First-Quarter 2021 Summary

Horizon Therapeutics plc

May 5, 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; the potential benefits and other impacts of the Viela Bio acquisition; development 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 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.

First-Quarter 2021 Summary

- Horizon Overview
- First-Quarter 2021 and Recent Company Highlights
- First-Quarter 2021 Financial Results
- Full-Year 2021 Guidance
- Pipeline Update
- Commercial Updates:
  - UPLIZNA®
  - TEPEZZA®
  - KRYSTEXXA®

Horizon: High-Growth Biotech with a Proven Track Record

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

Delivering **innovative therapies** to patients

With a **strong track record of strategic execution**

Generating **high returns** for shareholders

What Sets Horizon Apart

Excellence in Commercial Execution

We 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

First-Quarter 2021 and Recent Company Highlights

Significant Progress Executing on Our Strategy; Completed Strategic Acquisition of Viela Bio, Inc.

Financial Highlights

- **Q1 2021 net sales** of **$342.4M**; **adjusted EBITDA** of **$45.8M**
- **Updating full-year 2021 net sales guidance** to **$2.75B** to **$2.85B,** representing 27% growth at the midpoint; incorporates Viela
  - Reflects **TEPEZZA** full-year 2021 net sales guidance of **>$1.275B** and **KRYSTEXXA** full-year 2021 net sales guidance of **>$500M**
- **Updating full-year 2021 adjusted EBITDA guidance** to **$1.02B** to **$1.06B**; incorporates significant Viela R&D investment

Executing on Our Strategy

- **Completed Viela acquisition**; advances Horizon's strategy to expand the pipeline to sustain long-term growth by adding four pipeline candidates in nine development programs, as well as one on-market medicine
- **Resumed TEPEZZA supply** in April following short-term supply disruption due to U.S. government-mandated COVID-19 vaccine orders; made progress with **second drug product manufacturer**
- **Advancing Horizon's global expansion with European UPLIZNA launch preparations**; adding key EU infrastructure to support the potential launch of UPLIZNA in Europe in the near term as well as the potential launch of additional medicines over the long term
- **Presented new UPLIZNA data** at medical meetings (AAN and ACTRIMS) **demonstrating long-term safety** and **efficacy in NMOSD**
- **Initiated** enrollment in **KRYSTEXXA monthly dosing** trial; **completed enrollment** in **KRYSTEXXA PROTECT t**rial
- **Progressed TEPEZZA subcutaneous administration** clinical program
- **Continued adoption of immunomodulation with KRYSTEXXA**, prescribed for 35% to 40% of new patients starts

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.
AAN: American Academy of Neurology. ACTRIMS: American Committee for Treatment and Research in Multiple Sclerosis. NMOSD: Neuromyelitis optica spectrum disorder. PROTECT: Clinical trial evaluating the effect of KRYSTEXXA on serum uric acid levels in kidney transplant patients with uncontrolled gout.

First-Quarter 2021 Financial Results

($M, except for per share amounts and percentages)	Q1 2021	Q1 2020	% Change
Net sales	**$342.4**	**$355.9**	**(4)**
Net loss	(123.4)	(13.6)	NM
Non-GAAP net income	7.4	83.2	(91)
Adjusted EBITDA	**45.8**	**107.2**	**(57)**
Loss per share – diluted	(0.55)	(0.07)	NM
Non-GAAP earnings per share – diluted	0.03	0.40	(93)

Note:

- First-quarter 2021 results were negatively impacted by a short-term TEPEZZA supply disruption due to U.S. government-mandated COVID-19 vaccine orders

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.
NM: Not meaningful.

First-Quarter 2021 Orphan Segment Results

5% Year-Over-Year Increase in Net Sales Driven by KRYSTEXXA, RAVICTI, PROCYSBI and ACTIMMUNE

($M)	Q1 2021	Q1 2020	% Change
KRYSTEXXA	$106.7	$93.3	14
RAVICTI®(1)	72.8	61.2	19
PROCYSBI®	43.4	38.3	13
ACTIMMUNE®	28.8	26.5	8
TEPEZZA(2)	2.1	23.5	(91)
UPLIZNA(3)	1.8	-	NM
BUPHENYL®(1)	1.7	2.3	(28)
QUINSAIR™	0.2	0.3	(25)
Orphan Net Sales	**257.5**	**245.4**	**5**
Orphan Segment Operating Income	**1.1**	**54.4**	**(98)**

(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) First-quarter 2021 TEPEZZA net sales were negatively impacted by a short-term supply disruption due to U.S. government-mandated COVID-19 vaccine orders. First-quarter 2021 TEPEZZA net sales relate to an adjustment of 2020 gross-to-net reserves recorded in the first quarter of 2021.
(3) UPLIZNA was acquired on March 15, 2021.
NM: Not meaningful.

