First-Quarter 2019 Summary

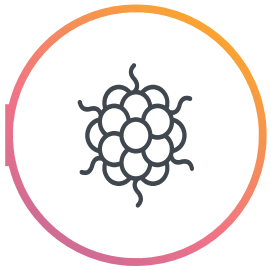
Horizon Therapeutics plc

May 8, 2019

Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to Horizon's full-year 2019 net sales and adjusted EBITDA guidance; expected financial performance and operating results in future periods; expected timing of clinical trials and regulatory submissions and decisions, including related to the potential BLA submission for teprotumumab; expected expansion of Horizon rare disease medicine pipeline and the impact thereof; potential market opportunity for 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 products; 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; risks inherent in developing novel medicine candidates, such as teprotumumab, and existing medicines for new indications; risks associated with regulatory approvals; risks in the ability to recruit, train and retain qualified personnel; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information.

Our Aspiration



Be a leading **rare disease biopharma** company

Deliver **innovative therapies** to patients

Generate **high returns** for shareholders

Horizon: A Leading Rare Disease Biopharma Company

Executing on Our Strategy

- Building a robust pipeline of rare disease medicines
- Building a leading R&D function
- Maximizing KRYSTEXXA® to enhance our leadership in uncontrolled gout

Significant Progress in 2018

- **Teprotumumab:** Fully enrolled Phase 3 trial; initiated commercial launch activities
- **Uncontrolled gout R&D programs:** Initiated immunomodulation strategy
- **Transformed R&D organization:** Recruitment of scientific leadership team
- **KRYSTEXXA:** Doubled commercial team and addressable patient population to accelerate vial growth

Leveraging Our Momentum in 2019+

- **Teprotumumab Phase 3 topline data announced February 2019:** Primary endpoint achieved at 82.9% vs. placebo of 9.5% ($p<0.001$); all secondary endpoints met
- **Advancing KRYSTEXXA immunomodulation and kidney transplant trials**
- **Advancing toward peak net sales expectations:**
  - **KRYSTEXXA:** >$750M[(1)]
  - **Teprotumumab:** >$750M[(1)]
- **Potential upside with future pipeline assets**

(1) Horizon peak sales estimate for U.S. net sales only.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

First-Quarter 2019 Summary

First-Quarter and Recent Company Highlights

Segment Results

R&D Update

Strong Financial Results and Strategic Execution

Financial and other highlights	• **Q1 net sales increased 25 percent** to $280.4M and **adjusted EBITDA increased 163 percent** to $88.4M • **Increased full-year 2019 guidance** to net sales of $1.26B to $1.28B and adjusted EBITDA of $450M to $465M • **Reduced gross debt by $550M** to better align with biopharma capital structure; net leverage at 1.3x as of March 31, 2019 • Changed our name to **Horizon Therapeutics plc** to better reflect our focus on developing medicines to treat rare diseases
Executing on our strategy: **To build a robust and differentiated pipeline and To maximize KRYSTEXXA growth**	• **Announced dramatic teprotumumab Phase 3 top-line results:** 82.9% of teprotumumab patients achieved primary endpoint (proptosis reduction) ($p<0.001$) compared to 9.5% of placebo patients and all secondary endpoints were achieved with statistical significance ($p\leq0.001$)(1) • **Presented additional teprotumumab Phase 3 data at AACE** and continue to expect BLA submission in mid-2019(2) • **MIRROR immunomodulation trial expected to begin in June;** will evaluate the use of methotrexate to enhance the response rate of KRYSTEXXA and increase the number of patients who can benefit • Selected lead candidate, **HZN-007 (PASylated uricase)**, for our next-generation biologic program for uncontrolled gout • Expect to initiate **KRYSTEXXA study in kidney transplant patients with uncontrolled gout in H2 2019**

Net Leverage: Net debt to LTM adjusted EBITDA.
AACE: American Association of Clinical Endocrinologists. BLA: Biologics License Application. MIRROR: **M**ethotrexate to **I**ncrease **R**esponse **R**ates in Patients with Uncontrolled G**O**ut **R**eceiving KRYSTEXXA.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
(1) Primary endpoint defined as proptosis responder rate defined as percentage of participants with ≥2 mm reduction.
(2) Data presented at AACE includes mean change from baseline over 24 weeks in proptosis measurement and overall responder rate, defined by proptosis reduction of ≥2 mm plus Clinical Activity Score improvement of ≥2 points.
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.

