This presentation contains forward-looking statements, including, but not limited to, statements related to expected financial performance and operating results in 2019 and future periods, including potential growth in net sales of certain of Horizon’s medicines and estimated net sales of new medicines after launch; plans with respect to product development efforts; expected timing of clinical trials and regulatory submissions and 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 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 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)

**KRYSТЕXXA:** 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

Total Shareholder Return at Dec. 31, 2019

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

Maximizing growth drivers through additional R&D programs
- New: KRYSTEXXA shorter-infusion study; designed to improve patient convenience
- New: Teprotumumab exploratory study in 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

---

(1) Horizon estimate.
(2) MIRROR open-label response rate of 79 percent compared to Phase 3 blinded, placebo-controlled clinical trial data of 42 percent.
(3) Net leverage as of Sept. 30, 2019.
Our Unique Biopharma Model is Delivering on Our Third Phase of Growth and Evolution

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

**Expanding Pipeline and Therapeutic Area Focus**
- Maximizing KRUSTEXXA opportunity
- Reinvesting cash flow into teprotumumab launch and growth
- Building pipeline and presence in core therapeutic areas
- 10 medicines; 6 for rare diseases

**Rare Disease Focus**
- Reinvested cash flow into acquiring rare disease portfolio
- Invested in repositioning and rejuvenating KRUSTEXXA
- 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 2019 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*

**Growth Drivers**

- **KRYSTEXXA:**  
  Peak Net Sales >$1B\(^{(1)}\)

- **Teprotumumab:**  
  Peak Net Sales >$1B\(^{(1)}\)

- Meaningful operating margin expansion, inclusive of increased R&D investment

---

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

\(^{(1)}\) Horizon estimate.  
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 understanding and clinical conviction to benefit more patients and optimize growth.

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

- KRYSTEXXA 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 KRYSTEXXA; projecting peak U.S. annual net sales of >$1B(1)
- We are further maximizing KRYSTEXXA through our immunomodulation clinical strategy so more patients can benefit

(1) 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 pipeline of early and late stage medicines to drive sustainable growth

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

BLA: Biologics License Application. PDUFA: Prescription Drug User Fee Act. 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>
<th>PHASE 3b/4</th>
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</thead>
<tbody>
<tr>
<td>KRYSTEXXA Immunomodulation</td>
<td>• MIRROR Open-Label (complete)</td>
<td></td>
<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td></td>
<td>• MIRROR Randomized Controlled Trial</td>
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<tr>
<td>KRYSTEXXA Nephrology</td>
<td>• PROTECT study in kidney transplant patients with uncontrolled gout</td>
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<tr>
<td>KRYSTEXXA Shorter-Infusion Duration&lt;sup&gt;(1)&lt;/sup&gt;</td>
<td>• Open-label study</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>PROCYSBI</td>
<td>• Delayed-release oral granules in packets; NDA under review</td>
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<tr>
<td>Teprotumumab Thyroid Eye Disease</td>
<td>• OPTIC-X trial: Phase 3 extension study</td>
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<tr>
<td>Teprotumumab Diffuse Cutaneous Scleroderma&lt;sup&gt;(1)&lt;/sup&gt;</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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<tr>
<td>HZN-007 Next-Gen Uncontrolled Gout&lt;sup&gt;(2)&lt;/sup&gt;</td>
<td>• Optimized uricase and PASylation for uncontrolled gout</td>
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<tr>
<td>HemoShear Gout Discovery Collaboration</td>
<td>• Exploration of novel approaches to treating gout</td>
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</tbody>
</table>

Teprotumumab 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 agreement with XL Protein.

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

<table>
<thead>
<tr>
<th>Date</th>
<th>Cash</th>
<th>Net Debt</th>
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</thead>
<tbody>
<tr>
<td>12/31/2016</td>
<td>$509M</td>
<td>$1,435M</td>
</tr>
<tr>
<td>12/31/2017</td>
<td>$751M</td>
<td>$1,269M</td>
</tr>
<tr>
<td>12/31/2018</td>
<td>$959M</td>
<td>$1,034M</td>
</tr>
<tr>
<td>09/30/2019</td>
<td>$884M</td>
<td>$534M</td>
</tr>
</tbody>
</table>

### Managing Debt and Leverage Efficiently

- **Reduced gross debt** by $575M to $1.418B at Dec. 31, 2019
- **Extended maturities** of $1B of debt to 2026/2027
- **Reduced interest expense** by >40 percent\(^{(1)}\)
- **Net leverage ratio** of 1.1x at Sept. 30, 2019, down from 2.9x\(^{(2)}\)