First-Quarter 2021 Inflammation Segment Results

Steady Operating Margins Provide Cash Flows to Invest in Growth Drivers and Expand Pipeline

($M)	Q1 2021	Q1 2020	% Change
PENNSAID 2%®	$45.8	$41.6	10
DUEXIS®	19.5	31.3	(38)
RAYOS®	15.3	18.2	(16)
VIMOVO®(1)	4.3	19.4	(78)
Inflammation Net Sales	**84.9**	**110.5**	**(23)**
Inflammation Segment Operating Income	**42.7**	**51.9**	**(18)**

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

Updating Full-Year 2021 Guidance

Updated Ranges Incorporate Viela, Which Was Acquired March 15, 2021

	Updated Guidance	Previous Guidance
Net Sales	**$2.75B to $2.85B**	$2.70B to $2.80B
Adjusted EBITDA	**$1.02B to $1.06B**	$1.14B to $1.18B

Key highlights

- Updated net sales and adjusted EBITDA guidance midpoints represent **year-over-year growth** of **27%** and **4%** respectively
  - The updated guidance ranges incorporate Viela, including significant R&D investment
- The Company continues to expect **TEPEZZA** full-year 2021 net sales of **>$1.275B**
- 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 Globally Expanding Biotech

Expanding our pipeline for sustainable growth

Maximizing the value of our key growth drivers TEPEZZA and KRYSTEXXA

Building a global presence

Progress and Expected Milestones in 2021

- ✓ Resume TEPEZZA commercial supply
- ✓ Complete Viela acquisition
- Advance the following key trials
  - ✓ TEPEZZA SC with Halozyme technology(1)
  - – TEPEZZA chronic TED; initiate mid-2021
  - ✓ KRYSTEXXA monthly dosing
  - – KRYSTEXXA retreatment; initiate Q2 2021
  - – HZN-825 dcSSc; initiate Q2 2021
  - – HZN-825 IPF; initiate mid-2021
  - – HZN-7734 SLE; initiate mid-2021
- Trial readouts
  - – KRYSTEXXA MIRROR RCT in Q4 2021
  - – KRYSTEXXA PROTECT in Q4 2021

Significant Anticipated Milestones Beyond 2021

- Key trial readouts
  - – TEPEZZA chronic TED
  - – TEPEZZA SC administration program
  - – KRYSTEXXA retreatment, shorter infusion duration and monthly dosing
  - – UPLIZNA MG
  - – UPLIZNA IgG4-related disease
  - – HZN-825 dcSSc
  - – HZN-825 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
- Advance toward peak net sales expectations
  - – TEPEZZA: >$3.5B(2); KRYSTEXXA: >$1B(2)

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.
dcSSc: Diffuse cutaneous systemic sclerosis. IPF: Idiopathic pulmonary fibrosis. MG: Myasthenia gravis. SC: Subcutaneous. SLE: Systemic lupus erythematosus
(1) TEPEZZA SC program initiated in 2020; completed dosing of a Phase 1 trial in 2021. (2) 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.

Pipeline Update

Advancing Horizon's Profile as an Innovation-Driven Biotech

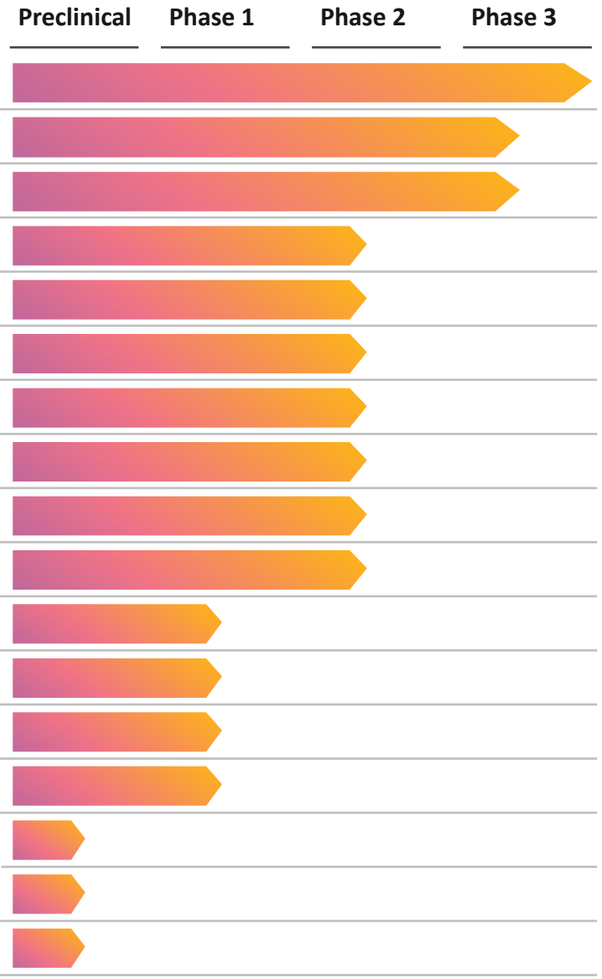
Acquisition of Viela Adds Significant Breadth and Depth to Horizon's Pipeline