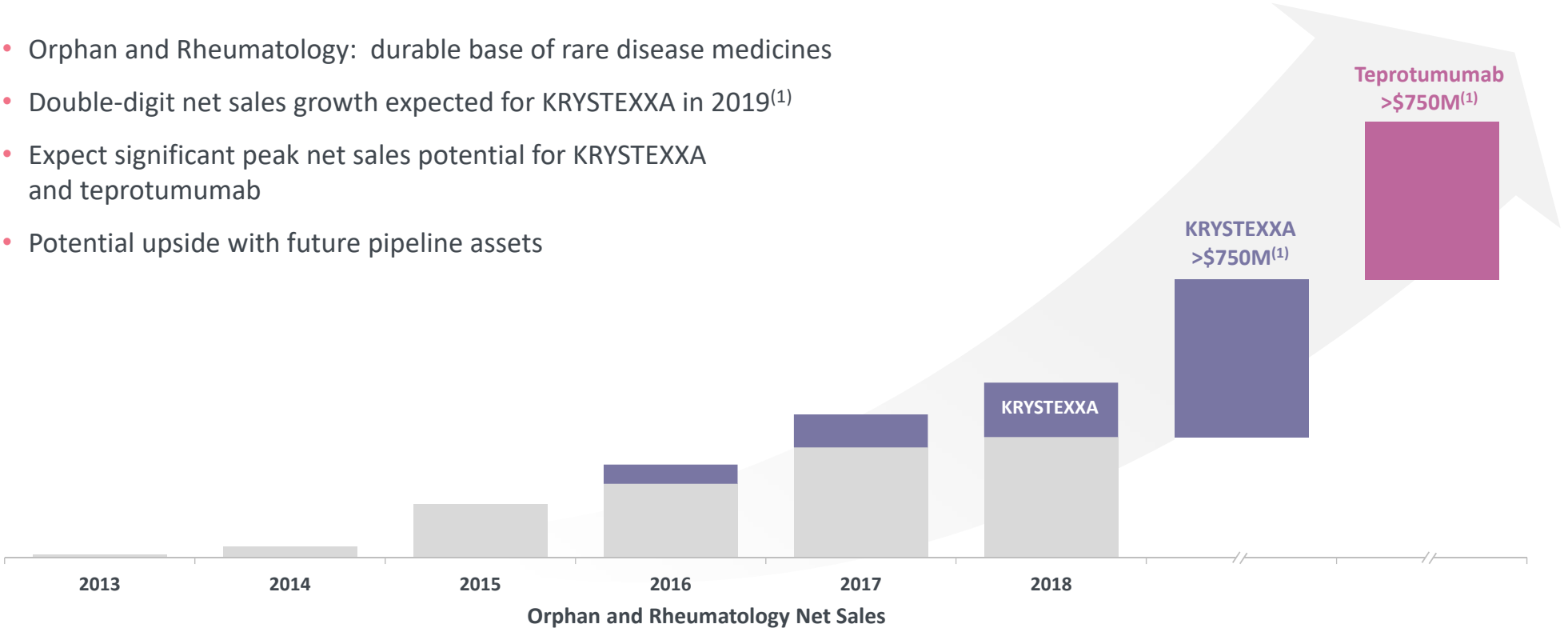
Q1 2019 Financial Results

($ in millions, except for per share amounts)	Q1 2019	Q1 2018	% Change
Net sales	$280.4	$223.9	25
Net loss	(32.9)	(148.7)	78
Non-GAAP net income	53.9	4.8	NM
Adjusted EBITDA	88.4	33.6	163
Loss per share – diluted	$(0.19)	$(0.90)	79
Non-GAAP earnings per share – diluted	$0.30	$0.03	NM

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.

Combined Estimated Annual Peak Net Sales of KRYSTEXXA and Teprotumumab Alone Would Double FY18 Net Sales

- Orphan and Rheumatology: durable base of rare disease medicines
- Double-digit net sales growth expected for KRYSTEXXA in 2019(1)
- Expect significant peak net sales potential for KRYSTEXXA and teprotumumab
- Potential upside with future pipeline assets



Teprotumumab is an investigational candidate and its safety and efficacy have not been established. Horizon cannot generate U.S. net sales of teprotumumab unless and until it obtains FDA approval.
Note: Company full-year 2018 net sales were $1.21B.
(1) Horizon estimate.

Increasing Full-Year 2019 Guidance

Full-year 2019 net sales and adjusted EBITDA guidance ranges:

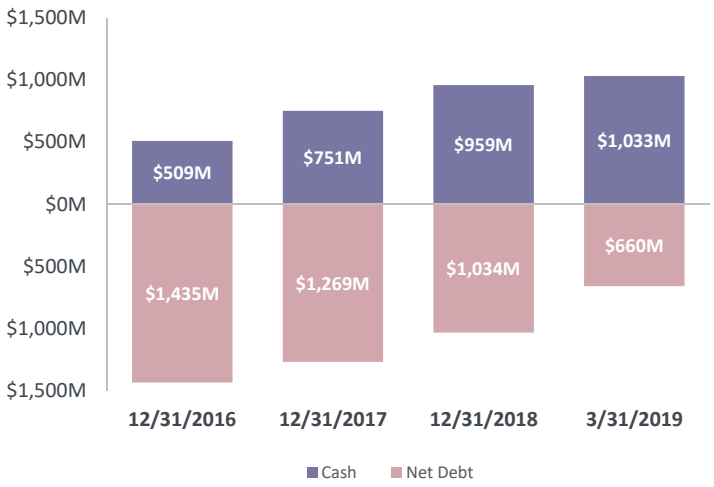
	New Guidance	Previous Guidance
Net Sales	**$1.26 to $1.28 Billion**	$1.23 to $1.25 Billion
Adjusted EBITDA	**$450 to $465 Million**	$440 to $455 Million

Note: Adjusted EBITDA is a non-GAAP measure.

