Horizon Pharma plc

Timothy P. Walbert
Chairman, President and
Chief Executive Officer
January 8, 2019
Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to expected growth in net sales of certain medicines, estimated peak annual net sales of certain medicines and medicine candidates; expected financial performance in future periods; expected timing of clinical trials and regulatory submissions and decisions; expected expansion of investment in Horizon Pharma’s rare disease medicine pipeline and marketing of KRISTEXXA and the impact thereof; potential corporate milestones and the timing thereof; potential market opportunity for Horizon Pharma’s medicines in approved and potential additional indications; and business and other statements that are not historical facts. These forward-looking statements are based on Horizon Pharma'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 Pharma’s actual full-year 2018, future financial and operating results may differ from its expectations or goals; Horizon Pharma’s ability to grow net sales from existing products; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; risks relating to Horizon Pharma’s ability to successfully implement its business strategies; risks inherent in developing novel medicine candidates, such as teprotumumab, and existing medicines for new indications; risks related to acquisition integration and achieving projected benefits; 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 Pharma operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon Pharma's filings and reports with the U.S. Securities and Exchange Commission. Horizon Pharma undertakes no duty or obligation to update any forward-looking statements contained in this presentation as a result of new information.
Agenda

1. Executing on Our Strategic Growth Objectives

2. Our Pipeline Programs:
   Teprotumumab, KRYS-TEXXA and Uncontrolled Gout

3. KRYS-TEXXA:
   Our On-Market Growth Driver

4. Key Takeaways
Our Aspiration

Be a leading rare disease biopharma company

Delivering innovative therapies to patients

Generating high returns for shareholders
Advancing Our Unique Biopharma Model

*Our Foundation is Commercial Execution; The Future is Our Pipeline*

**TRADITIONAL BIOTECH:**
- Conduct development program(s) using R&D expertise
- Obtain multiple financings with significant cash burn
- If successful, either sell or hire marketing expertise

**HORIZON PHARMA:**
A Rare Disease Biopharma Company

1. Establish commercial portfolio 2011-2016
2. Optimize growth trajectory through commercial expertise
3. Build solid financial position
4. Expand pipeline through internal development, licensing and acquisitions 2017 and beyond
Orphan and Rheumatology Segment

Driving Sustainable Long-term Net Sales Growth

- Durable base of rare disease medicines
- Expectation for significant peak sales for KRYSTEXXA and teprotumumab
- Potential upside with future pipeline assets

Note: 2018E for illustrative purposes only.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
(1) Horizon Pharma peak sales estimate for U.S. net sales only.
We Are Building Momentum

Significant Progress Executing Our Strategy

Building a Robust and Differentiated Pipeline

Developing a Leading R&D Organization

Maximizing KRYSTEXXA Growth
Executing on Teprotumumab

Phase 3 Data Read-Out Now Expected by End of Q1 2019

- Completed **Phase 3 trial enrollment** ahead of schedule
- Presented **72-week Phase 2 data** that demonstrated durability of response
- Expected **Phase 3 data read-out** by end of Q1 2019
- Tracking to a mid-2019 **BLA submission**
- Investing in **commercial launch activities** in anticipation of 2020 approval

**Potential U.S. Peak Net Sales >$750M**(1)

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(1) Horizon Pharma peak net sales estimate.
BLA: Biologic License Application.
Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
Advancing Our Gout R&D Programs to Sustain Our Leadership

- Encouraged by KRYSTEXXA plus methotrexate external case series demonstrating **nine of nine patients achieved response**
- Adapting our KRYSTEXXA plus methotrexate **MIRROR immunomodulation trial** to support potential for registration
- Progressing with **next-generation biologic programs for uncontrolled gout**
- Added collaboration with HemoShear to discover new gout therapies

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**Executing on our strategy to maximize value of KRYSTEXXA**
Transformed Our R&D Leadership Team to Add Scientific Expertise

- **Head of Development Sciences** to bolster new and innovative scientific capabilities
- **Head of External Research and Development** to assess acquisition and licensing opportunities
- **Rare Disease / Rheumatology Therapeutic Area Heads** to maximize KRYSTEXXA and execute on teprotumumab clinical development

**Expanded the R&D organization to significantly enhance its capabilities and enhance our business development process**
Driving Toward Our >$750M Peak Net Sales Estimate for KRYSTEXXA(1)

- Doubled our commercial team and addressable patient population and continue to invest in commercial infrastructure
- Opened more than 450 new accounts through Sept. 30, 2018, up 25 percent versus year-end 2017
- Expecting >65% net sales growth for 2018(1)
- Existing account vial growth increased 30% year-over-year(2)
- Generating significant interest in KRYSTEXXA by nephrologists
- Expecting double-digit KRYSTEXXA net sales growth in 2019(1)

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(1) Horizon Pharma estimate for U.S. net sales only.
(2) Year-to-date Sept. 30, 2018 vs. year-to-date Sept. 30, 2017.
Becoming a Leading Rare Disease Biopharma Company

Executing on Our Strategy

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

Made Significant Progress in 2018

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

Leveraging Our Momentum in 2019+

- Advancing toward peak net sales expectations:
  - **KRYSTEXXA**: >$750M\(^{(1)}\)
  - **Teprotumumab**: >$750M\(^{(1)}\)
- Potential upside with future pipeline assets

---

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

BUILT WITH PURPOSE
# Building a Robust Rare Disease Pipeline

<table>
<thead>
<tr>
<th>MEDICINE / CANDIDATE</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>
</tr>
</thead>
</table>
| KRYSTEXXA*           | Immunomodulation Studies:  
• MIRROR: KRYSTEXXA + methotrexate  
• RECIPE*: KRYSTEXXA + mycophenolate mofetil  
• TRIPLE*: KRYSTEXXA + azathioprine |  |  |  |  |  |
| HZN-001 (teprotumab)** | • OPTIC trial: Phase 3  
• OPTIC-X trial: Phase 3 extension |  |  |  |  |  |
| HZN-003              | • Optimized uricase and optimized PEGylation for uncontrolled gout |  |  |  |  |  |
| PASylated Uricase**   | • Optimized uricase and PASylation for uncontrolled gout |  |  |  |  |  |
| HemoShear Gout Discovery Collaboration | • Exploration of novel approaches to treating gout |  |  |  |  |  |