Eight Trials Scheduled to Initiate in 2021; One Already Started

Viela acquisition advances our position as an innovation-driven, high-growth biotech in several important ways:

1. Adds a deep, mid-stage biologics pipeline
2. Augments the Company's R&D organization with early-stage research and translational capabilities
3. Deepens Horizon's scientific knowledge in autoimmune and severe inflammatory diseases
4. Supports Horizon's global expansion strategy

Program	Potential Indication
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
	COVID-19 Acute Lung Injury
TEPEZZA	Subcutaneous Administration
	Diffuse Cutaneous Systemic Sclerosis
HZN-1116	Autoimmune Diseases
HZN-003	Next-Gen Uncontrolled Gout
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**
- 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**

(1) Phase 4

KRYSTEXXA Development Programs

Five Trials Planned or Underway to Maximize the Value of KRYSTEXXA

Improve Response Rate

MIRROR RCT: Randomized, placebo-controlled trial **underway** evaluating KRYSTEXXA response rate with 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: Open-label trial **expected** to initiate Q2 2021 to evaluate KRYSTEXXA plus MTX in patients who have previously failed KRYSTEXXA alone

Improve Patient Experience

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

Monthly dosing: 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.

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 mid-2021

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

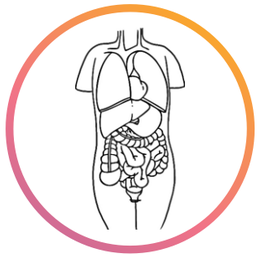
Diffuse Cutaneous Systemic Sclerosis

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

IGF-1R: Insulin-like growth factor 1 receptor. dcSSc: Diffuse cutaneous systemic sclerosis.

UPLIZNA Being Pursued in Three Additional Indications, Representing a Large Potential Market

UPLIZNA is an Anti-CD19 Humanized Monoclonal Antibody



Indication & Trial Phase	Myasthenia Gravis (MG)	IgG4-Related Disease (IgG4-RD)	Kidney Transplant Desensitization
	• A chronic, rare autoimmune neuromuscular disorder • Symptoms include weakness in voluntary skeletal muscles, especially those that control the eyes, mouth, throat and limbs • **Ongoing** Phase 3 trial	• A group of disorders marked by tumor-like swelling and fibrosis of affected organs, such as the pancreas, salivary glands and kidneys • **Ongoing** Phase 3 trial	• 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 (**paused** due to COVID-19)

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

Indication & Trial Phase	Diffuse Cutaneous Systemic Sclerosis (dcSSc)	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 start **expected** Q2 2021	• Commencing 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 start **expected** mid-2021

- >80% of patients with dcSSc 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

	Sjögren's Syndrome	Rheumatoid Arthritis	Kidney Transplant Rejection
			
Indication & Trial Phase	• 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 • **Ongoing** Phase 2b trial	• A chronic inflammatory disorder characterized by progressive destruction of joints • **Ongoing** Phase 2 trial; dose-ranging	• Occurs when the immune systems detect an organ transplant as a threat and attacks it • Results in organ rejection • **Ongoing** Phase 2 open-label trial

CD: Cluster of differentiation.

HZN-7734 in Development for Two Indications; HZN-1116 Expected to Enter Phase 1 Mid-2021

HZN-7734 is an Anti-ILT7 Human Monoclonal Antibody; HZN-1116 is a Monoclonal Antibody

Indication & Trial Phase	Systemic Lupus Erythematosus (SLE)	COVID-19-Related Acute Lung Injury (ALI)	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 **expected** to initiate mid-2021	• COVID-19-related ALI is the result of immune overactivation resulting in lung injury • **Ongoing** Phase 1 trial	**Expected** to enter single ascending dose Phase 1 trial in mid-2021 for autoimmune diseases

ILT: Immunoglobulin-like transcripts.

UPLIZNA

First and Only FDA-approved B-cell-depleting Antibody for the Treatment of Neuromyelitis Optica Spectrum Disorder (NMOSD)

UPLIZNA U.S. Relaunch Strategy and Global Expansion

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

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 support the Company's **global expansion strategy**
- **Adding key capabilities** to support the potential near-term launch of UPLIZNA as well as the potential launch of additional medicines over the long term

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 N-MOmentum Phase 2/3 Trial Presented at Premier Medical Meetings

American Academy of Neurology (AAN)

AAN 2021 Virtual Annual Meeting

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.