<table>
<thead>
<tr>
<th>Gross Leverage(^{(2)})</th>
<th>Sept. 30, 2018</th>
<th>Sept. 30, 2019</th>
<th>Target</th>
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<tbody>
<tr>
<td></td>
<td>4.9x</td>
<td>2.9x</td>
<td>&lt;3.0x</td>
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<thead>
<tr>
<th>Net Leverage(^{(2)})</th>
<th>Sept. 30, 2018</th>
<th>Sept. 30, 2019</th>
<th>Target</th>
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<tbody>
<tr>
<td></td>
<td>2.9x</td>
<td>1.1x</td>
<td>&lt;2.0x</td>
</tr>
</tbody>
</table>

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\(^{(1)}\) 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 teprotumumab
- Impressive Phase 3 results show 82.9 percent of teprotumumab patients with ≥2mm proptosis reduction

Thyroid Eye Disease is a debilitating, vision-threatening, autoimmune disease that severely 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.
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
What We Hear from Thyroid Eye Disease Patients

“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

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

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

Proptosis Responders (%)

Baseline Week 6 Week 12 Week 18 Week 24

7.1 56.1 75.6 82.9 82.9

p<0.001 p<0.001 p<0.001

Difference: 73.45 (95%CI 58.89, 88.01)

Teprotumab (N=41) Placebo (N=42)

Note: Throughout the 24-week treatment period, patients treated with teprotumab 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.

Teprotumab 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

Quality of Life

Mean change from baseline in GO-QoL questionnaire overall score

Clinical Activity Score

Percentage of participants with a CAS value of 0 or 1 in the study eye

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.
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.

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
Teprotumumab: With No Approved Treatment, the Patient Journey is Long and Ill-Defined

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

Primary Care
Ophthalmologist
Allergist or Optometrist
Endocrinologist

Repeat Doctor Visits and Tests
Before, During and After Diagnosis

Patient finally diagnosed with TED
Severity increases

Active Stage
1-3 Years
Steroids up to 8 grams
Steroids fail
Optic nerve compromised
Surgery

“Watch and Wait” Approach

Inactive Stage

Surgeries

Endocrinologist
Recognizes TED symptoms and refers to ophthalmologist

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

Teprotumumab Infused 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

Approximately 100-Person Field Team

### Physicians
- ~50-person sales force with buy-and-bill experience; 14+ medical scientific liaisons
- Disease and treatment education
- Referral facilitation
- Reimbursement support

### Patient Education & Support
- Leveraging Horizon’s extensive experience in patient services and dedicated marketing efforts
- 1-to-1 patient support from diagnosis through treatment
- Direct-to-patient digital disease awareness campaign
- Grassroots advocacy efforts

### Site of Care (Infusion Centers)
- National and regional teams supporting infusion centers
- Logistical support
- Referral network build out
- Site-of-care identification and segmentation
- Disease and treatment education
- Reimbursement education

### Payers
- Reimbursement team supporting access
- Disease, unmet need and treatment education
- Value proposition education to ensure optimal patient access

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\textsuperscript{(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

PDUFA Date: March 8, 2020

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 (top 130 targets 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


(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

Efficacy
82.9 percent achieved proptosis reduction of ≥2mm
Number needed to treat for proptosis response is 1.6

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

Safety
Significant benefits outweigh manageable risks

---

(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. [https://www.uws.edu/wp-content/uploads/2013/10/Number_Needed_to_Treat.pdf](https://www.uws.edu/wp-content/uploads/2013/10/Number_Needed_to_Treat.pdf)

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 patients eligible for teprotumumab each year.
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

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

Evaluating efficacy based on teprotumumab mechanism of action, which is to block IGF-1R
- Literature suggests that targeting IGF-1R could have an impact on the fibrotic process
- Initiating exploratory study to evaluate objective biomarker and clinical endpoints

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

**Gout**
- 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

9.5M
U.S. gout patients; growing low-single digits\(^{(2)}\)

3.5M
U.S. gout patients seeking treatment\(^{(2)}\)

~100K
Uncontrolled gout patients

~4K
Treated with KRYSTEXXA in 2019

---

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

KRySTEXXA: The Only Medicine Approved for Uncontrolled Gout (1)

Rapidly Reverses Disease Progression (2)

Before and After KRySTEXXA

Converts urate to water-soluble allantoin;
Renal excretion of allantoin is up to 10x more efficient than excretion of uric acid (3)

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

Increasing Our Peak U.S. Annual Net Sales Expectations to >$1B\(^{(1)}\)

**KRYSTEXXA Net Sales**
*Driven by Vial Growth*

**Growth Drivers**

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

---

(1) Horizon estimate.
(2) 2019 Company guidance of >25 percent KRYSTEXXA net sales growth.
KRUSTEXXA: 79 Percent Complete Response Rate Achieved in MIRROR Open-Label Trial

79% MIRROR OL complete response rate

VS.