*Investigator-initiated trial

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1. Teprotumab is a fully human monoclonal antibody (mAb) IGF-1R inhibitor in development for moderate-to-severe thyroid eye disease (TED).
2. Being developed under a collaboration agreement.
   - MIRROR: Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving KRYSTEXXA.
   - RECIPE*: Reducing Immunogenicity to PegloticaseE.
   - TRIPLE*: Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect.
   - OPTIC: Treatment of Graves’ Orbitopathy (Thyroid Eye Disease) to Reduce Proptosis with Teprotumab Infusions in a Randomized, Placebo-Controlled, Clinical Study. Teprotumab is an investigational candidate and its safety and efficacy have not been established.
Teprotumumab

MEANINGFUL GROWTH OPPORTUNITY IN AN AREA OF SIGNIFICANT UNMET NEED
Teprotumumab Exemplifies Our Pipeline Strategy

Building a Pipeline for Sustainable Long-Term Growth

<table>
<thead>
<tr>
<th>PIPELINE CANDIDATE CRITERIA</th>
<th>TEPROTUMUMAB</th>
</tr>
</thead>
</table>
| High unmet need with preference for rare diseases | ✓ No FDA-approved therapies exist for thyroid eye disease
| Compelling clinical trial data or proof of concept | ✓ Impressive Phase 2 results published in *The New England Journal of Medicine*
| Key regulatory designations | ✓ U.S. Orphan, Fast-Track and Breakthrough Therapy |
| Durable Intellectual Property | ✓ 12-year biologic exclusivity |

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

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
Thyroid Eye Disease (TED)

Debilitating autoimmune inflammatory disease of the eye
- Associated with Graves’ Disease, but TED is a separate and distinct disease
- Impacts more women than men; typically happens mid-life; smoking worsens severity

Begins as treatable active TED and progresses to inactive TED

Inflammation behind the eye causes proptosis (bulging of the eyes)
- Over time turns fibrotic, causing permanent structural damage

Proptosis causes multiple conditions such as diplopia (double vision), strabismus (misalignment), compressed optic nerve (can be sight threatening), ulcerations, pain; can be disfiguring and emotionally debilitating
Patients Living with TED Have Significant Challenges Living a Normal Life

“You would think, ‘Oh, not being able to close your eye, that’s not a big deal,’ but it was a big deal. It was so easy to irritate. I had to wear sunglasses to sleep; it felt like I was in a stupor.”

“TED has robbed me of a normal life and my looks. I don’t know how much more I can take.”

“My social life has basically been non-existent since the bulging started.”

“My colleagues know about the condition but it’s difficult talking to an acquaintance about it, or someone I just met…it can be kind of embarrassing.”

Source: Horizon Pharma market research and patient interviews.
Active TED: Current Approaches are Suboptimal

Pathogenic Mechanisms of Disease Not Targeted

<table>
<thead>
<tr>
<th>Current Treatment Approach: Steroids</th>
<th>An Unmet Need Exists</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Do not reverse underlying alterations of orbital tissue</td>
<td>• No disease modifying medication available</td>
</tr>
<tr>
<td>• Do not reverse proptosis or diplopia</td>
<td>• Many U.S. physicians “watch and wait” for active phase to end</td>
</tr>
<tr>
<td>• Significant side effects</td>
<td>• Significant need for a treatment that can prevent the progression of the disease and the need for multiple corrective surgeries</td>
</tr>
</tbody>
</table>
Inactive TED: Surgery Becomes Only Option

Once TED becomes inactive, long-term damage is done

Surgery becomes only option\(^{(1)}\)

- Complex with mixed results
- Often requires multiple surgeries per eye because accumulation of fibrotic tissue complicates operations
- Tens of thousands of dollars per surgery
- While corrective for some, can result in permanent eye misalignment, double vision, lazy eye or blindness

(1) Surgical treatment can include decompression surgery, eyelid surgery and corrective vision surgery.
Mechanism of Action of Teprotumumab for TED

TED 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 (bulging of the eyes) 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.
Breakthrough Pivotal Phase 2 Trial Results Demonstrated Proptosis Improvement

**Primary Endpoint**

- Teprotumumab (N=42)
  - Responders at Week 24 (%): p<0.001
  - Proptosis: 69.0%

- Placebo (N=45)
  - Responders at Week 24 (%): p<0.001
  - Proptosis: 20.0%


1. Primary endpoint is a composite endpoint defined as a ≥2 point reduction in CAS and a ≥2 mm reduction in proptosis.

Clinical Activity Score (CAS): A 7-point scale that measures change in orbital inflammation and pain.

Thyroid-associated ophthalmopathy is also known as thyroid eye disease. Teprotumumab is an investigational candidate and its safety and efficacy have not been established.

**Proptosis**

“In conclusion, a 24-week course of teprotumumab therapy provided clinical benefit in patients with active, moderate-to-severe thyroid-associated ophthalmopathy by reducing proptosis and the Clinical Activity Score and by improving the patients’ quality of life.”

For us, it’s personal.
## Confirmatory Phase 3 Clinical Trial

**Now Expect Phase 3 Top-line Data Read-out by End of Q1 2019**

### Phase 2 vs. Phase 3

- Enrollment criteria are the same
- Majority of 13 trial sites are the same
- Primary endpoint is proptosis (objective, measurable, agreed upon by FDA)

### 24-Week Treatment Period

<table>
<thead>
<tr>
<th>Treatment</th>
<th>Infusions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Teprotumumab</td>
<td>8 infusions: 1 every three weeks</td>
</tr>
<tr>
<td>Placebo</td>
<td>8 infusions: 1 every three weeks</td>
</tr>
</tbody>
</table>

### Estimated Milestones

- **By end of Q1 2019**
  - Top-line data
- **Mid 2019**
  - BLA submission
- **2020**
  - Potential FDA approval

### Primary endpoint at Week 24

Proptosis responder rate defined as percentage of participants with >2 mm reduction

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(1) Assuming positive data and assuming priority review given breakthrough and fast-track designations.