TEPEZZA

One of the Most Successful Rare Disease Medicine Launches Ever

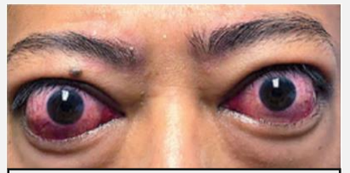
TEPEZZA is the First and Only Medicine Approved for Thyroid Eye Disease

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

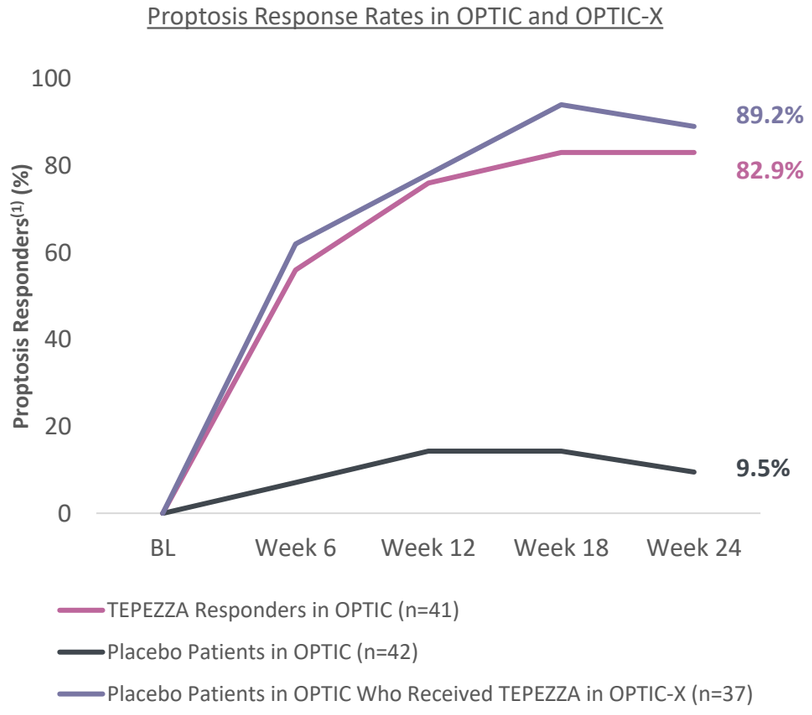
- TEPEZZA **blocks IGF-1R** and turns off signaling complex at the source of the disease

After

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

TEPEZZA: Impressive Clinical Trial Results in Acute TED and Growing Body of Evidence in Chronic TED

Acute TED: Patients Achieved Clinically Significant Proptosis Reduction



Chronic TED: Growing Body of Evidence Published and Presented

NANOS 2021 ANNUAL MEETING VIRTUAL • FEBRUARY 20-23

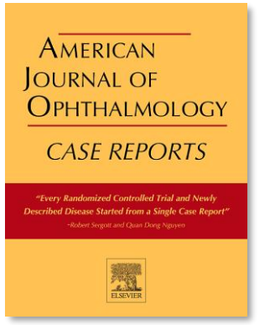
Case report showed TEPEZZA provided significant proptosis reduction in a chronic TED patient (23-years with Graves' disease)

The ROYAL COLLEGE of OPHTHALMOLOGISTS

TEPEZZA effectively reduced proptosis in patients with non-inflammatory / chronic TED(2)

AMERICAN SOCIETY OF OPHTHALMIC PLASTIC & RECONSTRUCTIVE SURGERY
OCULOFACIAL PLASTIC SURGERY

~30 TED patients across multiple reports presented at ASOPRS consistently saw benefit, inclusive of studies on chronic TED patients



AJO published the first chronic TED case where patient achieved a 6mm proptosis reduction after 3 infusions

TED: Thyroid Eye Disease. AJO: American Journal of Ophthalmology.
(1) Responder: Patients who achieved ≥ 2mm proptosis improvement from baseline. (2) Of the 10 patients studied, 2 had chronic TED and 4 had non-inflammatory disease.

We Are Investing to Drive the Continued Strong Growth of TEPEZZA

Expanding Supply Capacity

- **Resumed TEPEZZA supply** 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

Expanding Commercial Organization and Marketing Strategies

- **Doubled** commercial and field-based organization to **~200 employees**
- **Expanding marketing strategies** (including DTC) to drive increased awareness of TED

