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

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:
☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

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

<table>
<thead>
<tr>
<th>Title of each class</th>
<th>Trading Symbol(s)</th>
<th>Name of each exchange on which registered</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ordinary shares, nominal value $0.0001 per share</td>
<td>HZNP</td>
<td>The Nasdaq Global Select Market</td>
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</tbody>
</table>

Emerging growth company ☐

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐
Item 2.02 Results of Operations and Financial Condition.

On January 13, 2020, in advance of meetings and its presentation at the J.P. Morgan Healthcare Conference in San Francisco, California, Horizon Therapeutics plc issued a press release and is making publicly available a corporate presentation which include estimates of certain operating and financial results as of and for the year ended December 31, 2019, as well as other updates regarding its business. Copies of the press release and presentation are attached as Exhibits 99.1 and 99.2, respectively.

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

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits.

<table>
<thead>
<tr>
<th>Exhibit No.</th>
<th>Description</th>
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<tbody>
<tr>
<td>104</td>
<td>Cover Page Interactive Data File (embedded within the Inline XBRL document).</td>
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</table>
Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: January 13, 2020

HORIZON THERAPEUTICS PUBLIC LIMITED COMPANY

By: /s/ Paul W. Hoelscher

Paul W. Hoelscher
Executive Vice President, Chief Financial Officer
Horizon Therapeutics plc Increases Peak U.S. Annual Net Sales Expectations for Key Growth Drivers; Provides Update on Several Pipeline Programs

— Increases KRYSTEXXA® (pegloticase injection) Peak U.S. Annual Net Sales Expectations to More Than $1 Billion —

— Increases Teprotumumab Peak U.S. Annual Net Sales Expectations to More Than $1 Billion —

— Announces 79 Percent of Patients Achieved a Complete Response in MIRROR Open-Label Pilot Study, Supporting KRYSTEXXA Immunomodulation Strategy to Optimize Treatment Outcomes —

— Announces Two New Pipeline Programs —

DUBLIN — Jan. 13, 2020 — Horizon Therapeutics plc (Nasdaq: HZNP) announced today that it is increasing the peak U.S. annual net sales expectations for its key growth drivers KRYSTEXXA and teprotumumab, as well as providing several pipeline updates.

“As we enter 2020, Horizon is in its strongest position ever,” said Timothy Walbert, chairman, president and chief executive officer, Horizon. “We believe KRYSTEXXA and teprotumumab each has the potential for more than $1 billion in peak U.S. annual net sales. In addition, our strong balance sheet allows us to augment our pipeline to bolster long-term growth. Furthermore, we are evaluating ways to help more patients benefit from our medicines, including two new pipeline programs — one that explores more convenient delivery for KRYSTEXXA by significantly reducing infusion time, and the other for an additional indication for teprotumumab, specifically for the rare disease, diffuse cutaneous scleroderma.”

Continued Strong KRYSTEXXA Growth Drives Higher Peak Net Sales Expectation; New Immunomodulation Study Data and Shorter-Infusion Duration Development Program Offer Potential to Benefit More Uncontrolled Gout Patients

Based on current strong performance, the Company is increasing its peak U.S. annual net sales expectation for KRYSTEXXA to more than $1 billion, from the previous expectation of more than $750 million. The Company continues to project KRYSTEXXA full-year 2019 net sales growth of more than 25 percent.

The Company also announced topline results from its MIRROR open-label pilot study, which evaluated the use of the immunomodulator methotrexate with KRYSTEXXA to increase the response rate of KRYSTEXXA. The results of the study demonstrated that 79 percent, or 11 of 14 patients, achieved a complete response, defined as the proportion of serum uric acid (sUA) responders (sUA < 6 mg/dL) at Month 6. The combination was also well tolerated. Detailed results from the study will be presented at a future medical meeting. The 79 percent response rate is significantly higher than the 42 percent response rate in the KRYSTEXXA Phase 3 clinical program, which evaluated KRYSTEXXA alone.

KRYSTEXXA has demonstrated rapid reduction in sUA levels for people with uncontrolled gout; however, treatment with biologic medicines can, in some patients, trigger the body’s immune system to develop anti-drug antibodies. These anti-drug antibodies can reduce the effectiveness of the biologic therapy. Immunomodulators such as methotrexate, which is commonly used by rheumatologists, can help reduce this reaction.

Horizon Therapeutics plc
The MIRROR open-label pilot study follows other studies that showed an improved response rate when KRYSTEXXA is co-administered with methotrexate. There is a growing body of data supporting the potential of KRYSTEXXA plus immunomodulation to become the standard therapy opposed to KRYSTEXXA therapy alone. This includes an independent case series presented at the Annual European Congress of Rheumatology meeting in June 2019 which demonstrated that the administration of KRYSTEXXA with methotrexate resulted in a 100 percent response (10 of 10 patients) as defined by >90 percent of sUA levels being maintained at goal (<6.0 mg/dL) during the treatment period. Further, a case series presented at the American College of Rheumatology meeting in November 2019 demonstrated an 80 percent response (8 of 10 patients) as defined by receiving >3 infusions without loss of sUA response.

The Company is currently conducting a separate, placebo-controlled MIRROR trial evaluating the use of KRYSTEXXA and methotrexate. The trial, with 135 randomized patients, is designed to enable the potential for submission of results to the U.S. Food and Drug Administration (FDA) for update to the label.

In addition, the Company is planning to evaluate the impact of administering KRYSTEXXA over a significantly shorter infusion duration. The initial proof-of-concept work will begin mid-2020. Currently, KRYSTEXXA is infused over a two-hour or longer timeframe. A shorter infusion duration could meaningfully improve the experience and convenience for patients, physicians and sites of care.

Increasing Teprotumumab Peak Net Sales Expectation; Evaluating an Additional Indication for Diffuse Cutaneous Scleroderma, a Rare Disease with No Treatment Options

The FDA is currently evaluating a Biologics License Application (BLA) for teprotumumab for the treatment of Thyroid Eye Disease (TED) under Priority Review, with a Prescription Drug User Fee Act (PDUFA) action date of March 8, 2020. On Dec. 13, 2019, the Dermatologic and Ophthalmic Drugs Advisory Committee of the FDA voted unanimously (12-0) in favor of teprotumumab. Teprotumumab is a fully human monoclonal antibody that targets and blocks the insulin-like growth factor 1 receptor (IGF-1) with the potential to be the first and only medicine approved for this rare eye disease.

TED is a serious, progressive, vision-threatening rare autoimmune disease in which the muscles and fatty tissue behind the eye become inflamed and expand, which can lead to proptosis (eye bulging) and diplopia (double vision) and seriously impact activities of daily living and patients’ quality of life.