BLA: Biologic License Application.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
**Expected Annual Addressable TED Population**

**U.S. Peak Net Sales Potential of >$750M**

<table>
<thead>
<tr>
<th><strong>ANNUAL U.S. TREATABLE POPULATION</strong></th>
<th><strong>EPIDEMIOLOGY</strong></th>
<th><strong>U.S. PEAK NET SALES POTENTIAL OF &gt;$750M</strong></th>
</tr>
</thead>
</table>
| • 15,000 to 20,000 patients eligible for treatment | **Bottoms-up market model uses patient-level data**
• 10+ years worth of data
• Hospital admissions, insurance claims  | • No FDA-approved therapies exist
• Active disease lasts up to 3 years | • Current treatment paradigm is suboptimal
• Literature informative; however  | • Teprotumumab is potentially disease modifying |
| | • Limited data
• Varies widely | |

(1) Horizon Pharma estimate for U.S. net sales only.
(2) Company analysis of claims data and market research.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
Gout R&D Programs

ENHANCING OUR LEADERSHIP
IN UNCONTROLLED GOUT
Exploring Ways to Improve KRYSTEXXA Response Rate

**Immunomodulation Studies Underway**

<table>
<thead>
<tr>
<th>MIRROR</th>
<th>RECIPE</th>
<th>TRIPLE</th>
</tr>
</thead>
</table>
| • Company-sponsored trial  
• KRYSTEXXA plus methotrexate  
• Trial being adapted to support potential for registration  
• Methotrexate is the most commonly used immunomodulator by rheumatologists | • Investigator-initiated trial  
• KRYSTEXXA plus mycophenolate mofetil (MMF)  
• Commonly used immunomodulator | • Investigator-initiated trial  
• KRYSTEXXA plus azathioprine  
• Commonly used immunomodulator |

Encouraged by external case series demonstrating **nine of nine** patients achieved full response by combining KRYSTEXXA with methotrexate.
New Programs to Build on Our Market Leadership Position in Uncontrolled Gout

<table>
<thead>
<tr>
<th>Next-generation Uncontrolled Gout Programs</th>
<th>Novel Gout Discovery Program</th>
</tr>
</thead>
<tbody>
<tr>
<td>Potential to improve response rate, duration of treatment and provide more convenient administration through subcutaneous dosing</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>HZN-003</th>
<th>PASylated Uricase</th>
<th>HemoShear Collaboration</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 biological targets</td>
</tr>
<tr>
<td>• Potency allowing for subcutaneous dosing</td>
<td>• PASylation as a new approach to increasing half-life and reduce immunogenicity</td>
<td>• Exploring novel approaches to treating gout</td>
</tr>
</tbody>
</table>
KRYSTEXXA

FLAGSHIP MEDICINE WITH SIGNIFICANT GROWTH POTENTIAL
KRYSTEXXA is the Only Medicine Approved for Uncontrolled Gout\(^1\); Rapidly Reverses Disease Progression\(^2\)

**Before and After 5 Months of KRYSTEXXA**

- **42%** of patients had complete response defined as reduced serum uric acid\(^2\)(\(^3\))
- **45%** of KRYSTEXXA patients had complete resolution of tophi\(^4\)

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(1) Uncontrolled gout is defined as chronic gout that is refractory to conventional therapies. Addressable U.S. population of 100,000.
(3) Complete response defined as serum uric acid levels <6mg/DL and maintained for duration of therapy.
KRYSTEXXA: Differentiated Mechanism of Action in Uncontrolled Gout

Unlike other gout medicines, KRYSTEXXA converts urate, the source of uric acid crystals, into a water-soluble substance, allantoin.

Only ~10% of uric acid filtered through the kidney is excreted\(^{(1)}\).

The body can rapidly and easily eliminate nearly all allantoin.

Current oral urate-lowering therapies target patients’ sUA levels by addressing the over production or under excretion of uric acid.

Renal excretion of allantoin is up to 10x more efficient than excretion of uric acid\(^{(2)}\).

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\(^{(1)}\) Terkeltaub R, Bushinsky DA, Becker MA. Arthritis Res Ther. 2006;8 (suppl 1):34.


sUA: serum uric acid.
The KRYSTEXXA Story Exemplifies Our Commercial Execution

**2016**

We **ACQUIRE** under-appreciated medicines through our uniquely strong in-house business development capability

- Under-resourced and poorly marketed prior to acquisition

**2017**

We then **OPTIMIZE** the growth trajectory of our acquired medicines through focused commercial execution

- >2x pre-acquisition net sales
- 40% YOY vial growth

**2018+**

Next, we **MAXIMIZE** the value of our medicines through new markets and collaborative research

- Expanded addressable patient population to 100K
- >65% FY ’18 expected net sales growth
- >4x pre-acquisition net sales
- Expect double-digit growth in 2019
- >$750M estimated peak annual sales
- Working to enhance response rate

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(1) Horizon Pharma estimate.
YOY: year over year.
Accelerating KRYSTEXXA Growth

Double-digit KRYSTEXXA Net Sales Growth Expected in 2019\(^{(1)}\)

**Past**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Vials Sold (in millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q2 '16</td>
<td>$20</td>
</tr>
<tr>
<td>Q3 '16</td>
<td>$26</td>
</tr>
<tr>
<td>Q4 '16</td>
<td>$30</td>
</tr>
<tr>
<td>Q1 '17(^{(2)})</td>
<td>$32</td>
</tr>
<tr>
<td>Q2 '17</td>
<td>$38</td>
</tr>
<tr>
<td>Q3 '17</td>
<td>$43</td>
</tr>
<tr>
<td>Q4 '17</td>
<td>$44</td>
</tr>
</tbody>
</table>

**Present**

<table>
<thead>
<tr>
<th>Quarter</th>
<th>Vials Sold (in millions)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Q1 '18(^{(2)})</td>
<td>$47</td>
</tr>
<tr>
<td>Q2 '18</td>
<td>$59</td>
</tr>
<tr>
<td>Q3 '18</td>
<td>$70</td>
</tr>
</tbody>
</table>

**Future**

Three Pillars of KRYSTEXXA Growth

- Growth in existing rheumatology accounts
- Growth in new rheumatology accounts
- Accelerating nephrology growth

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\(^{(1)}\) Horizon Pharma estimate.