Pursuing Global Expansion

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

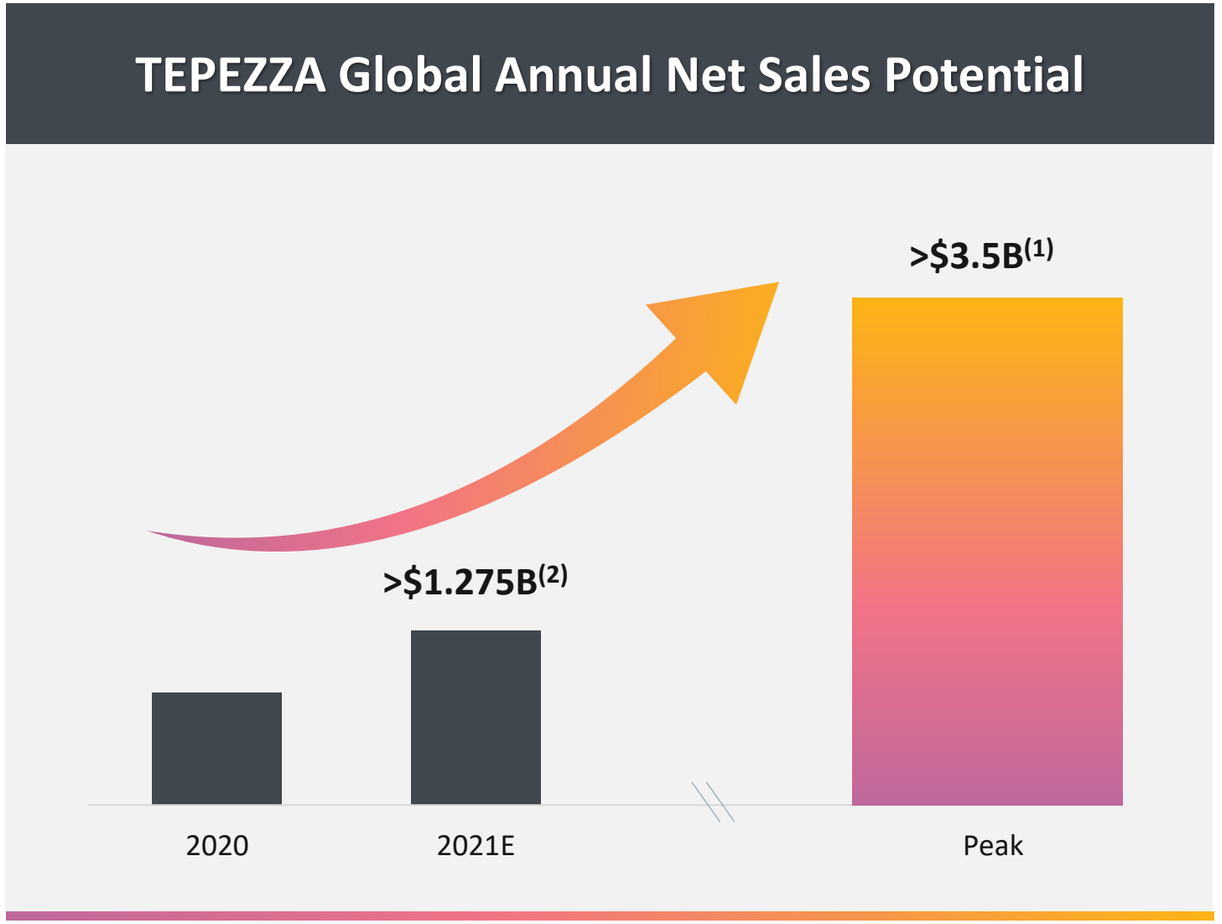
TED: Thyroid Eye Disease. DTC: Direct-to-consumer.

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 10-Year-Old Biologic to a High-Growth Medicine

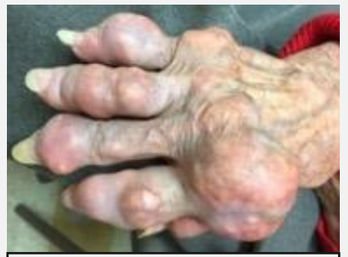
KRYSTEXXA is the Only Medicine Approved For Uncontrolled Gout

Uncontrolled Gout

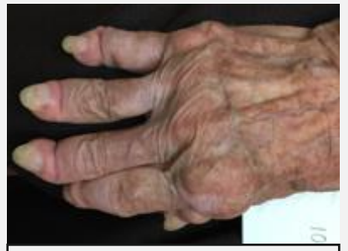
- Gout is the most common inflammatory arthritis; systemic disease with multiple co-morbidities
- **9.5 million estimated U.S. gout patients** growing at low-single digits per year(1)
- **>100K uncontrolled gout patients** in the U.S., growing in line with gout population(2)
- Opportunity for KRYSTEXXA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