Based on an improved understanding of the TED landscape informed by market research and launch preparation activities as well as the dramatic results achieved in the teprotumumab Phase 3 OPTIC trial, the Company is increasing its peak U.S. annual net sales expectation to more than $1 billion, from the previous expectation of more than $750 million.

The Company is evaluating additional indications for teprotumumab and is initiating an exploratory study in diffuse cutaneous scleroderma, a rare fibrotic disease with no treatment options. Diffuse cutaneous scleroderma is a subtype of scleroderma in which excess collagen production causes skin thickening and hardening, or fibrosis, over large areas of the body, usually the fingers, hands, arms, anterior trunk, legs and face. There can be significant associated organ damage, including to the gastrointestinal tract, kidneys, lungs and heart. Literature suggests that the mechanism of action of teprotumumab, which is to block the IGF-1 receptor, could have an impact on fibrotic processes, such as those that are relevant to diffuse cutaneous scleroderma. The Company expects to conduct an exploratory trial beginning in the first half of 2020 to evaluate objective biomarker and clinical endpoints to inform potential subsequent larger and longer duration clinical trials.
“We are extremely pleased to be one step closer to bringing teprotumumab to the thousands of patients with Thyroid Eye Disease who have been waiting for a treatment for this debilitating, painful and vision-threatening disease,” said Shao-Lee Lin, M.D., Ph.D., executive vice president, head of research and development and chief scientific officer, Horizon. “Understanding the potential of our medicines for additional diseases is also important. We believe teprotumumab may impact underlying mechanisms of fibrosis and could demonstrate utility beyond thyroid eye disease, including diffuse cutaneous scleroderma, a rare autoimmune disease with central characteristics of inflammation and fibrosis.”

About KRYSTEXXA

INDICATIONS AND USAGE
KRYSTEXXA® (pegolitace injection) is a PEGylated uric acid specific enzyme indicated for the treatment of chronic gout in adult patients refractory to conventional therapy.

Gout refractory to conventional therapy occurs in patients who have failed to normalize serum uric acid and whose signs and symptoms are inadequately controlled with xanthine oxidase inhibitors at the maximum medically appropriate dose or for whom these drugs are contraindicated.

Important Limitations of Use: KRYSTEXXA is not recommended for the treatment of asymptomatic hyperuricemia.

IMPORTANT SAFETY INFORMATION

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS
Anaphylaxis and infusion reactions have been reported to occur during and after administration of KRYSTEXXA. Anaphylaxis may occur with any infusion, including a first infusion, and generally manifests within 2 hours of the infusion. However, delayed-type hypersensitivity reactions have also been reported. KRYSTEXXA should be administered in healthcare settings and by healthcare providers prepared to manage anaphylaxis and infusion reactions. Patients should be premedicated with antihistamines and corticosteroids. Patients should be closely monitored for an appropriate period of time for anaphylaxis after administration of KRYSTEXXA. Serum uric acid levels should be monitored prior to infusions, and healthcare providers should consider discontinuing treatment if levels increase to above 6 mg/dL, particularly when 2 consecutive levels above 6 mg/dL. are observed.

The risk of anaphylaxis and infusion reactions is higher in patients who have lost therapeutic response.

Concomitant use of KRYSTEXXA and oral urate-lowering agents may blunt the rise of sUA levels. Patients should discontinue oral urate-lowering agents and not institute therapy with oral urate-lowering agents while taking KRYSTEXXA.

In the event of anaphylaxis or infusion reaction, the infusion should be slowed, or stopped and restarted at a slower rate.

Patients should be informed of the symptoms and signs of anaphylaxis and instructed to seek immediate medical care should anaphylaxis occur after discharge from the healthcare setting.

Horizon Therapeutics plc
CONTRAINDICATIONS: G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

Patients should be screened prior to starting KRYSTEXXA. Hemolysis and methemoglobinemia have been reported with KRYSTEXXA in patients with G6PD deficiency. KRYSTEXXA should not be administered to these patients.

GOUT FLARES

An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including treatment with KRYSTEXXA. If a gout flare occurs during treatment, KRYSTEXXA need not be discontinued. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

CONGESTIVE HEART FAILURE

KRYSTEXXA has not been studied in patients with congestive heart failure, but some patients in the clinical trials experienced exacerbation. Caution should be exercised when using KRYSTEXXA in patients who have congestive heart failure, and patients should be monitored closely following infusion.

ADVERSE REACTIONS

The most commonly reported adverse reactions in clinical trials with KRYSTEXXA were gout flares, infusion reactions, nausea, cutaneous ecchymosis, nasopharyngitis, constipation, chest pain, anaphylaxis and vomiting.

Please see Full Prescribing Information and Medication Guide for more information.

About Teprotumumab

Teprotumumab is a fully human monoclonal antibody (mAb) and a targeted inhibitor of the IGF-1R. Teprotumumab has received Priority Review, Orphan Drug, Fast Track and Breakthrough Therapy designations from the FDA. The clinical development program for teprotumumab in the treatment of TED includes statistically significant results from both the Phase 2 clinical study, which were published in The New England Journal of Medicine, as well as from the Phase 3 OPTIC confirmatory clinical trial. Both trials were conducted at leading centers in the U.S., Germany and Italy, with co-principal investigators Raymond Douglas, M.D., Ph.D., Cedars-Sinai Medical Center and George Kahaly, M.D., Ph.D., Johannes Gutenberg University Medical Centre. Horizon is also conducting the OPTIC-X extension trial to gather further insight into the long-term efficacy and safety of teprotumumab.

About Horizon

Horizon is focused on researching, developing and commercializing medicines that address critical needs for people impacted by rare and rheumatic diseases. Our pipeline is purposeful: we apply scientific expertise and courage to bring clinically meaningful therapies to patients. We believe science and compassion must work together to transform lives. For more information on how we go to incredible lengths to impact lives, please visit www.horizontherapeutics.com, follow us @HorizonNews on Twitter, like us on Facebook, or explore career opportunities on LinkedIn.
Forward Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to expected financial performance and operating results in future periods, including potential growth in net sales of certain of Horizon’s medicines; plans with respect to product development efforts; potential market opportunity for, regulatory approval of and benefits of Horizon’s medicines and medicine candidates; statements regarding the timing of an FDA decision on the teprotumumab BLA; expectations regarding the review of the BLA and the potential benefits of teprotumumab to patients; 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 and successfully launch new medicines; 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 and existing medicines for new indications; risks associated with regulatory approvals; risks in the ability to recruit, train and retain qualified personnel; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption “Risk Factors” and elsewhere in Horizon’s filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information.