\(^{(2)}\) Typical seasonality Q4 to Q1.
# Building on Our Momentum

## 2018 Progress and Potential Future Catalysts

<table>
<thead>
<tr>
<th>2018</th>
<th>2019</th>
<th>2020 and Beyond</th>
</tr>
</thead>
<tbody>
<tr>
<td>![Checkmark] RAVICTI sNDA submission for birth to two months</td>
<td>![Checkmark] Teprotumumab Phase 3 trial data by end of Q1</td>
<td>![Checkmark] Teprotumumab BLA decision and launch&lt;sup&gt;(1)&lt;/sup&gt;</td>
</tr>
<tr>
<td>![Checkmark] KRYSTEXXA RECIPE trial start</td>
<td>![Checkmark] Begin adapted KRYSTEXXA MIRROR trial in Q2</td>
<td>![Checkmark] KRYSTEXXA MIRROR registration trial data and submission</td>
</tr>
<tr>
<td>![Checkmark] KRYSTEXXA TRIPLE trial immunomodulation arm start</td>
<td>![Checkmark] Teprotumumab BLA submission mid-2019&lt;sup&gt;(1)&lt;/sup&gt;</td>
<td>![Checkmark] HZN-003 (optimized uricase and optimized PEGylation for uncontrolled gout) Phase 1 trial start</td>
</tr>
<tr>
<td>![Checkmark] Teprotumumab Phase 3 enrollment completed</td>
<td>![Checkmark] PASylated uricase lead candidate decision</td>
<td>![Checkmark] PASylated uricase Phase 1 trial start for uncontrolled gout</td>
</tr>
<tr>
<td>![Checkmark] KRYSTEXXA MIRROR trial start</td>
<td>![Checkmark] RAVICTI sNDA approval for birth to two months</td>
<td>![Checkmark] HemoShear lead candidate decision</td>
</tr>
<tr>
<td>![Checkmark] RAVICTI sNDA approval for birth to two months</td>
<td>![Checkmark] Milestone met</td>
<td>![Checkmark] Teprotumumab long-term data</td>
</tr>
</tbody>
</table>

<sup>(1)</sup> Assuming positive data and assuming priority review given breakthrough and fast-track designations.

RAVICTI: RAVICTI sNDA approval for birth to two months.

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MIRROR: Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving KRYSTEXXA.

RECIPE: REDucing Immunogenicity to Pegloticase.

TRIPLE: Tolerization REDuces Intolerance to Pegloticase and ProLongs the Urate Lowering Effect.

sNDA: Supplemental New Drug Application.

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**For us, it’s personal**

33
Strong Balance Sheet Supports Our Strategy

>$950M Cash and Cash Equivalents Estimated at Dec. 31, 2018\(^{(1)}\)

**Strong Cash Balance and Net Debt Position**

<table>
<thead>
<tr>
<th>Date</th>
<th>Cash</th>
<th>Net Debt</th>
</tr>
</thead>
<tbody>
<tr>
<td>12/31/2016</td>
<td>$1,435M</td>
<td>$1,000M</td>
</tr>
<tr>
<td>12/31/2017</td>
<td>$1,269M</td>
<td>$751M</td>
</tr>
<tr>
<td>9/30/2018</td>
<td>$807M</td>
<td>$509M</td>
</tr>
</tbody>
</table>

**Disciplined Approach to Debt**

- Strong cash position with an estimated >$950M of cash and cash equivalents at Dec. 31, 2018\(^{(1)}\)
- Earliest maturity is 2022 and is for the $400 million convertible note with a strike price of $28.66
- Since 2016, lowered interest rate on term loans by ~125 basis points, saving more than $10M in annual interest expense

**Managing debt and leverage efficiently; generating strong cash flow**

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Note: Net debt is a non-GAAP measure; see reconciliation slides at the end of the presentation for a reconciliation of GAAP to non-GAAP measures.

\(^{(1)}\) Horizon Pharma estimate. Includes $35 million of cash received from the Dec. 28, 2018, sale of the ex-North American and Japan rights of RAVICTI and AMMONAPS.
### Executing on Our Strategy
- Building a robust pipeline of rare disease medicines
- Building a leading R&D function
- Maximizing KRYSTEXXA to enhance our leadership in uncontrolled gout

### Made Significant Progress in 2018
- **Teprotumumab**: Fully enrolled Phase 3 trial and initiated commercial launch activities
- **Uncontrolled gout R&D programs**: Advancing immunomodulation strategy
- **Transformed R&D organization**: Addition of scientific leadership team
- **KRYSTEXXA**: Doubled commercial team and addressable patient population to significantly accelerate vial growth

### Leveraging Our Momentum in 2019+
- Advancing toward peak net sales expectations:
  - **KRYSTEXXA**: >$750M\(^{(1)}\)
  - **Teprotumumab**: >$750M\(^{(1)}\)
- Potential upside with future pipeline assets

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

Timothy P. Walbert
Chairman, President and
Chief Executive Officer
January 8, 2019
We Drive Value by Capitalizing on Our Defining Strengths

**Proven commercial execution**

*Example:*

<table>
<thead>
<tr>
<th>Year</th>
<th>Sales Growth</th>
</tr>
</thead>
<tbody>
<tr>
<td>2015</td>
<td>Pre-Acquisition</td>
</tr>
<tr>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>2018</td>
<td>&gt;65% YOY Projected Growth</td>
</tr>
<tr>
<td>PEAK</td>
<td>&gt;$750M</td>
</tr>
</tbody>
</table>

**Successful business development**

*Examples:*

- **Teprotumumab**
  - High unmet need; no FDA-approved therapies exist
  - Impressive Phase 2 efficacy results (p<0.001)
  - Completed enrollment for Phase 3 clinical trial, ahead of schedule
  - U.S. Orphan, Fast-Track and Breakthrough Therapy designations
  - >$750M peak sales potential

**Building our pipeline**

*Example:*

- **KRYSTEXXA® pegloticase**
  - Investigator-initiated trials
  - MIRROR: Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving KRYSTEXXA.
  - RECIPE: Reducing Immunogenicity to Pegloticase. TRIPLE: Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect.

**Maximizing our medicines’ value**

*Example:*

- Working to enhance KRYSTEXXA® response rate with 3 trials:
  - MIRROR
  - RECIPE\(^{(3)}\)
  - TRIPLE\(^{(3)}\)

- Exploring in-house next-generation opportunities

---

(1) Horizon Pharma estimate for U.S. net sales only. (2) Horizon Pharma estimate for U.S. net sales only.

