An Overview of Thyroid Eye Disease (TED), Teprotumumab and OPTIC Phase 3 Trial Topline Results

February 28, 2019
Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to Horizon's expected timing of clinical, regulatory and commercial events, including potential regulatory submissions related to, and potential commercialization of, teprotumumab, the potential benefits and market potential of teprotumumab, Horizon’s business strategy and plans 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; the risk that regulatory submissions and decisions may be delayed and that teprotumumab may not obtain approval by the U.S. Food and Drug Administration; the availability of coverage and adequate reimbursement and pricing from government and third-party payers; risks relating to Horizon’s ability to successfully implement its business strategies; risks inherent in developing novel medicine candidates, such as teprotumumab, and existing medicines for new indications; risks associated with regulatory approvals; risks in the ability to recruit, train and retain qualified personnel; competition, including potential generic competition; the ability to protect intellectual property and defend patents; regulatory obligations and oversight, including any changes in the legal and regulatory environment in which Horizon operates and those risks detailed from time-to-time under the caption "Risk Factors" and elsewhere in Horizon's filings and reports with the SEC. Horizon undertakes no duty or obligation to update any forward-looking statements contained in this presentation as a result of new information.
Agenda

1. Horizon Pharma: Building an Innovation-Driven Biopharma Company
   Timothy P. Walbert
   Chairman, President and Chief Executive Officer
   Horizon Pharma

2. Thyroid Eye Disease (TED): Disease Overview and Current Treatment Landscape
   Raymond S. Douglas, M.D., Ph.D.
   Professor of Surgery
   Director of Orbital and Thyroid Eye Disease Program
   Cedars-Sinai Medical Center

3. Teprotumumab: Review of Phase 2 Data at 24 and 72 Weeks
   Shao-Lee Lin, M.D., Ph.D.
   Executive Vice President, Head of R&D and Chief Scientific Officer
   Horizon Pharma

4. Teprotumumab: Phase 3 Trial Design and Topline Results
   Shao-Lee Lin, M.D., Ph.D.
   Executive Vice President, Head of R&D and Chief Scientific Officer
   Horizon Pharma

5. Conclusion
   Timothy P. Walbert
   Chairman, President and Chief Executive Officer
   Horizon Pharma

6. Q&A
Horizon Pharma: Building an Innovation-Driven Biopharma Company

Timothy P. Walbert
Chairman, President and Chief Executive Officer
Horizon Pharma
Key Takeaways for Today’s Call

1. Teprotumumab Phase 3 OPTIC trial achieved its primary endpoint, confirming Phase 2 and demonstrating that teprotumumab has the potential to be a disease-modifying therapy (1).

2. No FDA-approved therapies exist for TED; currently used therapies are not disease-modifying.

3. Active thyroid eye disease (TED) is a rare and debilitating inflammatory autoimmune disease of the eye; active TED impacts 15,000 to 20,000 U.S. patients annually (2).

4. Expect mid-2019 BLA submission and potential 2020 approval; fast-track and breakthrough designations:
   - Estimated U.S. peak net sales potential of >$750M (3).
   - Pre-launch planning underway.

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(2) Company analysis of claims data and market research.
(3) Horizon Pharma estimate.

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

Be a leading rare disease biopharma company

Delivering innovative therapies to patients

Generating high returns for shareholders
# Building a Robust Rare Disease Pipeline

<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><strong>KRISTEXX®</strong></td>
<td>* MIRROR immunomodulation study: KRISTEXX + methotrexate</td>
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<tr>
<td><strong>KRISTEXX</strong></td>
<td>* Study in kidney transplant patients with uncontrolled gout&lt;sup&gt;(1)&lt;/sup&gt;</td>
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<tr>
<td><strong>HZN-001 (teprotumumab)&lt;sup&gt;(2)&lt;/sup&gt;</strong></td>
<td>* OPTIC trial: Phase 3 complete</td>
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<tr>
<td><strong>HZN-003</strong></td>
<td>* Optimized uricase and optimized PEGylation for uncontrolled gout</td>
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<tr>
<td><strong>PASylated Uricase&lt;sup&gt;(3)&lt;/sup&gt;</strong></td>
<td>* Optimized uricase and PASylation for uncontrolled gout</td>
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<tr>
<td><strong>HemoShear Gout Discovery Collaboration</strong></td>
<td>* Exploration of novel approaches to treating gout</td>
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<sup>(1)</sup> Planned study, expected to begin in the second half of 2019.