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Horizon Therapeutics plc
Timothy Walbert
Chairman, President and Chief Executive Officer
Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to expected financial operating results in 2019 and future periods, including potential growth in net sales of certain of Horizon’s medicines and existing medicines after launch; plans with respect to product development efforts; expected timing of clinical trials and regulatory decisions; 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 involve significant risks and uncertainties. Actual results and the timing of events could differ materially from those anticipated in such statements as a result of these risks and uncertainties, which include, without limitation, risks that Horizon’s actual future financial operating results may differ from its expectations or goals; Horizon’s ability to grow net sales from existing medicines and successfully launch new medicines; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; Horizon’s ability to successfully implement its business strategies; risks inherent in developing novel medicine candidates and obtaining regulatory approvals; risks associated with regulatory approvals; risks in the ability to recruit, train and retain qualified personnel; including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and the legal and regulatory environment in which Horizon operates and other risks detailed from time to time 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.
Our Growth, Evolution and Strategy

Teprotumumab: Potential to be the First and Only Approved Medicine for Thyroid Eye Disease (TED)

KRYSTEXXA: Optimizing the Growth Trajectory of the Only Approved Medicine for Uncontrolled Gout

R&D Pipeline: Expanding to Support Sustainable Growth; Announcing Two New Programs

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Horizon: A Differentiated Investment Opportunity

We are a leading **profitable biopharmaceutical company**
- Differentiated commercial model; generating annual net sales of $1.29B\(^{(1)}\) 8 years post IPO
- Focused on rare diseases, rheumatology, nephrology, ophthalmology and endocrinology
- Two high-growth drivers with >$2B in combined peak U.S. annual net sales potential\(^{(2)}\)

Delivering **innovative therapies** to patients
- Deep development expertise with proven track record
- Building a pipeline through M&A to support sustainable long-term growth

Generating **high returns** for shareholders
- Outperformed NBI for 1, 3, 5 years
- Our prospects position us with a top-tier growth profile

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\(^{(1)}\) Midpoint of 2019 Company net sales guidance.
\(^{(2)}\) Horizon estimate.
Today We are in Our Strongest Position Ever

Key Takeaways

Increasing peak U.S. annual net sales expectations for our key growth drivers

- KRYSTEXXA: >$1B\textsuperscript{(1)}
- Teprotumumab: >$1B\textsuperscript{(1)}

Generated positive results of KRYSTEXXA MIRROR open-label immunomodulation trial

- New Data: 79 percent of patients achieved complete response\textsuperscript{(2)}
- MIRROR RCT underway to enable KRYSTEXXA label enhancement

Maximizing growth drivers through additional R&D programs

- New: KRYSTEXXA shorter-inferior trial designed to improve patient outcomes
- New: Teprotumumab explores diffuse cutaneous scleroderma

Strengthened capital structure

- Significantly reduced gross debt
- 1.1x net leverage\textsuperscript{(3)}; below target of 2.0x

\textsuperscript{[1]} Hanson estimate.
\textsuperscript{[2]} MIRROR open-label response rate of 79 percent compared to Phase 3 blinded, p< 0.02.
\textsuperscript{[3]} Net leverage as of Sept. 30, 2019.
Our Unique Biopharma Model is Delivering on Our Third Phase of Growth and Evaluation

Our Strategy: Maximizing Key Growth Drivers While Expanding Pipeline for Sustainable Growth

**Expanding Pipeline and Therapies**
- Maximizing KRYSTEdda opportunity
- Reinvesting cash flow into teprotumab
- Building pipeline and presence in core
- 10 medicines; 6 for rare diseases

**Rare Disease Focus**
- Reinvested cash flow into acquiring rare disease assets
- Invested in repositioning and rejuvenating KRYSTEXX
- Built out R&D capabilities

**Formation**
- Created sustainable, cash-flow positive company via initial portfolio
- Built out commercial capabilities
- IPO in 2011 with 2 medicines

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(1) Midpoint of 2010 Company net sales guidance.
(2) Net sales for year ended Dec. 31, 2014.
(3) Net sales for year ended Dec. 31, 2011.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Our Prospects Position Us with a Top-Tier Growth Profile

Net Sales Target
*Double-digit CAGR*

Non-GAAP Operating Income Target
*Strong Double-digit CAGR*

Note: Projections could change significantly as a result of any acquisitions or divestitures.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
We Employ a Holistic Approach to Maximize the Value of Our Medicines for Patients

- We DEEPLY UNDERSTAND the medicine, the disease, and the market dynamics, investing in clinical data to advance the science.
- We develop the right COMMERCIAL STRATEGY, TEAM, AND INFRASTRUCTURE to support our patients and drive uptake.
- We develop the right CLINICAL STRATEGY to improve physician and clinical conviction for patients and optimize outcomes.

**KRISTEXXA exemplifies our industry-leading holistic approach; we are leveraging this expertise with teprotumumab.**

- KRISTEXXA was an underperforming and undervalued asset at acquisition in January 2016.
- We transformed its growth trajectory through strong commercial execution, quadrupling annual net sales in 3 years.
- We are driving continued growth opportunities for KRISTEXXA, projecting peak U.S. annual net sales of $1B³.
- We are further maximizing KRISTEXXA through our immunomodulation clinical strategy so more patients can benefit.

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³ Horizon estimate.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Transformed Our R&D Organization to Deliver on Our Future Promise

Tremendous Progress in Two Years

2018

Built experienced R&D leadership team with deep drug development expertise; agile execution and proven track record

- Recruited industry veteran to lead and build R&D organization
- Added leadership team with broad expertise and capabilities/experience
- Experience across broad range of therapeutic areas and rare diseases
- 100+ molecules developed across team

2019

Accelerated delivery on near-term transformative priorities including teprotumumab development and improvement of KRYSTEXXA profile

- Teprotumumab: Accelerated development program and BLA submission
- KRYSTEXXA: Optimizing product profile targeting response rate
- Opened new South San Francisco facility
- Initiated HemoShear collaboration to discover new targeted therapies for gout

2020

Maximizing and expanding early and late stage opportunities to drive sustained growth

- Teprotumumab: March 8, 2020 PDUFA date; evaluating additional indications
- KRYSTEXXA: Continuing to optimize product profile and convenience
- Growing pipeline through acquisitions and partnerships

BLA: Biologics License Application.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Expanding Our Pipeline with Two New Programs to Maximize Our Current Portfolio