MIRROR: Methotrexate to Increase Response Rates in Patients with Uncontrolled Gout Receiving KRYSTEXXA.
RECIPE: Reducing Immunogenicity to Pegloticase. TRIPLE: Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
We Have Purposefully and Rapidly Transitioned to a Rare Disease Medicines Company

Developed a highly successful commercial business, generating attractive growth and cash flows to support BD and growth initiatives

Built a stable base of rare disease growth assets

Added high-growth on-market and pipeline rare disease medicines

Continue the evolution to generate long-term value
- Commercial execution
- Expanding our pipeline and building best-in-class R&D organization

Teprotumumab

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
We Have Rapidly Evolved into a Company Focused on Rare Disease Medicines

2013: Net sales of $74 Million
2 Medicines

2017: Net sales of $1.06 Billion
11 Medicines; 6 for Rare Diseases
Our Portfolio is Supported by Our Intellectual Property Expertise and Long-Life Protected Patents

**Orphan and Rheumatology**

- 11 OB listed patents extending to 2032
- Orphan Drug Exclusivity to 2020/2024
- Settled Par (first-filer) litigation with right to market July 1, 2025
- Settled Lupin litigation with right to market 180 days after Par
- 9 OB listed patents extending to 2036
- 4 new patents issued in 2018, with latest expiring in 2036
- Orphan Drug Exclusivity: U.S. 2020/2022; E.U. 2023
- 2 U.S. patents extending to 2022
- 7 U.S. patents, 4 Canadian patents; not approved in U.S.
- 25 U.S. patents extending to 2030, including 1 new patent issued in 3Q ‘18
- Biologic Exclusivity to 2022
- 8 OB listed patents extending to 2028
- Settled Actavis (first-filer) litigation with right to market Dec. 23, 2022

**Primary Care**

- 20 OB listed patents extending to 2030
- Settled Teligent, Amneal, Paddock (Perrigo), Taro and Lupin litigations by granting a right to market no sooner than Oct. 17, 2027
- In May 2017, U.S. District Court upheld ‘913 patent (extends to 2027) in case against Actavis
- 6 OB listed patents extending to 2026
- Settled Par (first-filer) litigation with right to market Jan. 1, 2023
- 14 OB listed patents (including esomeprazole patents) extending to 2031
- 11 OB listed patents (excluding esomeprazole patents) and 1 process patent
- In June 2017, U.S. District Court upheld both ‘285 patent (extends to 2022) and ‘907 patent (extends to 2023) in case against Dr. Reddy’s Laboratories, Mylan and Lupin
- Settled Actavis litigation with right to market Jan. 1, 2025

---

(1) Horizon Pharma divested the marketing rights to PROCYSBI and QUINSAIR in Europe, the Middle East and Africa on June 23, 2017. Horizon Pharma retains marketing rights for the two medicines in the U.S., Canada, Latin America and Asia. QUINSAIR is not approved in the United States.
Our Strong Financial Position Supports Our Growth Strategy

Cash and Cash Equivalents of $807M at Sept. 30, 2018

<table>
<thead>
<tr>
<th>Cash and cash equivalents</th>
<th>$807</th>
</tr>
</thead>
<tbody>
<tr>
<td>Senior secured term loans – due 2024</td>
<td>818</td>
</tr>
<tr>
<td>Senior notes – due 2023</td>
<td>475</td>
</tr>
<tr>
<td>Senior notes – due 2024</td>
<td>300</td>
</tr>
<tr>
<td>2.5% exchangeable senior notes – due 2022</td>
<td>400</td>
</tr>
<tr>
<td>Total principal amount of debt</td>
<td>$1,993</td>
</tr>
</tbody>
</table>

Net debt to LTM adjusted EBITDA leverage ratio of 2.9 times at Sept. 30, 2018

(1) Adjusted EBITDA and net debt are non-GAAP measures; see reconciliation slides at the end of the presentation for a reconciliation of GAAP to non-GAAP measures. LTM: last 12 months ended Sept. 30, 2018.

* Senior Secured Term Loans schedule includes 1 percent annual amortization ($8.5M of principal) and reflects a mandatory prepayment of $23.5M made in June 2018 that is applied 1) to prepay the next eight amortization payments from June 30, 2018; and 2) the remaining amortizations on a pro rata basis.
Supported By Our Strong Business Development Capability

- **September 2014**: Acquisition of Vidara Therapeutics
- **May 2015**: Acquisition of Hyperion Therapeutics
- **January 2016**: Acquisition of Crealta
- **October 2016**: Acquisition of Raptor
- **January 2018**: Acquired HZN-003 from MedImmune
  Partnered with XL-protein GmbH on PASylated Uricase Program
- **January 2019**: Collaboration with HemoShear Therapeutics

**Teprotumumab**
In Phase 3 development for thyroid eye disease

**HZN-003**
PASylated Uricase
For uncontrolled gout

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

MEANINGFUL GROWTH OPPORTUNITY IN AN AREA OF SIGNIFICANT UNMET NEED
How Do TED Patients Present?

Clinical Activity and Severity of TED

Moderate-to-Severe Active TED

- Lid swelling / redness
- Chemosis (swelling of conjunctiva)
- Swelling of plica and caruncle
- Conjunctivitis

Normal

Definable and Identifiable Criteria for Moderate-to-Severe TED

- Orbital prolapse of fat tissue
- Proptosis
- Lid retraction

Source: Hearst Digital Media.
Conjunctiva: The mucous membrane that covers the front of the eye and lines the inside of the eyelids.
Plica: A small fold of bulbar conjunctiva on the medial canthus of the eye.
Caruncle: Small, pink, globular nodule at the inner corner (the medial canthus) of the eye.
TED: Disease Progression; Potential Impact of Disease Modifying Therapy

Disease Severity

Unsurpassed

Treatment during active TED

Ideal Therapy

Up to 3 Years

Beyond 3 Years

ACTIVE TED

INACTIVE TED

### Phase 2 Trial Key Takeaways

*Shows Potential to Be Disease-Modifying and Durable*

<table>
<thead>
<tr>
<th>Early and Continued Response</th>
<th>Proptosis and Diplopia: Durable Response</th>
</tr>
</thead>
</table>
| • At Week 24, percentage of patients with reduction of $>2$ mm of proptosis and $>2$ points in CAS with $p<0.001$:  
  - Teprotumumab patients: 69 percent  
  - Placebo patients: 20 percent  
| • Proptosis:  
  - Week 24: 71 percent of patients were responders  
  - Week 72: 53 percent of responders maintained response approximately 1 year off treatment |
| • At Week 24, percentage of proptosis responders with $p<0.001$:  
  - Teprotumumab patients: 71 percent  
  - Placebo patients: 20 percent  
| • Diplopia:  
  - Week 24: 62 percent of patients were responders  
  - Week 72: 69 percent of responders maintained response approximately 1 year off treatment |

### Well Tolerated

Additional information on length of treatment and potential retreatment will be provided with OPTIC and OPTIC-X.

---

Clinical Activity Score (CAS): A 7-point scale that measures change in orbital inflammation and pain; a score of $>3$ indicates active TED.

Diplopia (double vision) response: improvement of at least one grade of diplopia.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
OPTIC: Treatment of Graves' Orbitopathy (TED) to reduce Proptosis with Teprotumumab Infusions in a randomized, placebo-controlled Clinical study.