<sup>(2)</sup> Teprotumumab is a fully human monoclonal antibody (mAb) IGF-1R inhibitor in development for active thyroid eye disease (TED).

<sup>(3)</sup> Being developed under a collaboration agreement.

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

**OPTIC**: Treatment of Graves’ Orbitopathy (Thyroid Eye Disease) to Reduce Proptosis with Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
## Teprotumumab Exemplifies Our Pipeline Strategy

**Building a Pipeline for Sustainable Long-Term Growth**

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

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

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
TED: Disease Overview and Current Treatment Landscape

Raymond S. Douglas, M.D., Ph.D.
Professor of Surgery
Director of Orbital and Thyroid Eye Disease Program
Cedars-Sinai Medical Center
Thyroid Eye Disease (TED)

**Rare and debilitating** autoimmune 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
Pathology of TED

TED Pathology\(^\text{(1)}\)

- 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

IGF-1R: Insulin-like growth factor-1 receptor. TSHR: Thyroid stimulating hormone receptor.
Epidemiology and Risk Factors of TED

TED is Not a Complication of Graves’ Disease (GD)

- TED is a separate and distinct disease although it is commonly associated with GD (hyperthyroidism)
- TED can occur before, during or after diagnosis of GD; can occur without thyroid disease
  - TED can present with hyperthyroid, hypothyroid or euthyroid
  - Phase 2 and Phase 3 trial patients had well-controlled thyroid disease

TED: Disease Progression

- **Active TED** (Up to 3 Years)
  - Inflammation

- **Inactive TED** (Beyond 3 Years)
  - Fibrosis

How Do TED Patients Present?

Clinical Activity and Severity of TED

Definable and Identifiable Criteria for Active TED

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

- 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.
Proptosis (Bulging of the Eye)

Swelling or bulging of the eye that can result in:

- **Diplopia** *(double vision)*
- **Difficulty closing eye** *(sleep, ulcerations)*
- **Strabismus** *(eye misalignment)*
- **Optic nerve compression and potentially blindness**

### Healthy Eye and Orbital Tissue in Normal Condition

- Eye is well protected by lid
- Thin periocular muscles
- Optic nerve can easily pass through apex
- Orbit contains a small amount of tissue and fat

### In Presence of Active TED

- Inflamed and enlarged muscles due to fluid accumulation
- Compression of the optic nerve at orbital apex
- Increase in orbital tissue and fat
- Lid retraction
- Eye protrusion
- Lid and conjunctival redness

Diplopia *(double vision)*
Difficulty closing eye *(sleep, ulcerations)*
Strabismus *(eye misalignment)*
Optic nerve compression and potentially blindness

Swelling or bulging of the eye that can result in:

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Swelling or bulging of the eye that can result in:

- Diplopia *(double vision)*
- Difficulty closing eye *(sleep, ulcerations)*
- Strabismus *(eye misalignment)*
- Optic nerve compression and potentially blindness
Diplopia (Double Vision)

- Two images of a single object are seen resulting from unequal action of the eye muscles
- Misalignment of one or both eyes
- Headache
- Nausea

Source: AllAboutVision.com and WebMD.
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.
Who Diagnoses TED and How is TED Treated?

**Physicians Involved in Treatment and Diagnosis**

- Primary Care
- Endocrinologist
- Ophthalmologist
- Oculoplastic Surgeon

**How Is TED Treated Today?**

- Active TED → No Approved Treatments
- Inactive TED → Treat with Surgery

For us, it's personal
Active TED: Current Approaches are Suboptimal

Pathogenic Mechanisms of Disease Not Targeted

<table>
<thead>
<tr>
<th>Current Treatment Approach: Steroids</th>
<th>Significant Unmet Need Exists</th>
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<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>
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</table>
Inactive TED: Surgery Only Current Option

Once TED becomes inactive, long-term damage is done

Surgery currently the 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.
Potential Impact of Disease-Modifying Therapy

Disease Progression

Active TED

Inactive TED

Untreated

Treatment during active TED

Ideal Therapy

Up to 3 Years

Beyond 3 Years

Teprotumumab: Review of Phase 2 Data at 24 and 72 Weeks

Shao-Lee Lin, M.D., Ph.D.
Executive Vice President, Head of R&D and Chief Scientific Officer
Horizon Pharma
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