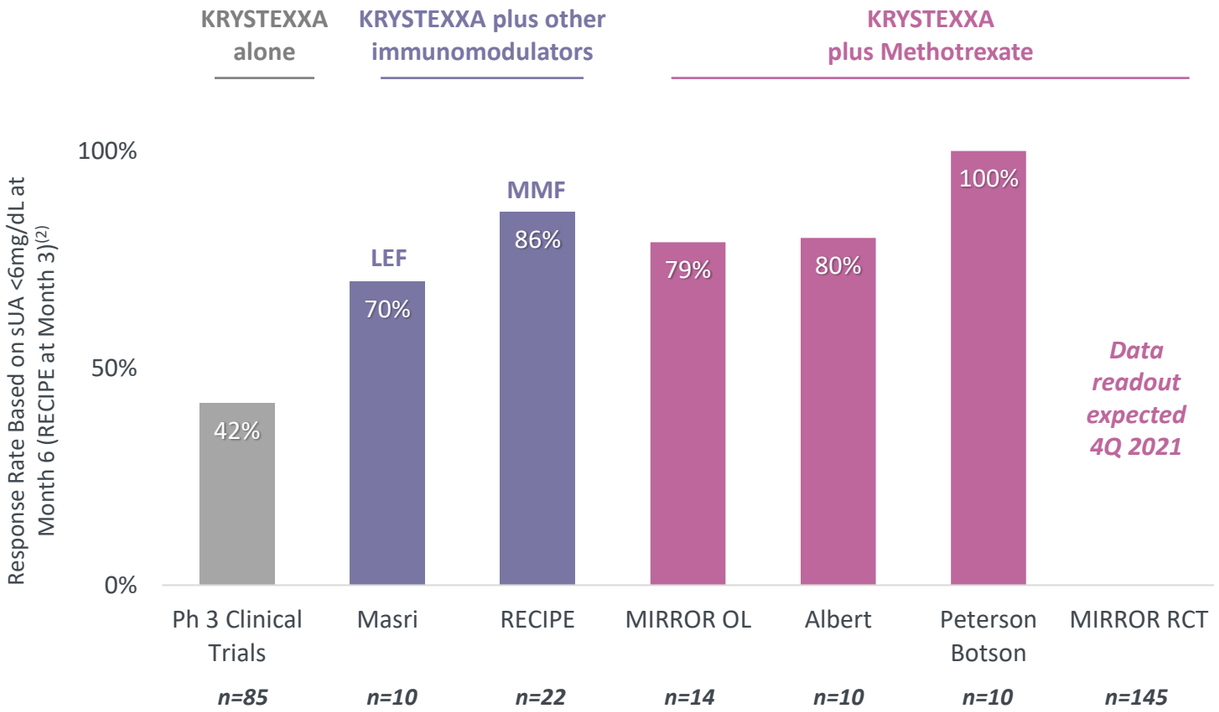
After

(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

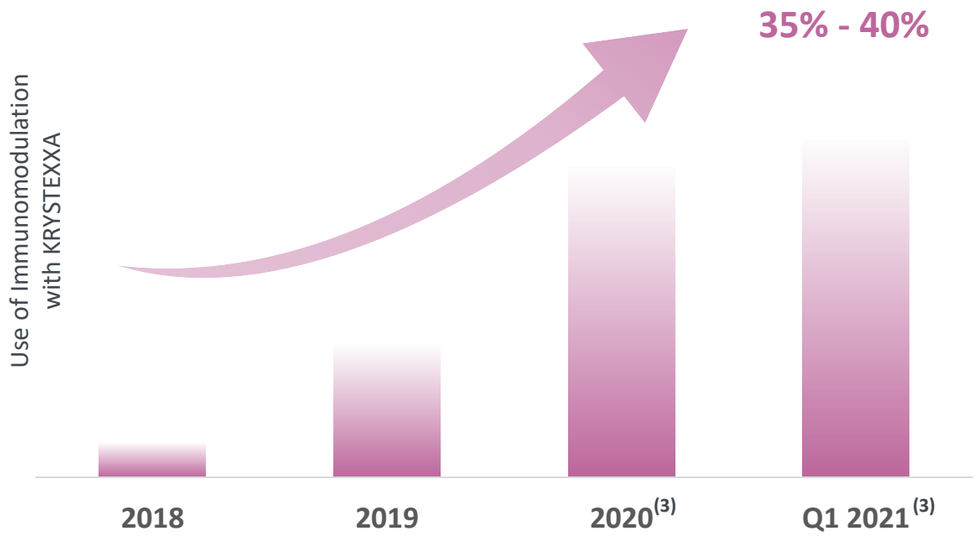
KRYSTEXXA Immunomodulation Strategy is Resonating with Physicians