Q3W: Once every 3 weeks

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

OPTIC-X Extension Trial Design
Additional Information on Length of Treatment and Potential Retreatment

Week 24

Teprotumumab (n=38)
8 infusions (Q3W)

Placebo (n=38)
8 infusions (Q3W)

Would a non-responder benefit from longer therapy?

Week 72

48 Week Follow-up

If disease recurs, will another course of teprotumumab help?

Teprotumumab
Up to 8 infusions (Q3W)
Orphan and Rheumatology
Gout Is Often Associated with Multiple Negative Consequences

Patients with high uric acid levels have multiple comorbidities; gout patients have an average of four comorbidities.

Uric acid deposits can occur almost anywhere in the body – bones and joints, as well as organs, such as the heart and kidney.

Gout Patients with Comorbidity (%)

- Diabetes Mellitus: 28.9%
- Coronary Artery Disease: 37.4%
- Chronic Kidney Disease: 47.1%
- Hyperlipidemia: 62.6%
- Hypertension: 88.7%

Nephrology Represents a Significant Opportunity For KRYSTEXXA

Clinical need:

• 25-50% of Chronic Kidney Disease (CKD) patients have gout(1)
• Gout is more prevalent as CKD advances
• Nephrologists have a high sense of urgency to protect the kidney
• Conventional gout therapies place further burden on the kidneys and have significant dosing limitations in CKD patients(2)(3)

(1) Nephrologists estimates; based on Horizon Pharma qualitative research.
(2) Gout and Hyperuricemia in Chronic Kidney Disease, National Kidney Foundation. 2015.

KRYSTEXXA meets the need:

• Mechanism of action is a significant area of differentiation
• Tested and proven effective and safe for uncontrolled gout patients with CKD(4)
• CKD patients can be effectively treated without dose adjustment(4)

Many nephrologists are unaware of KRYSTEXXA

“You’ve given me something in a sea of nothing.”
– Nephrologist Comment, 2017 Blinded Market Research
RAVICTI

*Increasing Penetration of the Diagnosed Patient Population*

**Indicated for urea cycle disorders (UCDs)**
UCDs are rare and life-threatening genetic diseases resulting in body’s inability to remove ammonia from the blood stream\(^1\)

**U.S. market**
~2,600 people with UCDs; ~1,000 diagnosed population\(^2\)

**U.S. market share**
~54% of diagnosed patients

**Growth drivers**
- Increase awareness and diagnosis of UCDs
- Drive conversion from older-generation nitrogen-scavengers to RAVICTI
- Increase awareness of label expansion to position RAVICTI as first-line therapy

---

\(^1\) See full prescribing information at www.RAVICTI.com.
\(^2\) Horizon Pharma estimate.
**PROCYSBI**

*Driving Additional Uptake*

**Indicated for nephropathic cystinosis (NC)**
- NC is a rare and life-threatening 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

**U.S. market**
~500-600 diagnosed patients; ~400-450 diagnosed patients on cystine-depleting therapy\(^{(2)}\)

**U.S. market share**
~55% of diagnosed patients

**Growth drivers**
- Drive conversion of patients from older-generation therapy
- Drive uptake of diagnosed but untreated patients
- Increase awareness of label expansion (>1 year) to position PROCYSBI as first line of therapy
- Identify undiagnosed patients

---

\(^{(1)}\) See full prescribing information at [www.PROCYSBI.com](http://www.PROCYSBI.com).

\(^{(2)}\) Horizon Pharma estimate.
ACTIMMUNE

Establishing Role of ACTIMMUNE in Broader Range of CGD Patients

Indicated for chronic granulomatous disease (CGD)

• 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

U.S. CGD market

\~1,600 people\(^{(2)}\)

Growth drivers

• Increase awareness and diagnosis of CGD
• Increase persistence of and adherence to treatment

(1) See full prescribing information at www.ACTIMMUNE.com.
(2) Horizon Pharma estimate.
RECONCILIATIONS OF GAAP TO NON-GAAP MEASURES
Note Regarding Use of Non-GAAP Financial Measures

EBITDA, or earnings before interest, taxes, depreciation and amortization, and adjusted EBITDA are used and provided by Horizon Pharma as non-GAAP financial measures. Horizon Pharma provides certain other financial measures such as non-GAAP net income, non-GAAP diluted earnings per share, non-GAAP gross profit and gross profit ratio, non-GAAP operating expenses, non-GAAP operating income, non-GAAP tax rate, non-GAAP operating cash flow and net debt, each of which include adjustments to GAAP figures. These non-GAAP measures are intended to provide additional information on Horizon Pharma’s performance, operations, expenses, profitability and cash flows. Adjustments to Horizon Pharma’s GAAP figures as well as EBITDA exclude acquisition and/or divestiture-related expenses, charges related to the discontinuation of ACTIMMUNE development for Friedreich’s ataxia, gain from divestiture, gain from sale of assets, an upfront fee for a license of a patent, litigation settlements, loss on debt extinguishment, costs of debt refinancing, drug manufacturing harmonization costs, restructuring and realignment costs, as well as non-cash items such as share-based compensation, depreciation and amortization, royalty accretion, non-cash interest expense, long-lived asset impairment charges, impacts of contingent royalty liability remeasurements and other non-cash adjustments. Certain other special items or substantive events may also be included in the non-GAAP adjustments periodically when their magnitude is significant within the periods incurred. Horizon maintains an established non-GAAP cost policy that guides the determination of what costs will be excluded in non-GAAP measures. Horizon Pharma believes that these non-GAAP financial measures, when considered together with the GAAP figures, can enhance an overall understanding of Horizon Pharma’s financial and operating performance. The non-GAAP financial measures are included with the intent of providing investors with a more complete understanding of the Company’s historical and expected 2018 financial results and trends and to facilitate comparisons between periods and with respect to projected information. In addition, these non-GAAP financial measures are among the indicators Horizon Pharma’s management uses for planning and forecasting purposes and measuring the Company’s performance. For example, adjusted EBITDA is used by Horizon Pharma as one measure of management performance under certain incentive compensation arrangements. These non-GAAP financial measures should be considered in addition to, and not as a substitute for, or superior to, financial measures calculated in accordance with GAAP. The non-GAAP financial measures used by the Company may be calculated differently from, and therefore may not be comparable to, non-GAAP financial measures used by other companies. Horizon Pharma has not provided a reconciliation of its full-year 2018 adjusted EBITDA outlook to an expected net income (loss) outlook because certain items such as acquisition/divestiture-related expenses and share-based compensation that are a component of net income (loss) cannot be reasonably projected due to the significant impact of changes in Horizon Pharma's stock price, the variability associated with the size or timing of acquisitions/divestitures and other factors. These components of net income (loss) could significantly impact Horizon Pharma’s actual net income (loss).
## GAAP to Non-GAAP Reconciliation