Announcing KRYSTEXXA MIRROR Open-Label Data

<table>
<thead>
<tr>
<th>MEDICINE / PROGRAM</th>
<th>DESCRIPTION</th>
<th>PRE-CLINICAL</th>
<th>PHASE 1</th>
<th>PHASE 2</th>
<th>PHASE 3</th>
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<tr>
<td>KRYSTEXXA Immunomodulation</td>
<td>• MIRROR Open-Label (complete) • MIRROR Randomized Controlled Trial</td>
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<td>KRYSTEXXA Nephrology</td>
<td>• PROTECT study in kidney transplant patients with uncontrolled gout</td>
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<td>KRYSTEXXA Shorter-Infusion Duration(1)</td>
<td>• Open-label study</td>
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<td>PROCYSBI</td>
<td>• Delayed-release oral granules in packets; NDA under review</td>
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<td>Teprotumumab Thyroid Eye Disease</td>
<td>• OPTIC-X trial: Phase 3 extension study</td>
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<td>Teprotumumab Diffuse Cutaneous Scleroderma(1)</td>
<td>• Exploratory study</td>
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<td>HZN-003 Next-Gen Uncontrolled Gout</td>
<td>• Optimized uricase and optimized PEGylation for uncontrolled gout</td>
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<td>HZN-007 Next-Gen Uncontrolled Gout(2)</td>
<td>• Optimized uricase and PASylation for uncontrolled gout</td>
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<td>HemoShear Gout Discovery Collaboration</td>
<td>• Exploration of novel approaches to treating gout</td>
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*Tepronumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale. (1) Planned study expected to begin in 2020. (2) Being developed under a collaboration.*

MIRROR: Trials 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.

OPTIC-X: Open-label extension study following Phase 3 trial evaluating Teprotumumab for the treatment of Thyroid Eye Disease.
Significantly Strengthened Our Capital Structure in 2019

Reduced Gross Debt by $575M in 2019

**Strong Cash Balance and Net Debt Position**

- **Gross Leverage**
  - Sept. 30, 2018: 4.9x
  - Sept. 30, 2019: 2.9x

- **Net Leverage**
  - Sept. 30, 2018: 2.9x
  - Sept. 30, 2019: 1.1x

Gross Leverage: Gross debt to last-12-months adjusted EBITDA.
Net Leverage: Net debt to last-12-months adjusted EBITDA.

(1) 2018 cash interest expense vs. pro forma annualized 2019 cash interest expense.
(2) 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.
Teprotumumab
Potential Growth Opportunity in Area of Significant Unmet Need
Teprotumumab Has the Potential to Be the First and Only Approved Medicine for Thyroid Eye Disease

March 8, 2020 PDUFA Date; Unanimous FDA Advisory Committee Vote
- 12-0 FDA Advisory Committee vote in December in favor of benefit/risk profile of teprotumab
- Impressive Phase 3 results show 82.9 percent of teprotumumab patients with ≥2mm proptosis

Thyroid Eye Disease is a debilitating, vision-threatening, autoimmune disease that impacts quality of life
- Inflammation and tissue expansion behind the eye cause proptosis (bulging of the eyes)
- Annual U.S. incidence of 15-20K patients eligible for teprotumumab

Significant market education efforts continuing for U.S. commercial launch
- Multi-functional, highly experienced team has been working with stakeholders since July 2019

Raising peak U.S. annual net sales estimate to >$1B

[1] Horizon estimate. Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale. PDUFA: Prescription Drug User Fee Act.
Thyroid Eye Disease: Rare, Debilitating, Vision-Threatening; Severely Impacts Quality of Life

Inflammation and tissue expansion behind the eye causes **proptosis**, the most disfiguring sign of TED

Can impair ability to close eyes, resulting in **pain**, corneal ulcerations

Associated with **diplopia** (double vision), which is a result of misalignment of eyes

**Impacts quality of life:**
Working, driving, reading, sleeping
“One of the most heartbreaking complaints we hear from patients with severe TED is, my grandkids are afraid of me.”

Kimberly Dorris
Executive Director and CEO of Graves' Disease and Thyroid Foundation

Source: Written testimony submitted to the FDA to support the approval of teprotumumab

“I varied from total blindness during surgery to vision that qualified as legally blind. These problems prevented me from performing my duties as a police sergeant.”

Ronald Barela
Lives with Thyroid Eye Disease

Source: Spoken testimony provided at Dec. 13 FDA Advisory Committee Meeting
Active TED Progresses to Inactive TED; Permanent Damage May Require Surgery

Begins as active Thyroid Eye Disease for 1-3 years; Progresses to inactive Thyroid Eye Disease

Disease Activity

- Efficacious therapy
- Untreated
- Surgery

Up to 3 years
Beyond 3 years

- Active
- Inactive

Phase 3 Trial: 82.9 Percent of Patients Achieved Primary Endpoint of Proptosis Response

Proptosis Response (Reduction of ≥2 mm) at Week 24

Proptosis Reduction of 3.32 mm at Week 24

Note: Throughout the 24-week treatment period, patients treated with teprotumumab had an average proptosis reduction of 3.83 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 follicular phase day 21 to day 1 baseline score interactions.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Phase 3 Trial: All Secondary Endpoints Met with Statistical Significance

**Diplopia**
Percentage of participants with improvement from baseline of at least one grade in diplopia

<table>
<thead>
<tr>
<th>Week</th>
<th>Teprotumumab (N=41)</th>
<th>Placebo (N=42)</th>
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<tbody>
<tr>
<td>Baseline</td>
<td>4</td>
<td>50</td>
</tr>
<tr>
<td>Week 6</td>
<td>18</td>
<td>68</td>
</tr>
<tr>
<td>Week 12</td>
<td>21</td>
<td>68</td>
</tr>
<tr>
<td>Week 18</td>
<td>29</td>
<td>68</td>
</tr>
</tbody>
</table>

**Quality of Life**
Mean change from baseline in GO-QoL questionnaire overall score

<table>
<thead>
<tr>
<th>Week</th>
<th>Teprotumumab (N=41)</th>
<th>Placebo (N=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>5.3</td>
<td>10.2</td>
</tr>
<tr>
<td>Week 6</td>
<td>5.2</td>
<td>13.9</td>
</tr>
<tr>
<td>Week 12</td>
<td>1.8</td>
<td>17.3</td>
</tr>
</tbody>
</table>

**Clinical Activity**
Percentage of participants with CAS of 0 or 1 in each study evaluation cycle

<table>
<thead>
<tr>
<th>Week</th>
<th>Teprotumumab (N=41)</th>
<th>Placebo (N=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>22</td>
<td>22</td>
</tr>
<tr>
<td>Week 6</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Week 12</td>
<td>10</td>
<td>10</td>
</tr>
</tbody>
</table>

Diplopia: Double vision. Note: Only participants who had baseline diplopia (diplopia score >0) were included in the diplopia analysis.