42% Phase 3 complete response rate

Well-tolerated

Response Rate of KRUSTEXXA plus Methotrexate Significantly Higher than KRUSTEXXA Alone

<table>
<thead>
<tr>
<th></th>
<th>KRUSTEXXA Alone</th>
<th>KRUSTEXXA plus Methotrexate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Phase 3 Clinical Trials</td>
<td>42%</td>
<td>79%</td>
</tr>
<tr>
<td>MIRROR OL</td>
<td>79%</td>
<td>80%</td>
</tr>
<tr>
<td>Albert Case Series</td>
<td>80%</td>
<td>100%</td>
</tr>
<tr>
<td>Peterson Botson Case Series</td>
<td>100%</td>
<td>100%</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.
KRYSTEXXA: MIRROR RCT Underway to Support Potential Label Expansion

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

### MIRROR Randomized Clinical Trial Design

135 Patients Evaluated for 24 Weeks

- KRYSTEXXA + methotrexate (n=90)
  - 12 infusions: 1 every two weeks
- KRYSTEXXA + placebo (n=45)
  - 12 infusions: 1 every two weeks

Initiated Q2 2019; Data Readout Expected in 2021

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

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) at Month 6
KRYSTEXXA: Improving the Patient Experience through a Shorter-Infusion Study

**Current state**

KRYSTEXXA infusion duration currently 2+ hours

**Opportunity**

Open-label study evaluating the impact of administering KRYSTEXXA 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\textsuperscript{(1)}
- **Teprotumumab:** >$1B\textsuperscript{(1)}

### Maximizing growth drivers through additional R&D programs

- **New:** KRYSTEXXA shorter-infusion study; designed to improve patient convenience
- **New:** Teprotumumab exploratory study in diffuse cutaneous scleroderma

### 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

### Strengthened capital structure

- Significantly reduced gross debt in 2019 with 1.1x net leverage\textsuperscript{(3)}; below target of 2.0x

---

\textsuperscript{(1)} Horizon estimate.
\textsuperscript{(2)} MIRROR open-label response rate of 79 percent compared to Phase 3 blinded, placebo-controlled clinical trial data of 42 percent.
\textsuperscript{(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 $1.3 Billion
Diversified Portfolio; 6 for Rare Diseases

LTM: Last twelve months.
Mechanism of Action of Teprotumumab for Thyroid Eye Disease

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

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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

Educating Patients on TED

**Eyelids shouldn’t need help**

**LISTEN TO YOUR EYES**
SYMPTOMS LIKE RETRACTED EYELIDS CAUSED BY BULGING EYES COULD MEAN YOUR THYROID EYE DISEASE MAY BE GETTING WORSE

The pain or numbness in your eyes not only makes it harder to do things like read, watch TV, or go to work, it also means your condition may be getting more serious. Find an eye care specialist who will get to know you and your eyes to determine the cause of your symptoms.

**Share Your TED Story**

Your story may be used on social media and in other venues to help raise awareness of the impact of TED.

Share your "TED story":

Name:

American Autoimmune Related Diseases Association, Inc.
Lighthouse Guild
New R&D Programs to Build on Our Market Leadership Position in Uncontrolled Gout

Next-Generation Uncontrolled Gout Programs
Potential to improve response rate and 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\(^{(1)}\)
- Optimized uricase and PASylation for uncontrolled gout
- PASylation as a new approach to increasing half-life and reducing immunogenicity
- Potency allowing potential for subcutaneous dosing

Novel Gout Discovery Program
- Strong capability to identify and validate novel biological targets
- Exploring novel approaches to treating gout

HemoShear Collaboration

\(^{(1)}\) Being developed under a collaboration agreement with XL Protein.
## Durable Orphan Franchise

<table>
<thead>
<tr>
<th>Indication</th>
<th>Urea cycle disorders (UCDs)</th>
<th>Nephropathic cystinosis (NC)</th>
<th>Chronic granulomatous disease (CGD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>U.S. Market</td>
<td>~2,600 people with UCDs</td>
<td>~500-600 diagnosed patients</td>
<td>~1,600 people with CGD</td>
</tr>
<tr>
<td></td>
<td>~1,000 diagnosed population</td>
<td>~400-450 diagnosed patients</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td>on cystine-depleting therapy</td>
<td></td>
</tr>
<tr>
<td>Growth Strategy</td>
<td>Conversion from older-generation nitrogen-scavengers to RAVICTI</td>
<td>Conversion from older-generation cysteamine-depleting therapy to PROCYSBI</td>
<td>Increase awareness and diagnosis of CGD</td>
</tr>
<tr>
<td></td>
<td>Increase awareness of label expansion to position RAVICTI as first-line therapy</td>
<td>Increase awareness of label expansion to position PROCYSBI as first-line therapy</td>
<td>Drive adoption of “triple prophylaxis” therapy – antifungal + antibiotic + immunomodulation (IFNg)</td>
</tr>
<tr>
<td></td>
<td>Increase awareness and diagnosis of UCDs</td>
<td>Drive uptake of untreated patients and optimal dosing</td>
<td>Increase persistence of and adherence to treatment</td>
</tr>
</tbody>
</table>