**EBITDA and Adjusted EBITDA – Three and Nine Months Ended Sept. 30**

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>GAAP net income (loss)</strong></td>
<td>$26,030</td>
<td>$(63,971)</td>
<td>$(164,134)</td>
<td>$(364,078)</td>
</tr>
<tr>
<td>Depreciation</td>
<td>1,523</td>
<td>1,476</td>
<td>4,627</td>
<td>5,037</td>
</tr>
<tr>
<td>Amortization, accretion and step-up:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible amortization expense</td>
<td>67,725</td>
<td>68,666</td>
<td>202,069</td>
<td>208,118</td>
</tr>
<tr>
<td>Accretion of royalty liabilities</td>
<td>14,945</td>
<td>12,720</td>
<td>44,460</td>
<td>38,415</td>
</tr>
<tr>
<td>Amortization of deferred revenue</td>
<td>-</td>
<td>(235)</td>
<td>-</td>
<td>(636)</td>
</tr>
<tr>
<td>Inventory step-up expense</td>
<td>83</td>
<td>21,170</td>
<td>17,212</td>
<td>95,659</td>
</tr>
<tr>
<td>Interest expense, net (including amortization of debt discount and deferred financing costs)</td>
<td>30,437</td>
<td>31,706</td>
<td>91,921</td>
<td>95,297</td>
</tr>
<tr>
<td>(Benefit) expense for income taxes</td>
<td>(1,733)</td>
<td>7,181</td>
<td>1,863</td>
<td>(42,138)</td>
</tr>
<tr>
<td><strong>EBITDA</strong></td>
<td>$139,010</td>
<td>$78,723</td>
<td>$198,018</td>
<td>$35,674</td>
</tr>
<tr>
<td>Other non-GAAP adjustments:</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition/divestiture-related costs</td>
<td>425</td>
<td>5,561</td>
<td>6,185</td>
<td>168,985</td>
</tr>
<tr>
<td>Restructuring and realignment costs</td>
<td>4,582</td>
<td>(290)</td>
<td>14,889</td>
<td>4,903</td>
</tr>
<tr>
<td>Litigation settlements</td>
<td>1,500</td>
<td>-</td>
<td>5,750</td>
<td>-</td>
</tr>
<tr>
<td>Impairment of long-lived assets</td>
<td>1,603</td>
<td>-</td>
<td>39,455</td>
<td>22,270</td>
</tr>
<tr>
<td>Remeasurement of royalties for medicines acquired through business combinations</td>
<td>-</td>
<td>(2,151)</td>
<td>(2,944)</td>
<td></td>
</tr>
<tr>
<td>Share-based compensation</td>
<td>28,428</td>
<td>31,698</td>
<td>86,981</td>
<td>87,935</td>
</tr>
<tr>
<td>Charges relating to discontinuation of Friedreich’s ataxia program</td>
<td>254</td>
<td>(1,116)</td>
<td>1,476</td>
<td>(4,219)</td>
</tr>
<tr>
<td>Drug substance harmonization costs</td>
<td>301</td>
<td>5,654</td>
<td>1,579</td>
<td>10,698</td>
</tr>
<tr>
<td>Upfront and milestone payments related to license agreements</td>
<td>(100)</td>
<td>-</td>
<td>(10)</td>
<td>-</td>
</tr>
<tr>
<td>Fees related to term loan refinancings</td>
<td>40</td>
<td>16</td>
<td>82</td>
<td>4,114</td>
</tr>
<tr>
<td>Loss on debt extinguishment</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>533</td>
</tr>
<tr>
<td>Gain on sale of assets</td>
<td>(12,303)</td>
<td>-</td>
<td>(12,303)</td>
<td>-</td>
</tr>
<tr>
<td>Gain on divestiture</td>
<td>(112)</td>
<td>-</td>
<td>(5,968)</td>
<td></td>
</tr>
<tr>
<td>Royalties for medicines acquired through business combinations</td>
<td>(13,831)</td>
<td>(12,031)</td>
<td>(39,611)</td>
<td>(34,970)</td>
</tr>
<tr>
<td><strong>Total of other non-GAAP adjustments</strong></td>
<td>10,899</td>
<td>29,380</td>
<td>102,322</td>
<td>251,337</td>
</tr>
<tr>
<td><strong>Adjusted EBITDA</strong></td>
<td>$149,909</td>
<td>$108,103</td>
<td>$300,340</td>
<td>$287,011</td>
</tr>
</tbody>
</table>
# GAAP to Non-GAAP Reconciliation

## EBITDA and Adjusted EBITDA – Full-Years 2017 and 2016

($ in thousands)

<table>
<thead>
<tr>
<th></th>
<th>Twelve Months Ended December 31,</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>2017</td>
</tr>
</tbody>
</table>

### EBITDA and Adjusted EBITDA:

<table>
<thead>
<tr>
<th>Description</th>
<th>2017</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>GAAP net loss</td>
<td>$(410,526)</td>
<td>$(166,834)</td>
</tr>
<tr>
<td>Depreciation</td>
<td>6,631</td>
<td>4,962</td>
</tr>
<tr>
<td>Amortization, accretion and inventory step-up:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible amortization expense</td>
<td>276,784</td>
<td>216,875</td>
</tr>
<tr>
<td>Accretion of royalty liabilities</td>
<td>51,263</td>
<td>40,616</td>
</tr>
<tr>
<td>Amortization of deferred revenue</td>
<td>(860)</td>
<td>(836)</td>
</tr>
<tr>
<td>Inventory step-up expense</td>
<td>119,151</td>
<td>71,137</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>126,523</td>
<td>86,610</td>
</tr>
<tr>
<td>Expense Benefit for income taxes</td>
<td>(102,749)</td>
<td>(61,251)</td>
</tr>
<tr>
<td>EBITDA</td>
<td>$66,217</td>
<td>$191,279</td>
</tr>
</tbody>
</table>