GO-QoL: Graves’ Ophthalmopathy Quality of Life.

CAS: Clinical Activity Score is a 7-point scale that measures change in orbital inflammation and pain; a score of >3 indicates active Thyroid Eye Disease.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Positive Benefit/Risk Profile for Teprotumumab in Thyroid Eye Disease

**Benefits**

- Clinically significant reduction in proptosis
- Significant improvement in diplopia
- Reduced inflammation
  - Orbital pain, eyelid and conjunctival swelling and redness
- Improved patients’ quality of life
  - Functional vision
  - Appearance

**Manageable Safety Profile**

- Hyperglycemia and infusion reactions
- Potential for IBD exacerbation
- Hearing impairment
- Muscle spasms
- Infection
- Potential for embryo-fetal toxicity based on animal studies

*IBD: Inflammatory bowel disease.*
*Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.*
Teprotumumab: With No Approved Treatment, the Patient Journey is Long and Ill-Defined

Primary Care
Ophthalmologist
Allergist or Optometrist
Endocrinologist

Repeat Doctor Visits and Tests
Before, During and After Diagnosis

Active Stage
1-3 Years

Patient finally diagnosed with TED → Severity increases

Steroids up to 8 grams → Steroids fail
Optic nerve compromised → Surgery

“Watch and Wait” Approach

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Teprotumumab: Horizon is Simplifying the Process for Patients, Physicians and Sites of Care

Simplifying the Patient Journey

- **Endocrinologist**
  Recognizes TED symptoms and refers to ophthalmologist

- **Ophthalmologist / Oculoplastic Surgeon / Neuro-Ophthalmologist**
  Confirms diagnosis and refers patient to site of care

- **Teprotumumab at Site of Care**

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Teprotumumab: Building a Robust Infrastructure to Support All Aspects of the Patient Journey with an Approximately 100-Person Field Team

<table>
<thead>
<tr>
<th>Physicians</th>
<th>Patient Education &amp; Support</th>
<th>Site of Care (Infusion Centers)</th>
<th>Reimbursement Support</th>
</tr>
</thead>
<tbody>
<tr>
<td>~50-person sales force with buy-and-bill experience; 14+ medical scientific liaisons</td>
<td>Leveraging Horizon’s extensive experience in patient services and dedicated marketing efforts</td>
<td>National and regional teams supporting infusion centers</td>
<td>Disease, unreimbursed support</td>
</tr>
<tr>
<td>• Disease and treatment education</td>
<td>• 1-to-1 patient support from diagnosis through treatment</td>
<td>• Logistical support</td>
<td>• Disease, unreimbursed support</td>
</tr>
<tr>
<td>• Referral facilitation</td>
<td>• Direct-to-patient digital disease awareness campaign</td>
<td>• Referral network build out</td>
<td>• Value proposition to ensure optimal access</td>
</tr>
<tr>
<td>• Reimbursement support</td>
<td>• Grassroots advocacy efforts</td>
<td>• Site-of-care identification and segmentation</td>
<td></td>
</tr>
</tbody>
</table>

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Teprotumumab: Well Prepared for the Potential Commercial Launch

Expected Peak U.S. Annual Net Sales of >$1B(1)

Pre-Launch
Efforts Driving Awareness and Excitement; Paving Way for Launch

2H19 to Present

- **Multi-functional team** established; meeting with key stakeholders since July
- >6,000 physician targets reached (95% of top-decile prescribers); 1,300 top targets engaged 5.5x
- Launched multimedia **DTC and DTP disease awareness programs** (150K unique DTC visitors; >500 patients enrolled)
- Identified, met with and educated >300 sites of care; began establishing referral network infrastructure
- Conducted extensive payer meetings representing two-thirds of total lives with positive indication of access
- Presented teprotumumab clinical results and TED education sessions at >10 medical meetings since Phase 3 data readout
- **Significant engagement** with advocacy and patient communities

Launch and Post-Launch Plans

- **Sufficient product supply** available for commercial launch
- Building payer and site of care networks
- **Targeting top-tier ophthalmologists and endocrinologists (60/40 split):** high empathy, urgency and volume (manage 4,500 TED patients)
- Launching branded campaign that is motivating to physicians and patients
- Launch-year dynamics:
  - Manual, temporary reimbursement coding process
  - Payer approval process and pull-through
  - Continuing to establish referral infrastructure

PDUFA Date: March 8, 2020

---

(1) Horizon estimate.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
Teprotumumab: Compelling Value Proposition

**Unmet Need**
No prior treatments for Thyroid Eye Disease
Multiple complex surgeries often required

**Rare Disease**
U.S. addressable incidence of 15K to 20K patients\(^{(2)}\)

**Efficacy**
82.9 percent achieved proptosis reduction of ≥2mm
Number needed to treat for proptosis response is 1.6\(^{(1)}\)

**Acute Treatment**
6-month course of therapy with long-term durability

---

\(^{(1)}\) Number needed to treat (NNT) is a method used to describe the effectiveness of a treatment, signifying how many patients need to be treated in order to get one additional patient better who would not have gotten better without the treatment. A perfect NNT would be 1; the larger the number, the fewer people will be helped. As a general rule of thumb, an NNT of 5 or under for treating a symptomatic condition is usually considered to be acceptable. [Link to NNT](https://www.usatoday.com/story/news/nation/2013/10/06/number-need-to-treat/3574466/)

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.

\(^{(2)}\) Horizon estimate of teprotumumab sales
## Diffuse Cutaneous Scleroderma
- Chronic autoimmune disease marked by fibrosis, including hardening of skin and internal organ involvement
- Rare disease with no approved or effective treatments
- Patients typically suffer extensive fibrosis that can progress to internal organ damage
- Primarily managed by rheumatologists

## Epidemiology
- ~100K patients in U.S. diagnosed with scleroderma\(^1\)
- Of U.S. diagnosed patients, ~30K patients are diagnosed with diffuse cutaneous scleroderma\(^1\)

---

\(^1\) Horizon estimate.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.
KRYSTEXXA

Our Flagship Medicine with Significant Growth Potential
Gout: A Systemic Disease Often Associated with Multiple Negative Consequences

- Most common inflammatory arthritis\(^{(1)}\)
- Characterized by multiple comorbidities, including chronic kidney disease and hypertension
- Systemic disease; uric acid deposits can occur almost anywhere in the body

Uncontrolled Gout

- Chronic gout refractory (unresponsive) to conventional therapies

---

\(^{(1)}\) Zhu Y, Pandya BI, Choi HK.