- UCDs are rare and life-threatening genetic diseases resulting in the body’s inability to remove ammonia from the blood stream\(^{(1)}\)
- UCDs cause hyperammonia that can lead to intellectual disability, seizures, coma or death\(^{(2)}(3)\)

- NC is a rare and life-threatening, progressive, multisystem metabolic disorder\(^{(1)}\)
- 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

- CGD is a life-threatening immune disease that leads to recurrent severe bacterial and fungal infections\(^{(1)}\)
- Patients have increased susceptibility to severe and recurrent bacterial and fungal infections, along with the formation and development of granulomas in most organs

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\(^{(1)}\) 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.

\(^{(2)}\) Summar, 2001

\(^{(3)}\) Haeberle, 2019

\(^{(4)}\) Horizon estimate.
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.
- **May 2015**: Acquisition of Hyperion Therapeutics, Inc.
- **January 2016**: Acquisition of Crealta Holdings LLC
- **October 2016**: Acquisition of Raptor Pharmaceutical Corp.
- **May 2017**: Acquisition of River Vision Development Corp.
- **January 2018**: - Acquisition of HZN-003 from MedImmune LLC - Partnered with XL-protein GmbH on HZN-007 (PASylated Uricase)
- **January 2019**: - Acquisition of HZN-003 from MedImmune LLC - Partnered with XL-protein GmbH on HZN-007 (PASylated Uricase)

**Teprotumumab**
- Late-stage development candidate for thyroid eye disease

**Gout Discovery Collaboration**
Our Portfolio Is Supported by Our Intellectual Property Expertise and Long-Life Protected Patents

### Orphan and Rheumatology

<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>RAVICTI®</td>
<td>[Details not provided]</td>
</tr>
<tr>
<td>PROCYSBI®</td>
<td>[Details not provided]</td>
</tr>
<tr>
<td>ACTIHUMNE®</td>
<td>[Details not provided]</td>
</tr>
<tr>
<td>KRYSTEXXA®</td>
<td>[Details not provided]</td>
</tr>
<tr>
<td>RAYOS® (Prelorine) Delayed-release Tablets</td>
<td>Settled Actavis (first-filer) litigation with right to market Dec. 23, 2022</td>
</tr>
</tbody>
</table>

### Inflammation

<table>
<thead>
<tr>
<th>Product</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>PENNSAID®</td>
<td>Settled Teligent, Amneal, Paddock (Perrigo), Taro and Lupin litigations by granting a right to market no sooner than Oct. 17, 2027</td>
</tr>
<tr>
<td>DUEXIS®</td>
<td>Settled Par (first-filer) litigation with right to market Jan. 1, 2023</td>
</tr>
<tr>
<td>VIMOVO®</td>
<td>On-going (first-filer) litigation with Dr. Reddy’s Laboratories</td>
</tr>
<tr>
<td></td>
<td>Settled litigation with the following parties: Mylan, Actavis and Lupin with right to market Aug. 1, 2024</td>
</tr>
</tbody>
</table>
## GAAP to Non-GAAP Reconciliation

### EBITDA and Adjusted EBITDA – Three and Nine Months Ended September 30, 2019

<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>GAAP net income (loss)</td>
<td>$18,234</td>
<td>$33,381</td>
</tr>
<tr>
<td>Depreciation</td>
<td>1,658</td>
<td>1,523</td>
</tr>
<tr>
<td>Amortization and step-up:</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>Interest expense, net (including amortization of debt discount and deferred financing costs)</td>
<td>20,428</td>
<td>30,437</td>
</tr>
<tr>
<td>(Benefit) expense for income taxes</td>
<td>(30,564)</td>
<td>(1,266)</td>
</tr>
<tr>
<td><strong>EBITDA</strong></td>
<td>$67,418</td>
<td>$125,302</td>
</tr>
<tr>
<td>Other non-GAAP adjustments:</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>4,582</td>
</tr>
<tr>
<td>Impairment of long-lived assets</td>
<td>-</td>
<td>1,603</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>41,371</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><strong>63,004</strong></td>
<td><strong>24,607</strong></td>
</tr>
<tr>
<td><strong>Adjusted EBITDA</strong></td>
<td><strong>$130,422</strong></td>
<td><strong>$149,909</strong></td>
</tr>
</tbody>
</table>
### GAAP to Non-GAAP Reconciliation

**EBITDA and Adjusted EBITDA – Full-Year 2018**

<table>
<thead>
<tr>
<th>GAAP to Non-GAAP Reconciliation</th>
<th>Twelve Months Ended December 31, 2018</th>
</tr>
</thead>
</table>

$ in thousands

- **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

### 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>