Aiming to Maximize the Number of Patients That Benefit from KRYSTEXXA

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



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



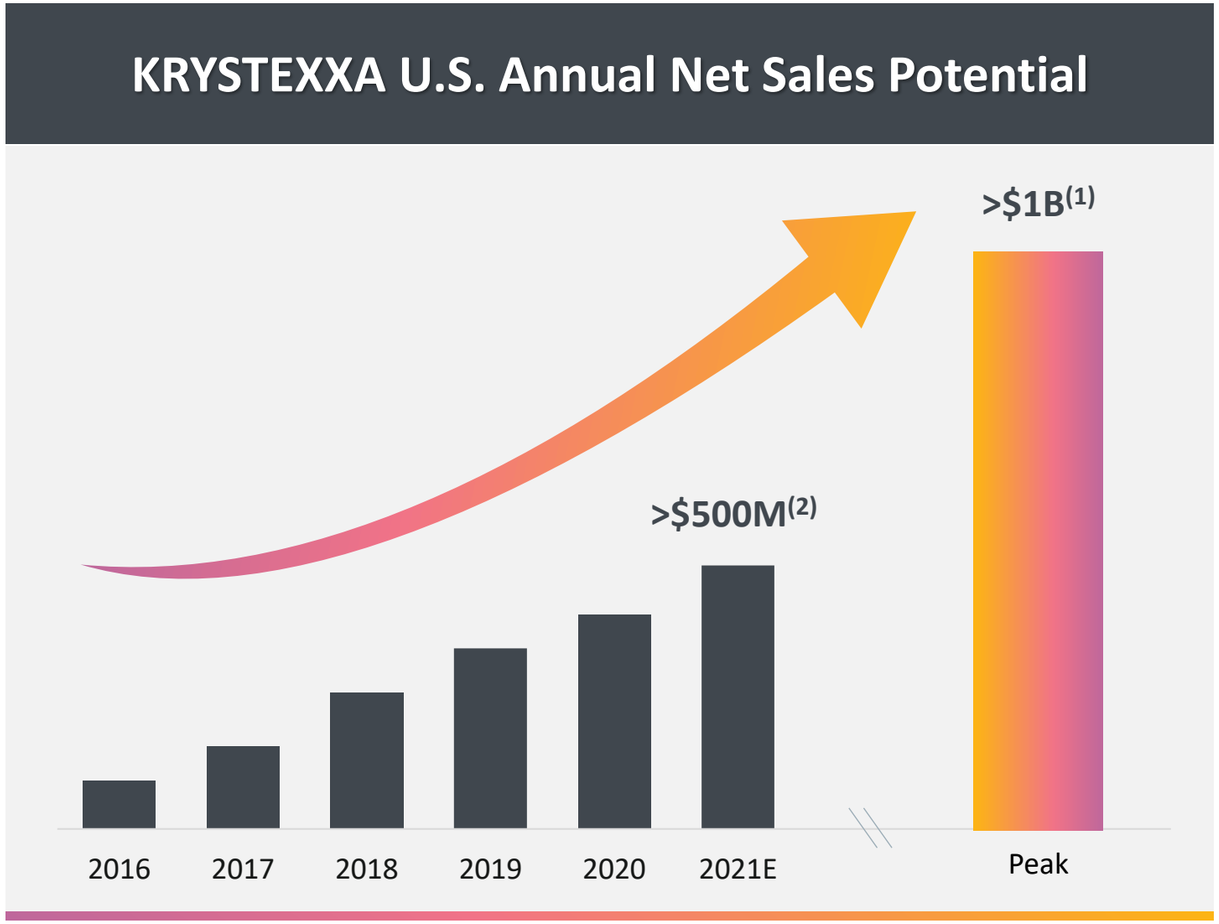
(1) Reflects KRYSTEXXA plus immunomodulation results. (2) Albert and Masri based on patient receiving ≥12 infusions. (3) Horizon analysis of HUB and claims data of KRYSTEXXA-treated patients also receiving immunomodulators.
RECIPE is an investigator-initiated randomized (3:1) placebo-controlled trial 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. ACR: American College of Rheumatology. 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.

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 gross profit and gross profit ratio, non-GAAP operating expenses, non-GAAP operating income, non-GAAP tax expense 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 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 Months Ended March 31

$ in thousands	Three Months Ended March 31, 2021	2020
GAAP net loss	**$ (123,351)**	**$ (13,591)**
Depreciation	4,451	7,165
Amortization and step-up:		
Intangible amortization expense	66,369	58,575
Inventory step-up expense	911	-
Interest expense, net (including amortization of debt discount and deferred financing costs)	13,460	17,344
Benefit for income taxes	(47,751)	(19,026)
EBITDA	**$ (85,911)**	**$ 50,467**
Other non-GAAP adjustments:		
Acquisition/divestiture-related costs	49,108	(6)
Restructuring and realignment costs	6,093	-
Impairment of long-lived assets	12,371	-
Share-based compensation	61,166	56,421
Upfront, progress and milestone payments related to license and collaboration agreements	3,000	-
Fees related to refinancing activities	-	54
Drug substance harmonization costs	-	290
Total of other non-GAAP adjustments	**131,738**	**56,759**
Adjusted EBITDA	**$ 45,827**	**$ 107,226**