### Other non-GAAP adjustments:

<table>
<thead>
<tr>
<th>Description</th>
<th>2017</th>
<th>2016</th>
</tr>
</thead>
<tbody>
<tr>
<td>Remeasurement of royalties for medicines acquired through business combinations</td>
<td>21,774</td>
<td>386</td>
</tr>
<tr>
<td>Acquisition/divestiture-related costs</td>
<td>177,035</td>
<td>52,874</td>
</tr>
<tr>
<td>Restructuring and realignment costs</td>
<td>4,883</td>
<td>-</td>
</tr>
<tr>
<td>Gain on divestiture</td>
<td>(6,267)</td>
<td>-</td>
</tr>
<tr>
<td>Loss on debt extinguishment</td>
<td>978</td>
<td>-</td>
</tr>
<tr>
<td>Fees related to term loan refinancings</td>
<td>5,220</td>
<td>-</td>
</tr>
<tr>
<td>Share-based compensation</td>
<td>121,553</td>
<td>114,144</td>
</tr>
<tr>
<td>Litigation settlement</td>
<td>-</td>
<td>65,000</td>
</tr>
<tr>
<td>Reversal of pre-acquisition reserve upon signing of contract</td>
<td>-</td>
<td>(6,900)</td>
</tr>
<tr>
<td>Impairment of in-process research and development</td>
<td>-</td>
<td>66,000</td>
</tr>
<tr>
<td>Charges relating to discontinuation of the Friedreich’s ataxia program</td>
<td>22,509</td>
<td>23,513</td>
</tr>
<tr>
<td>Upfront and milestone payments related to license agreements</td>
<td>12,386</td>
<td>2,000</td>
</tr>
<tr>
<td>Drug substance harmonization costs</td>
<td>10,651</td>
<td>-</td>
</tr>
<tr>
<td>Royalties for medicines acquired through business combinations</td>
<td>(47,003)</td>
<td>(37,593)</td>
</tr>
<tr>
<td>Total of other non-GAAP adjustments</td>
<td>323,519</td>
<td>279,424</td>
</tr>
<tr>
<td>Adjusted EBITDA</td>
<td>$389,736</td>
<td>$470,703</td>
</tr>
</tbody>
</table>
## GAAP to Non-GAAP Reconciliation

### Operating Income

<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>2018</td>
<td>2017</td>
</tr>
<tr>
<td>GAAP operating income (loss)</td>
<td>$54,246</td>
<td>$(25,751)</td>
</tr>
<tr>
<td>Non-GAAP adjustments:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acquisition/divestiture-related costs</td>
<td>425</td>
<td>5,561</td>
</tr>
<tr>
<td>Restructuring and realignment costs</td>
<td>4,582</td>
<td>(290)</td>
</tr>
<tr>
<td>Litigation settlements</td>
<td>1,500</td>
<td>-</td>
</tr>
<tr>
<td>Amortization, accretion and step-up:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intangible amortization expense</td>
<td>67,725</td>
<td>68,666</td>
</tr>
<tr>
<td>Accretion of royalty liabilities</td>
<td>14,945</td>
<td>12,720</td>
</tr>
<tr>
<td>Inventory step-up expense</td>
<td>83</td>
<td>21,170</td>
</tr>
<tr>
<td>Impairment of long-lived assets</td>
<td>1,603</td>
<td>-</td>
</tr>
<tr>
<td>Remeasurement of royalties for medicines acquired through business combinations</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Share-based compensation</td>
<td>28,428</td>
<td>31,698</td>
</tr>
<tr>
<td>Depreciation</td>
<td>1,523</td>
<td>1,476</td>
</tr>
<tr>
<td>Charges relating to discontinuation of Friedreich's ataxia program</td>
<td>254</td>
<td>(1,116)</td>
</tr>
<tr>
<td>Drug substance harmonization costs</td>
<td>301</td>
<td>5,654</td>
</tr>
<tr>
<td>Gain on sale of assets</td>
<td>(12,303)</td>
<td>-</td>
</tr>
<tr>
<td>Upfront and milestone payments related to license agreements</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Fees related to term loan refinancings</td>
<td>40</td>
<td>16</td>
</tr>
<tr>
<td>Royalties for medicines acquired through business combinations</td>
<td>(13,831)</td>
<td>(12,031)</td>
</tr>
<tr>
<td>Total of non-GAAP adjustments</td>
<td>95,275</td>
<td>133,524</td>
</tr>
<tr>
<td>Non-GAAP operating income</td>
<td>$149,521</td>
<td>$107,773</td>
</tr>
<tr>
<td>Orphan and Rheumatology segment operating income</td>
<td>91,537</td>
<td>65,561</td>
</tr>
<tr>
<td>Primary care segment operating income</td>
<td>57,984</td>
<td>42,212</td>
</tr>
<tr>
<td>Total segment operating income</td>
<td>$149,521</td>
<td>$107,773</td>
</tr>
<tr>
<td>Amortization of deferred revenue</td>
<td>-</td>
<td>(225)</td>
</tr>
<tr>
<td>Foreign exchange gain (loss)</td>
<td>35</td>
<td>275</td>
</tr>
<tr>
<td>Other income, net</td>
<td>353</td>
<td>280</td>
</tr>
<tr>
<td>Adjusted EBITDA</td>
<td>$149,909</td>
<td>$108,103</td>
</tr>
</tbody>
</table>
### GAAP to Non-GAAP Reconciliation

**Net Debt**

<table>
<thead>
<tr>
<th></th>
<th>As of</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>September 30,</td>
<td>December 31,</td>
<td></td>
</tr>
<tr>
<td></td>
<td>2018</td>
<td>2017</td>
<td></td>
</tr>
<tr>
<td>Long-term debt-current portion</td>
<td>$ -</td>
<td>$ 10,625</td>
<td></td>
</tr>
<tr>
<td>Long-term debt, net of current</td>
<td>1,563,239</td>
<td>1,576,646</td>
<td></td>
</tr>
<tr>
<td>Exchangeable notes, net</td>
<td>327,573</td>
<td>314,384</td>
<td></td>
</tr>
<tr>
<td><strong>Total Debt</strong></td>
<td>1,890,812</td>
<td>1,901,655</td>
<td></td>
</tr>
<tr>
<td>Debt discount</td>
<td>92,473</td>
<td>108,054</td>
<td></td>
</tr>
<tr>
<td>Deferred financing fees</td>
<td>9,741</td>
<td>11,041</td>
<td></td>
</tr>
<tr>
<td><strong>Total Principal Amount Debt</strong></td>
<td>1,993,026</td>
<td>2,020,750</td>
<td></td>
</tr>
<tr>
<td>Less: cash and cash equivalents</td>
<td>807,047</td>
<td>751,368</td>
<td></td>
</tr>
<tr>
<td><strong>Net Debt</strong></td>
<td>$ 1,185,979</td>
<td>$ 1,269,382</td>
<td></td>
</tr>
</tbody>
</table>