Evolving Our Capital Structure to Be in Line with Aspirational Peers

Reduces Gross Debt by $550M; Net Leverage 1.3x

Strong Cash Balance and Net Debt Position



Managing debt and leverage efficiently

Disciplined Approach to Debt

- **Gross debt** of $1.443 billion principal amount at May 1, 2019, down from $1.993 billion at Dec. 31, 2018(1)
  - Earliest maturity: 2022 for $400 million exchangeable notes (conversion price of $28.66)
- **Net Leverage Ratio** of 1.3x at March 31, 2019, down from 2.3x at Dec. 31, 2018
- **March 2019 Equity Offering:** Raised $345 million to use for debt reduction along with balance sheet cash

Target Leverage Ratios:

- Gross: <3.0x
- Net: <2.0x

LTM: Last twelve months.
Net Leverage: Net debt to LTM adjusted EBITDA.
(1) Following the notice of partial optional redemption, $250.0 million of the 2023 Senior Notes were redeemed on May 1, 2019.
Note: Net debt and LTM adjusted EBITDA are non-GAAP measures; see reconciliation slides at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.

Orphan and Rheumatology Segment

Strong Q1 2019 Orphan and Rheumatology Net Sales Driven by KRYSTEXXA, RAVICTI, PROCYSBI and RAYOS

($ in millions)	Q1 2019	Q1 2018	% Change
RAVICTI®(1)(2)	$49.9	$49.1	2
PROCYSBI®	39.6	34.9	13
ACTIMMUNE®	21.7	24.9	(13)
BUPHENYL®(1)	2.8	5.7	(52)
QUINSAIR™	0.2	0.1	39
Orphan	**$114.2**	**$114.7**	**(1)**
KRYSTEXXA®	52.3	46.7	12
RAYOS®	19.4	10.7	82
LODOTRA®(1)	-	0.1	NM
Rheumatology	**$71.7**	**$57.5**	**25**
Orphan and rheumatology segment net sales(2)	***$185.9***	***$172.2***	***8***
Orphan and rheumatology segment operating income	***$46.7***	***$43.1***	***8***

NM: Not meaningful.
(1) On Dec. 28, 2018, the Company sold the rights to RAVICTI and AMMONAPS (AMMONAPS is known as BUPHENYL in the United States) outside of North America and Japan to Medical Need Europe AB. In addition, effective Jan. 1, 2019, the RAYOS and LODOTRA license and supply agreements were amended, including the transfer of LODOTRA to Vectura Group plc (LODOTRA is known as RAYOS in the United States). Beginning in 2019, the Company no longer recognizes revenue from RAVICTI and AMMONAPS sales outside of North America and Japan, or from sales of LODOTRA.
(2) Excluding the first-quarter 2018 divested net sales, first-quarter 2019 RAVICTI net sales increased 5 percent and the orphan and rheumatology segment net sales increased 10 percent.

Driving Toward Our >$750M Peak Net Sales Estimate for KRYSTEXXA[(1)]

- **Existing account vials grew ~30%** year-over-year in Q1 2019
- Expecting **double-digit net sales growth** in 2019[(1)]
- Opened **>600 new accounts in the last twelve months**
- **Generating significant interest** from nephrologists

(1) Horizon estimate.

Primary Care Segment

Q1 2019 Results: Primary Care Segment

($ in millions)	Q1 2019	Q1 2018	% Change
PENNSAID® 2%	$50.2	$26.8	87
DUEXIS®	29.5	15.7	88
VIMOVO®	14.0	8.4	68
MIGERGOT®	0.8	0.8	12
Primary care segment net sales	***$94.5***	***$51.7***	***83***
Primary care segment operating income	***$41.4***	***($9.6)***	***NM***

NM: Not meaningful.