KRystexxa: The Only Medicine Approved for Uncontrolled Gout
Rapidly Reverses Disease Progression

Before and After KRystexxa

Converting urate to water-soluble allantoin;
Renal excretion of allantoin is up to 10x more efficient than excretion of uric acid

[1] Uncontrolled gout is chronic gout refractory (unresponsive) to conventional therapies.
KRYPTEXXA: Our Commercial Strategy Has Accelerated Volume Growth

*Increasing Our Peak U.S. Annual Net Sales Expectations to >$1B<sup>(1)</sup>*

---

**KRYSTEXXA Net Sales**

*Driven by Vial Growth*

<table>
<thead>
<tr>
<th>Year</th>
<th>Net Sales (M)</th>
<th>Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>2016</td>
<td>$91M</td>
<td>72%</td>
</tr>
<tr>
<td>2017</td>
<td>$157M</td>
<td>65%</td>
</tr>
<tr>
<td>2018</td>
<td>$239M</td>
<td>&gt;25%&lt;sup&gt;(2)&lt;/sup&gt;</td>
</tr>
<tr>
<td>2019</td>
<td></td>
<td>&gt;$1B&lt;sup&gt;(1)&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

---

<sup>(1)</sup> Horizon estimate.

<sup>(2)</sup> 2019 Company guidance of >25% KRYSTEXXA net sales growth.
KRYS T EXXA: 79 Percent Complete Response Rate Achieved in MIRROR Open-Label

79%
MIRROR OL complete response rate

VS.

42%
Phase 3 complete response rate

Well-tolerated

Response Rate of KRYS T EXXA plus Methotrexate Significantly Higher than KRYS T EXXA Alone

<table>
<thead>
<tr>
<th></th>
<th>KRYS T EXXA Alone</th>
<th>KRYS T EXXA plus Methotrexate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 3 Clinical Trials</td>
<td>47%</td>
<td>79%</td>
</tr>
<tr>
<td>MIRROR OL</td>
<td>79%</td>
<td>80%</td>
</tr>
<tr>
<td>Albert</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>


Note: Data from separate clinical trials may not be directly comparable due to differences in study protocols, conditions, and patient populations.
KRYSLEXXA: MIRROR RCT Underway to Support Potential Label Expansion

- Immunomodulation has potential to increase KRYSLEXXA response rate
  - Increases physician confidence
  - Allows patients to stay on therapy longer
- Following MIRROR RCT readout, potential to expand label

<table>
<thead>
<tr>
<th>MIRROR Randomized Clinical Trial Design</th>
</tr>
</thead>
</table>

**135 Patients Evaluated for 24 Weeks**

<table>
<thead>
<tr>
<th>Arm</th>
<th>Description</th>
<th>Infusions Details</th>
</tr>
</thead>
<tbody>
<tr>
<td>KRYSLEXXA + methotrexate</td>
<td>(n=90)</td>
<td>12 infusions: 1 every two weeks</td>
</tr>
<tr>
<td>KRYSLEXXA + placebo</td>
<td>(n=45)</td>
<td>12 infusions: 1 every two weeks</td>
</tr>
</tbody>
</table>

Initiated Q2 2019; Data Readout Expected in 2021

**Primary Endpoint at Week 24:**
Proportion of serum uric acid (sUA) responders (sUA <6 mg/dL)
KRYSTEXXA: PROTECT Study Designed to Support Nephrologists’ Understanding

Evaluating KRYSTEXXA to Improve Management of Uncontrolled Gout in Kidney Transplant Patients

- Gout is **10x** more frequent in kidney transplant patients
- **PROTECT** is designed to provide data for most severe chronic kidney disease patients

**PROTECT Trial Design**

20 Kidney Transplant Patients with Uncontrolled Gout Evaluated for 2 Years

- KRYSTEXXA (n=20)
- 12 infusions: 1 every two weeks

*Initiated Q3 2019; Data Readout Expected in 2021*

**Primary Endpoint at Week 24:**
Proportion of serum uric acid (sUA) responders (sUA <6 mg/dL)

PROTECT: Clinical trial evaluating the effect of KRYSTEXXA on serum uric acid levels in kidney transplant patients with uncontrolled gout.
KRUSTEXXA: Improving the Patient Experience through a Shorter-Infusion Study

Current state
KRUSTEXXA infusion duration currently 2+ hours

Opportunity
Open-label study evaluating the impact of administering KRUSTEXXA for a shorter-infusion duration
Potential to meaningfully improve patient, physician and site-of-care experiences
Today We are in Our Strongest Position Ever

Key Takeaways

Increasing peak U.S. annual net sales expectations for our key growth drivers
- KRYSTEXXA: >$1B\(^{[1]}\)
- Teprotumumab: >$1B\(^{[1]}\)

Maximizing growth drivers through additional R&D programs
- **New:** KRYSTEXXA shorter-infusion dosing designed to improve patient convenience
- **New:** Teprotumumab explore for diffuse cutaneous scleroderma

Generated positive results of KRYSTEXXA MIRROR open-label immunomodulation trial
- **New Data:** 79 percent of patients achieved complete response\(^{[2]}\)
- MIRROR RCT underway to enable KRYSTEXXA label enhancement

Strengthened capital structure
- Significantly reduced gross debt in 2019 with 1.1x net leverage\(^{[3]}\); below target of 2.0x

---

MIRROR: Trials evaluating the use of KRYSTEXXA in combination with methotrexate to increase the response rate.  
RCT: Randomized controlled trial.  
Teprotumumab is an investigational candidate and its safety and efficacy have not been established, and it is not approved for sale.  
\(^{[1]}\) Horizon estimate.  
\(^{[2]}\) MIRROR open-label response rate of 79 percent compared to Phase 3 blinded, pl of 42 percent.  
\(^{[3]}\) Net leverage as of Sept. 30, 2019.
Appendix

Additional Information and Reconciliations of GAAP to Non-GAAP Measures
We Have Rapidly Evolved into a Company Focused on Rare Disease Medicines

2013: Net sales of $74 Million
2 Medicines

LTM Sept. 30, 2019: Net sales of
Diversified Portfolio; 6 for Rare

LTM: Last twelve months.
Thyroid Eye Disease Pathology

- The body attacks its own orbital cells which overexpress IGF-1R
- The IGF-1R and TSHR are linked and form a signaling complex
- This leads to severe inflammation and expansion of tissue, muscle and fat cells behind the eye
- Causes proptosis and optic nerve compression

Teprotumumab Mechanism of Action

- Fully human monoclonal antibody inhibitor of IGF-1R
- Blocks IGF-1R and turns off signaling complex at the disease
- Intended to reduce inflammation and prevent excess growth behind the eye

IGF-1R: Insulin-like growth factor-1 receptor, TSHR: Thyroid stimulating hormone receptor.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
Educating Patient Community on Thyroid Eye Disease

Partnering with Key Advocacy Organizations

Learning About Patient Needs

My TED Story

Add your voice to the Thyroid Eye Disease (TED) community. Tell us how you have seen TED affect those you love and how the TED community is helping to ensure those who are living with TED to put their voice first.