GAAP to Non-GAAP Reconciliation

EBITDA and Adjusted EBITDA – Full-Year 2020

$ in thousands	Twelve Months Ended December 31, 2020
GAAP net income	**$ 389,796**
Depreciation	24,303
Amortization and step-up:	
Intangible amortization expense	255,148
Inventory step-up expense	-
Interest expense, net (including amortization of debt discount and deferred financing costs)	59,616
Expense for income taxes	11,849
EBITDA	**$ 740,712**
Other non-GAAP adjustments:	
Acquisition/divestiture-related costs	49,196
Restructuring and realignment costs	(141)
Impairment of long-lived assets	1,713
Gain on sale of assets	(4,883)
Share-based compensation	146,627
Upfront, progress and milestone payments related to license and collaboration agreements	33,000
Fees related to refinancing activities	54
Loss on debt extinguishment	31,856
Drug substance harmonization costs	542
Total of other non-GAAP adjustments	257,964
Adjusted EBITDA	**$ 998,676**

GAAP to Non-GAAP Reconciliation

Operating Income – Three Months Ended March 31

$ in thousands	Three Months Ended March 31, 2021	2020
GAAP operating loss	**$ (160,018)**	**$ (16,491)**
Non-GAAP adjustments:		
Acquisition/divestiture-related costs	49,391	284
Restructuring and realignment costs	6,093	-
Amortization and step-up:		
Intangible amortization expense	66,369	58,575
Inventory step-up expense	911	-
Impairment of long-lived assets	12,371	-
Share-based compensation	61,166	56,421
Depreciation	4,451	7,165
Upfront, progress and milestone payments related to license and collaboration agreements	3,000	-
Fees related to refinancing activities	-	54
Drug substance harmonization costs	-	290
Total of non-GAAP adjustments	**203,752**	**122,789**
Non-GAAP operating income	**$ 43,734**	**$ 106,298**
Orphan segment operating income	1,054	54,356
Inflammation segment operating income	42,680	51,942
Total segment operating income	**$ 43,734**	**$ 106,298**
Foreign exchange (loss)/gain	(848)	776
Other income, net	2,941	152
Adjusted EBITDA	**$ 45,827**	**$ 107,226**

GAAP to Non-GAAP Reconciliation

Net Loss and Non-GAAP Net Income – Three Months Ended March 31

$ in thousands	Three Months Ended March 31, 2021	2020
GAAP net loss	**$ (123,351)**	**$ (13,591)**
Non-GAAP adjustments:		
Acquisition/divestiture-related costs	49,108	(6)
Restructuring and realignment costs	6,093	-
Amortization and step-up:		
Intangible amortization expense	66,369	58,575
Inventory step-up expense	911	-
Amortization of debt discount and deferred financing costs	773	5,569
Impairment of long-lived assets	12,371	-
Share-based compensation	61,166	56,421
Depreciation	4,451	7,165
Upfront, progress and milestone payments related to license and collaboration agreements	3,000	-
Fees related to refinancing activities	-	54
Drug substance harmonization costs	-	290
Total of pre-tax non-GAAP adjustments	**204,242**	**128,068**
Income tax effect of pre-tax non-GAAP adjustments	(73,504)	(31,262)
Total of non-GAAP adjustments	**130,738**	**96,806**
Non-GAAP Net income	**$ 7,387**	**$ 83,215**

GAAP to Non-GAAP Reconciliation

GAAP and Non-GAAP Earnings (Loss) Per Share – Basic and Diluted – Three Months Ended March 31

$ in thousands except share and per share data	Three Months Ended March 31, 2021	Three Months Ended March 31, 2020
Non-GAAP Earnings Per Share:		
Weighted average ordinary shares - Basic	**223,920,768**	**190,072,112**
Non-GAAP Earnings Per Share - Basic:		
GAAP loss per share - Basic	**$ (0.55)**	**$ (0.07)**
Non-GAAP adjustments	0.58	0.51
Non-GAAP earnings per share - Basic	**$ 0.03**	**$ 0.44**
Non-GAAP Net income	**$ 7,387**	**$ 83,215**
Effect of assumed exchange of Exchangeable Senior Notes, net of tax	-	1,875
Numerator - non-GAAP Net income	**$ 7,387**	**$ 85,090**
Weighted average ordinary shares - Diluted		
Weighted average ordinary shares - Basic	223,920,768	190,072,112
Ordinary share equivalents	10,190,012	22,984,847
Denominator - weighted average ordinary shares – Diluted	**234,110,780**	**213,056,959**
Non-GAAP Earnings Per Share - Diluted		
GAAP loss per share - Diluted	**$ (0.55)**	**$ (0.07)**
Non-GAAP adjustments	0.58	0.51
Diluted earnings per share effect of ordinary share equivalents	-	(0.04)
Non-GAAP earnings per share - Diluted	**$ 0.03**	**$ 0.40**