Our Rare Disease Pipeline

Built With Purpose

Building a Robust Rare Disease Pipeline

MEDICINE / PROGRAM	DESCRIPTION	PRE-CLINICAL	PHASE 1	PHASE 2	PHASE 3	PHASE 3b / 4
KRYSTEXXA	• MIRROR immunomodulation study: KRYSTEXXA + methotrexate(1)					
KRYSTEXXA	• Study in kidney transplant patients with uncontrolled gout(2)					
HZN-001 (teprotumumab)(3)	• OPTIC trial: Phase 3 (complete) • OPTIC-X trial: Phase 3 extension					
HZN-003	• Optimized uricase and optimized PEGylation for uncontrolled gout					
HZN-007(4)	• Optimized uricase and PASylation for uncontrolled gout					
HemoShear Gout Discovery Collaboration	• Exploration of novel approaches to treating gout					

(1) Planned study, expected to begin in June.
(2) Planned study, expected to begin in the second half of 2019.
(3) Teprotumumab is a fully human monoclonal antibody (mAb) IGF-1R inhibitor in development for active thyroid eye disease (TED).
(4) Being developed under a collaboration agreement.
MIRROR: **M**ethotrexate to **I**ncrease **R**esponse **R**ates in Patients with Uncontrolled G**O**ut **R**eceiving KRYSTEXXA.
OPTIC: Treatment of Graves' **O**rbitopathy (Thyroid Eye Disease) to Reduce **P**roptosis with **T**eprotumumab **I**nfusions in a Randomized, Placebo-Controlled, **C**linical Study.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

Teprotumumab Exemplifies Our Pipeline Strategy

Building a Pipeline for Sustainable Long-Term Growth

PIPELINE CANDIDATE CRITERIA	TEPROTUMUMAB
High unmet need with preference for rare diseases	☑ No FDA-approved therapies exist for thyroid eye disease ☑ Standard of care ineffective; safety concerns ☑ Surgery is invasive, complex and often ineffective
Compelling clinical trial data or proof of concept	☑ Impressive Phase 2 results published in *The New England Journal of Medicine* ☑ Dramatic Phase 3 results; achieved primary and all secondary endpoints
Key regulatory designations	☑ U.S. Orphan, Fast-Track and Breakthrough Therapy
Durable intellectual property	☑ 12-year biologic exclusivity

Teprotumumab meets ALL pipeline candidate criteria and has potential to be first FDA-approved therapy to treat active thyroid eye disease

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

Teprotumumab Phase 3 Top-Line Results

OPTIC study met its primary endpoint (82.9% vs 9.5%; p<0.001), demonstrating a dramatic impact on proptosis

All secondary endpoints met with statistical significance (p≤0.001)

- Overall responder rate at Week 24 (primary endpoint of Phase 2)(1)
- CAS responder rate at Week 24
- Change in proptosis through Week 24
- Diplopia improvement at Week 24
- Change in GO-QOL through Week 24

Safety profile consistent with Phase 2

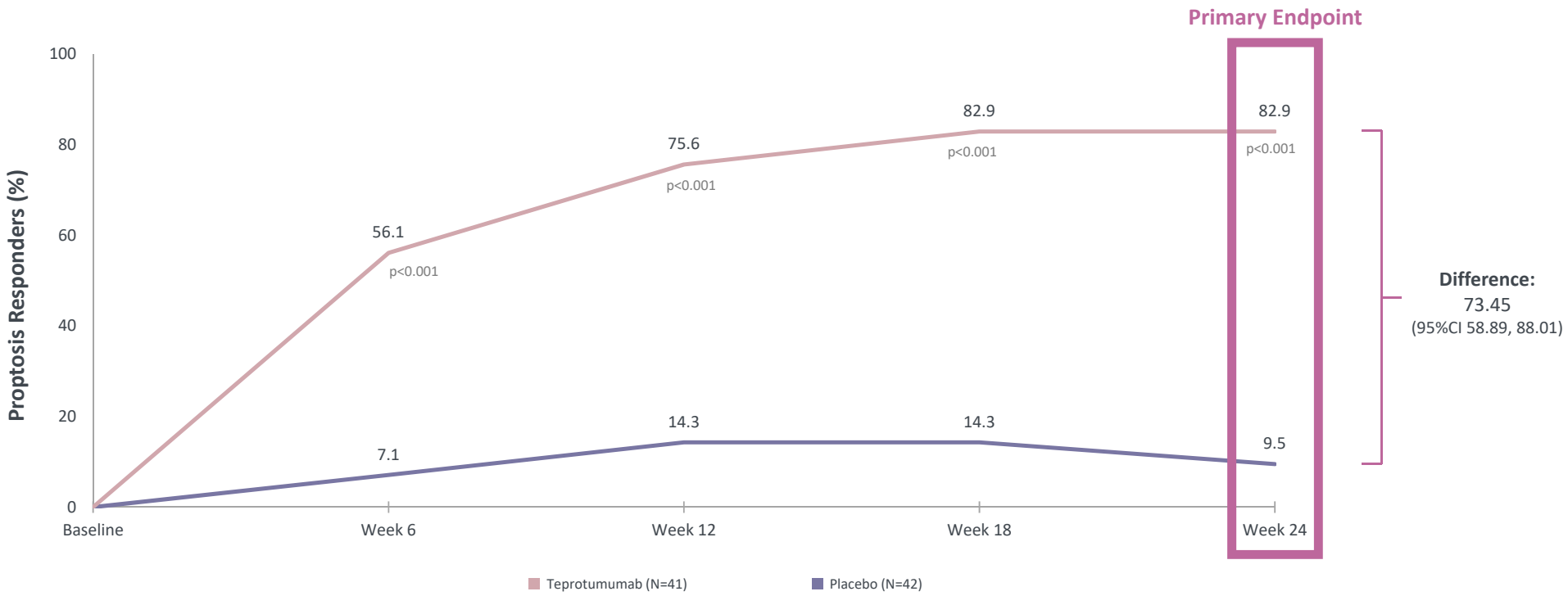
- No new safety observations
- Drop-out rate was low (<5%) and balanced across arms