Share Your TED Story

TEDct
Thyroid Eye Disease Charitable Trust

Prevent Blindness

NORD
National Organization for Rare Disorders

American Autoimmune
Becker-Hebert Association, Inc.

Lighthouse Guild
# Next-Generation Uncontrolled Gout Programs

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

<table>
<thead>
<tr>
<th>HZN-003</th>
<th>HZN-007(^{(1)})</th>
<th>HemoShear Coll.</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Optimized uricase and optimized PEGylation for uncontrolled gout</td>
<td>• Optimized uricase and PASylation for uncontrolled gout</td>
<td>• Strong capability to identify and validate novel biologicals</td>
</tr>
<tr>
<td>• Potency allowing potential for subcutaneous dosing</td>
<td>• PASylation as a new approach to increasing half-life and reducing immunogenicity</td>
<td>• Exploring novel approaches to treating gout</td>
</tr>
</tbody>
</table>

\(^{(1)}\) Being developed under a collaboration agreement with XL Protein.
<table>
<thead>
<tr>
<th>Durable Orphan Franchise</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RAVICTI</strong> (polyglutamate) Oral Liquid</td>
</tr>
<tr>
<td><strong>Procysbi</strong> (cysteamine bitartrate) delayed-release capsules</td>
</tr>
<tr>
<td><strong>Actimmune</strong> (immunoglobulin)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Indication</strong></th>
<th><strong>Urea cycle disorders (UCDs)</strong></th>
<th><strong>Nephropathic cystinosis (NC)</strong></th>
<th><strong>Chronic granulomatous disease (CGD)</strong></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>UCDs</strong></td>
<td>UCDs are rare and life-threatening genetic diseases resulting in the body’s inability to remove ammonia from the blood stream. UCDs cause hyperammonia that can lead to intellectual disability, seizures, coma or death.</td>
<td>NC is a rare and life-threatening, progressive, multisystem metabolic disorder. Without cysteamine-depleting treatment, high intracellular cystine concentrations can occur in virtually all organs and tissues, leading to irreversible cellular damage, progressive multi-organ failure and death.</td>
<td>CGD is a life-threatening disease that leads to recurrent infections and fungal infections. Patients have increased risk of severe and recurrent bacterial infections, along with the development of granulomas.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>U.S. Market</strong></th>
<th>~2,600 people with UCDs</th>
<th>~500-600 diagnosed patients</th>
<th>~1,600 people</th>
</tr>
</thead>
<tbody>
<tr>
<td>~1,000 diagnosed population</td>
<td>~400-450 diagnosed patients on cystine-depleting therapy</td>
<td>Increase awareness and diagnosis of UCDs</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th><strong>Growth Strategy</strong></th>
<th>Conversion from older-generation nitrogen-scavengers to RAVICTI</th>
<th>Increase awareness of label expansion to position RAVICTI as first-line therapy</th>
<th>Increase awareness and diagnosis of UCDs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Increase awareness of label expansion to position Procysbi as first-line therapy</td>
<td>Drive uptake of untreated patients and optimal dosing</td>
<td>Increase awareness and diagnosis of UCDs</td>
<td></td>
</tr>
</tbody>
</table>

---

(1) See full prescribing information at [www.RAVICTI.com](http://www.RAVICTI.com), [www.Procysbi.com](http://www.Procysbi.com) and [www.Actimmune.com](http://www.Actimmune.com). Information found on or accessible through these websites is not a part of or incorporated by reference in this presentation.
Inflammation Segment: Provides Cash Flow to Support Investments in Our Orphan and Rheumatology Medicines

- Three medicines:
  - DUEXIS® and VIMOVO®: indicated for treatment of osteoarthritis (OA) and rheumatoid arthritis
  - PENNSAID® 2%: indicated for treatment of OA of the knee
We Have Transformed into a Rare Disease Focused Company through Acquisitions

- **September 2014**: Acquisition of Vidara Therapeutics Intl.
- **October 2015**: Acquisition of Hyperion Therapeutics, Inc.
- **February 2016**: Acquisition of Crealta Holdings LLC
- **October 2016**: Acquisition of Raptor Pharmaceutical Corp.
- **January 2017**: Acquisition of River Vision Development Corp.
- **January 2018**: Collaboration with HemTherautics

- **October 2017**: HZN-003 and HZN-007 for uncontrolled gout
- **February 2018**: Teprotumumab, late-stage development candidate for thyroid eye disease
Our Portfolio Is Supported by Our Intellectual Property Expertise and Long-Life Protected Patents

<table>
<thead>
<tr>
<th>Orphan and Rheumatology</th>
<th>Inflammation</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>RAVICTI</strong></td>
<td><strong>PENNSAID</strong></td>
</tr>
</tbody>
</table>
| - Settled Par (first-filer) litigation with right to market July 1, 2025  
  - Settled Lupin litigation with right to market 180 days after Par | - Settled Teilgent, Amneal, Paddock (Perriq litigations by granting a right to market n Oct. 17, 2027 |
| **Procysbi** | **DUEXIS** |
| - 9 08-listed patents extending to 2036  
  - Orphan Drug Exclusivity: U.S. 2020-2022 | - Settled Par (first-filer) litigation with right to market |
| **ACTHMUNE** | **VIMOVO** |
| - 2 U.S. patents extending to 2022 | - On-going (first-filer) litigation with Dr. Re |
| **KRSTEXX** | - Settled litigation with the following parties: Lupin with right to market Aug 1, 2024 |
| - 18 U.S. patents extending to 2030; composition of matter to 2026  
  - Biologic Exclusivity to 2022 | |
| **RAYOS** | |
| - Settled Actavis (first-filer) litigation with right to market Dec. 23, 2022 | |
## GAAP to Non-GAAP Reconciliation

