**$ (0.49)**
Non-GAAP adjustments	0.95	0.85	1.51	1.36
Diluted earnings per share effect of ordinary share equivalents	-	(0.03)	-	(0.07)
Non-GAAP earnings per share - Diluted	**$ 1.62**	**$ 0.40**	**$ 1.66**	**$ 0.80**