BLA submission targeted for mid-2019

(1) Percent of participants with ≥2 point reduction in Clinical Activity Score (CAS) and ≥2 mm reduction in proptosis from baseline, provided there is no corresponding deterioration (≥2-point/mm increase) in CAS or proptosis in the fellow eye.
OPTIC: Treatment of Graves' **O**rbitopathy (Thyroid Eye Disease) to Reduce **P**roptosis with **T**eprotumumab **I**nfusions in a Randomized, Placebo-Controlled, **C**linical Study.
CAS: Clinical Activity Score, a 7-point scale that measures change in orbital inflammation and pain; a score of >3 indicates active TED.
GO-QOL: Graves' Ophthalmopathy Quality of Life.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

Teprotumumab Phase 3 Primary Endpoint

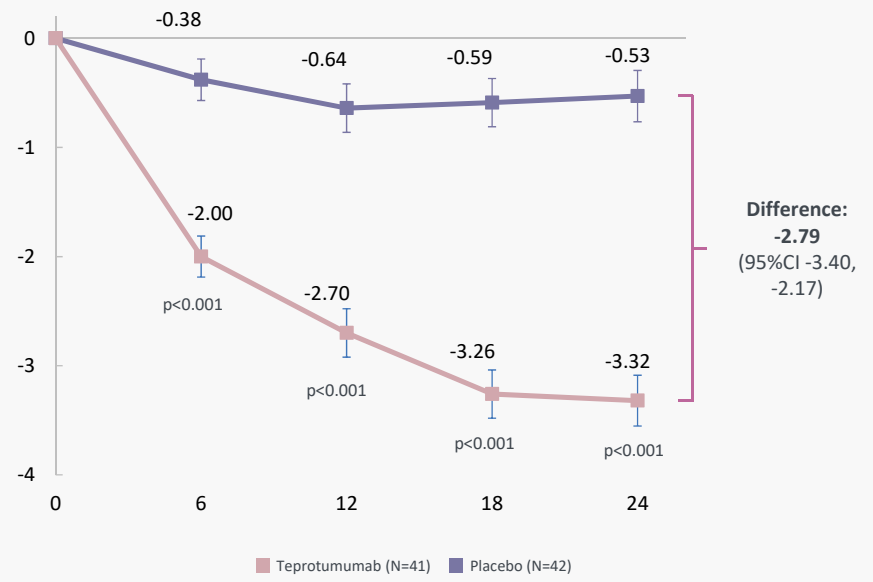
Proptosis Response (Reduction of ≥2 mm) over Time



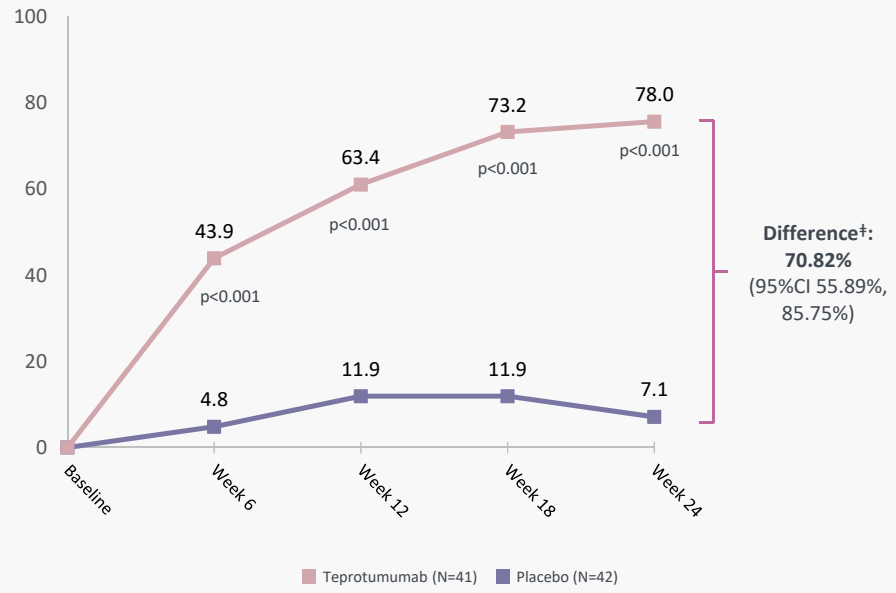
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