### EBITDA and Adjusted EBITDA – Three and Nine Months Ended September 30

<table>
<thead>
<tr>
<th></th>
<th>Three Months Ended September 30</th>
<th>Nine Months Ended September 30</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2019</td>
<td>2018</td>
</tr>
<tr>
<td><strong>GAAP net income (loss)</strong></td>
<td>$18,324</td>
<td>$33,381</td>
</tr>
<tr>
<td><strong>Depreciation</strong></td>
<td>1,658</td>
<td>1,523</td>
</tr>
<tr>
<td><strong>Amortization and step-up:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible amortization expense</td>
<td>57,662</td>
<td>61,144</td>
</tr>
<tr>
<td>Inventory step-up expense</td>
<td>-</td>
<td>83</td>
</tr>
<tr>
<td><strong>Interest expense, net (including amortization of debt discount and deferred financing costs)</strong></td>
<td>20,438</td>
<td>30,437</td>
</tr>
<tr>
<td><strong>(Benefit) expense for income taxes</strong></td>
<td>$(36,564)</td>
<td>$(1,266)</td>
</tr>
<tr>
<td><strong>EBITDA</strong></td>
<td>$67,418</td>
<td>$125,302</td>
</tr>
<tr>
<td><strong>Other non-GAAP adjustments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition/divestiture-related costs</td>
<td>67</td>
<td>302</td>
</tr>
<tr>
<td>Restructuring and realignment costs</td>
<td>-</td>
<td>4,562</td>
</tr>
<tr>
<td>Impairment of long-lived assets</td>
<td>-</td>
<td>3,603</td>
</tr>
<tr>
<td>(Gain)/Loss on sale of assets</td>
<td>-</td>
<td>(12,303)</td>
</tr>
<tr>
<td>Share-based compensation</td>
<td>18,151</td>
<td>28,428</td>
</tr>
<tr>
<td>Litigation settlements</td>
<td>-</td>
<td>1,500</td>
</tr>
<tr>
<td>Upfront, progress and milestone payments related to license and collaboration agreements</td>
<td>3,073</td>
<td>(100)</td>
</tr>
<tr>
<td>Fees related to refinancing activities</td>
<td>262</td>
<td>40</td>
</tr>
<tr>
<td>Loss on debt extinguishment</td>
<td>41,171</td>
<td>-</td>
</tr>
<tr>
<td>Drug substance harmonization costs</td>
<td>80</td>
<td>301</td>
</tr>
<tr>
<td>Charges relating to discontinuation of Friedreich’s ataxia program</td>
<td>-</td>
<td>254</td>
</tr>
<tr>
<td><strong>Total of other non-GAAP adjustments</strong></td>
<td>63,004</td>
<td>24,607</td>
</tr>
<tr>
<td><strong>Adjusted EBITDA</strong></td>
<td>$130,422</td>
<td>$149,909</td>
</tr>
<tr>
<td>Description</td>
<td>Amount</td>
<td></td>
</tr>
<tr>
<td>----------------------------------------------------------------------------</td>
<td>----------</td>
<td></td>
</tr>
<tr>
<td>GAAP net loss</td>
<td>$(38,380)</td>
<td></td>
</tr>
<tr>
<td>Depreciation</td>
<td>6,126</td>
<td></td>
</tr>
<tr>
<td>Amortization and step-up:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible amortization expense</td>
<td>243,634</td>
<td></td>
</tr>
<tr>
<td>Inventory step-up expense</td>
<td>17,312</td>
<td></td>
</tr>
<tr>
<td>Interest expense, net (including amortization of</td>
<td></td>
<td></td>
</tr>
<tr>
<td>debt discount and deferred financing costs)</td>
<td>121,692</td>
<td></td>
</tr>
<tr>
<td>Benefit for income taxes</td>
<td>(44,752)</td>
<td></td>
</tr>
<tr>
<td><strong>EBITDA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>$ 305,652</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Other non-GAAP adjustments:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition/divestiture-related costs</td>
<td>4,296</td>
<td></td>
</tr>
<tr>
<td>Restructuring and realignment costs</td>
<td>15,350</td>
<td></td>
</tr>
<tr>
<td>Share-based compensation</td>
<td>114,860</td>
<td></td>
</tr>
<tr>
<td>Impairment of long-lived assets</td>
<td>46,096</td>
<td></td>
</tr>
<tr>
<td>Litigation settlements</td>
<td>5,750</td>
<td></td>
</tr>
<tr>
<td>Drug substance harmonization costs</td>
<td>2,855</td>
<td></td>
</tr>
<tr>
<td>Fees related to refinancing activities</td>
<td>937</td>
<td></td>
</tr>
<tr>
<td>Upfront and milestone payments related to license and collaboration</td>
<td>(10)</td>
<td></td>
</tr>
<tr>
<td>agreements</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Charges relating to discontinuation of Friedrich's ataxia program</td>
<td>(1,464)</td>
<td></td>
</tr>
<tr>
<td>Gain on sale of assets</td>
<td>(42,985)</td>
<td></td>
</tr>
<tr>
<td><strong>Total of other non-GAAP adjustments</strong></td>
<td><strong>145,785</strong></td>
<td></td>
</tr>
<tr>
<td><strong>Adjusted EBITDA</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>$ 451,417</strong></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
## GAAP to Non-GAAP Reconciliation

### Net Debt

<table>
<thead>
<tr>
<th></th>
<th>September 30, 2019</th>
<th>December 31, 2018</th>
<th>September 30, 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>Long-term debt, net of current</td>
<td>$1,000,819</td>
<td>$1,564,485</td>
<td>$1,563,239</td>
</tr>
<tr>
<td>Exchangeable notes, net</td>
<td>346,541</td>
<td>332,199</td>
<td>327,573</td>
</tr>
<tr>
<td><strong>Total Debt</strong></td>
<td>1,347,360</td>
<td>1,896,684</td>
<td>1,890,812</td>
</tr>
<tr>
<td>Debt discount</td>
<td>65,234</td>
<td>87,038</td>
<td>92,473</td>
</tr>
<tr>
<td>Deferred financing fees</td>
<td>5,432</td>
<td>9,304</td>
<td>9,741</td>
</tr>
<tr>
<td><strong>Total Principal Amount of Debt</strong></td>
<td>1,418,026</td>
<td>1,993,026</td>
<td>1,993,026</td>
</tr>
<tr>
<td>Less: cash and cash equivalents</td>
<td>883,964</td>
<td>958,712</td>
<td>807,047</td>
</tr>
<tr>
<td><strong>Net Debt</strong></td>
<td>$534,062</td>
<td>$1,034,314</td>
<td>$1,185,979</td>
</tr>
</tbody>
</table>