New Phase 3 Data Presented at AACE in April

Proptosis Reduction of 3.32 mm at Week 24[(1)]



Overall Responder Rate (Proptosis + CAS) of 78 Percent[(2)]



AACE: American Association of Clinical Endocrinologists. CAS: Clinical Activity Score, a 7-point scale that measures change in orbital inflammation and pain; a score of >3 indicates active TED.
Note: Throughout the 24 week treatment period, patients treated with teprotumumab had an average proptosis reduction of 2.82 mm compared with 0.54 mm for those who received placebo (p<0.001).
(1) Change from baseline in proptosis as a continuous variable is based on Mixed-Model Repeated-Measures (MMRM) analysis of covariance (ANCOVA) model with an unstructured covariance matrix including the following terms: baseline score, tobacco use status (non-user, user), treatment group, visit, and visit-by-treatment and visit-by-baseline-score interactions.
(2) Overall responders defined as reduction of ≥2 mm proptosis + ≥2 points CAS improvement. Overall responders was the primary endpoint of the Phase 2 trial.
‡Stratified Difference in Response Rates. Estimates from the two strata (tobacco user, tobacco non-user) are combined with Cochran-Mantel-Haenszel weights.

Phase 3 Safety Overview

- Safety profile similar to Phase 2 with no new safety observations
- Drop-out rate was low (<5%) and balanced across arms
- No deaths
- Vast majority of treatment-emergent adverse events were mild to moderate in intensity and no non-serious events led to discontinuation

	Placebo (N=42)	Teprotumumab (N=41)
TEAEs	29 (69.0%)	35 (85.4%)
SAEs	1 (2.4%)[1]	2 (4.9%)[2]

(1) Placebo: visual field defect requiring orbital decompression surgery (patient discontinued study)

(2) Teprotumumab: pneumothorax (considered not related to study drug; patient had history of throat cancer with radiation treatment), infusion reaction (patient discontinued study)

Note: Table represents number of subjects with TEAEs and SAEs.
TEAE: Treatment emergent adverse event.
SAE: Serious adverse event.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

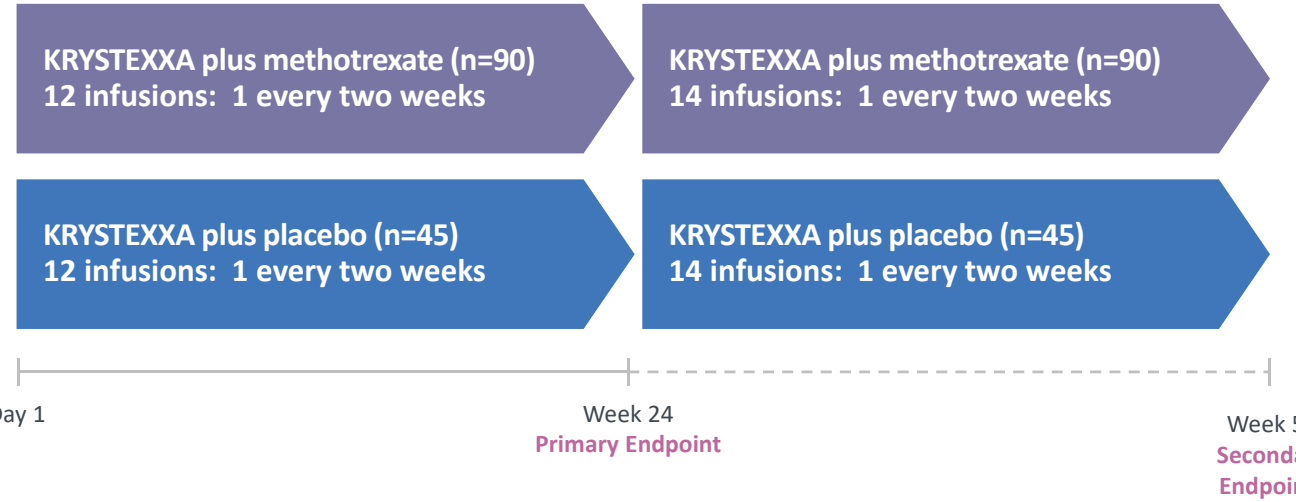
KRYSTEXXA Immunomodulation Trial (MIRROR)

Goal is to Improve Patient Response Rates

Overview

- **Total patients: 135**
- **2:1 randomization**
- **Run-in period: Methotrexate 15/mg per week or blinded placebo for four weeks**
- **Adapted to support registration**

24-Week Treatment Period



Primary Endpoint at Week 24:

Proportion of serum uric acid (sUA) responders (sUA < 6 mg/dL) at six months

Secondary Endpoints at Week 52:

Proportion of serum uric acid (sUA) responders (sUA < 6 mg/dL) at twelve months

Proportion of responders on tophi, defined as resolution of tophi based on photographic evidence of resolution at twelve months

MIRROR: **M**ethotrexate to **I**ncrease **R**esponse **R**ates in Patients with Uncontrolled G**O**ut **R**eceiving KRYSTEXXA.

New Programs to Build on Our Market Leadership Position in Uncontrolled Gout

Next-generation Uncontrolled Gout Programs

Potential to improve response rate, duration of treatment and provide more convenient administration through subcutaneous dosing

HZN-003

- Optimized uricase and optimized PEGylation for uncontrolled gout
- Potency allowing potential for subcutaneous dosing

HZN-007

- Optimized uricase and PASylation for uncontrolled gout
- PASylation as a new approach to increasing half-life and reduce immunogenicity
- Potency allowing potential for subcutaneous dosing

Novel Gout Discovery Program

HemoShear Collaboration

- Strong capability to identify and validate novel biological targets
- Exploring novel approaches to treating gout

Building on Our Momentum

2019 Progress and Potential Future Catalysts

2019

- [x] Teprotumumab Phase 3 trial data by end of Q1
- [x] PASylated uricase lead candidate decision
- [ ] Begin registrational KRYSTEXXA MIRROR trial in June
- [ ] Teprotumumab BLA submission mid-2019
- [ ] Begin trial evaluating KRYSTEXXA in kidney transplant patients with uncontrolled gout

2020 and Beyond

- [ ] Teprotumumab BLA decision and launch(1)
- [ ] Teprotumumab long-term data
- [ ] KRYSTEXXA MIRROR registrational trial data and submission
- [ ] HZN-003 (optimized uricase and optimized PEGylation for uncontrolled gout) Phase 1 trial start
- [ ] HZN-007 Phase 1 trial start for uncontrolled gout
- [ ] HemoShear lead candidate decision

[x] Milestone met

(1) Assuming priority review given breakthrough and fast-track designations.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
MIRROR: **M**ethotrexate to **I**ncrease **R**esponse **R**ates in Patients with Uncontrolled G**O**ut **R**eceiving KRYSTEXXA.

Historical Information and 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 rate, non-GAAP operating cash flow and net debt, each of which include adjustments to GAAP figures. These non-GAAP measures are intended to provide additional information on Horizon performance, operations, expenses, profitability and cash flows. Adjustments to Horizon's GAAP figures as well as EBITDA exclude acquisition and/or divestiture-related expenses, charges related to the discontinuation of ACTIMMUNE development for Friedreich's ataxia, gain from divestiture, gain from sale of assets, upfront 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, 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 2019 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 2019 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, 2019	2018
GAAP net loss	**$ (32,863)**	**$ (148,656)**
Depreciation	1,473	1,552
Amortization and step-up:		
Intangible amortization expense	57,417	60,883
Inventory step-up expense	115	17,076
Interest expense, net (including amortization of debt discount and deferred financing costs)	27,530	30,454
(Benefit) expense for income taxes	(1,920)	945
EBITDA	**$ 51,752**	**$ (37,746)**
Other non-GAAP adjustments:		
Acquisition/divestiture-related costs	1,345	4,653
Restructuring and realignment costs	20	3,342
Share-based compensation	27,548	27,833
Loss on debt extinguishment	5,586	-
Impairment of long-lived assets	-	33,647
Drug substance harmonization costs	80	804
Fees related to refinancing activities	142	27
Upfront and milestone payments related to license and collaboration agreements	2,000	90
Charges relating to discontinuation of Friedreich's ataxia program	(79)	950
Total of other non-GAAP adjustments	**36,642**	**71,346**
Adjusted EBITDA	**$ 88,394**	**$ 33,600**

GAAP to Non-GAAP Reconciliation

EBITDA and Adjusted EBITDA – Full-Year 2018

$ in thousands	Twelve Months Ended December 31, 2018
GAAP net loss	**$ (38,380)**
Depreciation	6,126
Amortization and step-up:	
Intangible amortization expense	243,634
Inventory step-up expense	17,312
Interest expense, net (including amortization of debt discount and deferred financing costs)	121,692
Benefit for income taxes	(44,752)
EBITDA	**$ 305,632**
Other non-GAAP adjustments:	
Acquisition/divestiture-related costs	4,396
Restructuring and realignment costs	15,350
Share-based compensation	114,860
Impairment of long-lived assets	46,096
Litigation settlements	5,750
Drug substance harmonization costs	2,855
Fees related to refinancing activities	937
Upfront and milestone payments related to license and collaboration agreements	(10)
Charges relating to discontinuation of Friedreich's ataxia program	(1,464)
Gain on sale of assets	(42,985)
Total of other non-GAAP adjustments	**145,785**
Adjusted EBITDA	**$ 451,417**

GAAP to Non-GAAP Reconciliation

Operating Income

$ in thousands	Three Months Ended March 31, 2019	2018
GAAP operating loss	**$ (1,795)**	**$ (117,298)**
Non-GAAP adjustments:		
Depreciation	1,473	1,552
Amortization and step-up:		
Intangible amortization expense	57,417	60,883
Inventory step-up expense	115	17,076
Acquisition/divestiture-related costs	1,202	4,625
Restructuring and realignment costs	20	3,342
Share-based compensation	27,548	27,833
Impairment of long-lived assets	-	33,647
Drug substance harmonization costs	80	804
Fees related to refinancing activities	142	27
Upfront and milestone payments related to license and collaboration agreements	2,000	90
Charges relating to discontinuation of Friedreich's ataxia program	(79)	950
Total of non-GAAP adjustments	**89,918**	**150,829**
Non-GAAP operating income	**$ 88,123**	**$ 33,531**
Orphan and Rheumatology segment operating income	46,677	43,104
Primary care segment operating income	41,446	(9,573)
Total segment operating income	**$ 88,123**	**$ 33,531**
Foreign exchange loss	(61)	(110)
Other income, net	332	179
Adjusted EBITDA	**$ 88,394**	**$ 33,600**

GAAP to Non-GAAP Reconciliation

Net Loss and Non-GAAP Net Income

$ in thousands	Three Months Ended March 31, 2019	2018
GAAP net loss	**$ (32,863)**	**$ (148,656)**
Non-GAAP adjustments:		
Acquisition/divestiture-related costs	1,345	4,653
Restructuring and realignment costs	20	3,342
Amortization and step-up:		
Intangible amortization expense	57,417	60,883
Inventory step-up expense	115	17,076
Amortization of debt discount and deferred financing costs	5,912	5,496
Impairment of long-lived assets	-	33,647
Share-based compensation	27,548	27,833
Loss on debt extinguishment	5,586	-
Upfront and milestone payments related to license and collaboration agreements	2,000	90
Depreciation	1,473	1,552
Fees related to refinancing activities	142	27
Drug substance harmonization costs	80	804
Charges relating to discontinuation of Friedreich's ataxia program	(79)	950
Total of pre-tax non-GAAP adjustments	**101,559**	**156,353**
Income tax effect of pre-tax non-GAAP adjustments	(14,751)	32,995
Other non-GAAP income tax adjustments	-	(35,893)
Total of non-GAAP adjustments	**86,808**	**153,455**
Non-GAAP Net Income	**$ 53,945**	**$ 4,799**

GAAP to Non-GAAP Reconciliation

GAAP and non-GAAP earnings (loss) per share – Basic and Diluted

$ in thousands	Three Months Ended March 31, 2019	Three Months Ended March 31, 2018
Non-GAAP Earnings Per Share:		
Weighted average ordinary shares - Basic	**172,789,209**	**164,549,502**
Non-GAAP Earnings Per Share - Basic:		
GAAP loss per share - Basic	**$ (0.19)**	**$ (0.90)**
Non-GAAP adjustments	0.50	0.93
Non-GAAP earnings per share - Basic	**$ 0.31**	**$ 0.03**
Weighted average ordinary shares - Diluted		
Weighted average ordinary shares - Basic	172,789,209	164,549,502
Ordinary share equivalents	7,496,024	3,201,430
Weighted average shares - Diluted	**180,285,233**	**167,750,932**
Non-GAAP Earnings Per Share - Diluted		
GAAP loss per share - Diluted	**$ (0.19)**	**$ (0.90)**
Non-GAAP adjustments	0.50	0.93
Diluted earnings per share effect of ordinary share equivalents	(0.01)	-
Non-GAAP earnings per share - Diluted	**$ 0.30**	**$ 0.03**

GAAP to Non-GAAP Reconciliation

Net Debt

$ in thousands	As of March 31, 2019	As of December 31, 2018
Long-term debt-current portion[(1)]	$ 250,000	$ -
Long-term debt, net of current	1,021,263	1,564,485
Exchangeable notes, net	336,858	332,199
Total Debt	**1,608,121**	**1,896,684**
Debt discount	78,465	87,038
Deferred financing fees	6,440	9,304
Total Principal Amount Debt	**1,693,026**	**1,993,026**
Less: cash and cash equivalents	1,032,808	958,712
Net Debt	**$ 660,218**	**$ 1,034,314**

(1) On March 31, 2019, $250.0 million was reclassified from "long-term debt, net of current" to "long-term debt – current portion" following the notice of partial optional redemption of $250.0 million of 2023 Senior Notes to the trustee under the indenture governing the 2023 Senior Notes and the holders of the 2023 Senior Notes, which notes were subsequently redeemed on May 1, 2019.


HORIZON