- 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

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.
Phase 2 Trial Design

Patient Criteria
- Active TED
- 18 to 75 years
- <9 months since active TED onset with no prior treatment
- CAS ≥4
- FT4 and FT3 ≤50 percent above or below normal limits

Teprotumumab (N=42)
8 infusions: 1 every three weeks

Placebo (N=45)
8 infusions: 1 every three weeks

Screening
Randomization

Primary endpoint at Week 24
Percentage of participants with >2 mm reduction in proptosis and
>2 point reduction in Clinical Activity Score (CAS)

CAS: Clinical Activity Score, a 7-point scale that measures change in orbital inflammation and pain; a score of >3 indicates active TED.
FT4: Free thyroxine.
FT3: Free triiodothyronine.
Teprotumumab is an investigational candidate, and safety and efficacy have not been established.
Phase 2 Trial Measures Used

Clinical Activity Score (CAS)

1. Spontaneous orbital pain
2. Gaze evoked orbital pain
3. Eyelid swelling that is considered to be due to active GO
4. Eyelid erythema
5. Conjunctival redness that is considered to be due to active GO
6. Chemosis
7. Inflammation of caruncle OR plica

Diplopia Score

0. No diplopia
1. Intermittent, i.e., diplopia in primary position of gaze, when tired or when first awakening
2. Inconstant, i.e., diplopia at extremes of gaze
3. Constant, i.e., continuous diplopia in primary or reading position

GO: Graves’ Orbitopathy, also known as thyroid eye disease, or TED.
Chemosis: Swelling of conjunctiva, which is the mucous membrane that covers the front of the eye and lines the inside of the eyelids.
Caruncle: Small, pink, globular nodule at the inner corner (the medial canthus) of the eye.
Plica: A small fold of bulbar conjunctiva on the medial canthus of the eye.
Diplopia: Double vision.
Phase 2 Trial Results

Shows Potential to Be Disease-Modifying and Durable

**Impressive Response**

- 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**
- At Week 24, percentage of proptosis responders with p<0.001:
  - Teprotumumab patients: **71 percent**
  - Placebo patients: **20 percent**

**Proptosis and Diplopia: Durable Response**

- Proptosis:
  - Week 24: **71 percent** of patients were responders
  - Week 72: **53 percent** of responders maintained response approximately 1 year off treatment
- Diplopia:
  - Week 24: **62 percent** of patients were responders
  - Week 72: **69 percent** of responders maintained response approximately 1 year off treatment

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 safety and efficacy have not been established.
# Phase 2 Safety Overview

- Most adverse events were mild, transient and did not require treatment
  - The most frequent adverse events reported (≥5 percent of teprotumumab and greater than placebo) were nausea, muscle spasms, diarrhea, alopecia, hyperglycemia, dry skin, dysgeusia, headache, paresthesia, hearing impairment and weight loss
- Hyperglycemia (grade 2 or 3) occurred in some diabetics receiving teprotumumab, and it was well controlled after adjustment of diabetes medication

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=45)</th>
<th>Teprotumumab (N=42)</th>
</tr>
</thead>
<tbody>
<tr>
<td>TEAEs</td>
<td>32 (72.7%)</td>
<td>32 (74.4%)</td>
</tr>
<tr>
<td>SAEs(^1)</td>
<td>1 (2.3%)</td>
<td>5 (11.6%)</td>
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</tbody>
</table>


SAE: Serious adverse event. TEAE: Treatment emergent adverse event.

\(^1\)SAE (placebo): Optic neuropathy.

\(^2\)SAEs (teprotumumab): severe diarrhea in a patient with history of UC; IBD; E coli infection treated with IV antibiotics; Hashimoto’s encephalopathy (Provisional diagnosis after episodic mental confusion with no other neurologic symptoms); urinary retention (after patient had inguinal herniorrhaphy).

Teprotumumab is an investigational candidate, and safety and efficacy have not been established.
Teprotumumab: Phase 3 Trial Design and Topline Results

Shao-Lee Lin, M.D., Ph.D.
Executive Vice President, Head of R&D and Chief Scientific Officer
Horizon Pharma
Top-line Results

- **OPTIC study met its primary endpoint (82.9% vs 9.5%, p<0.001), demonstrating a dramatic impact on proptosis**
  - All secondary endpoints also met statistical significance (p≤0.001)
    - Overall responder rate at Week 24 (primary endpoint of Phase 2)\(^{(1)}\)
    - CAS responder rate at Week 24
    - Change in proptosis through Week 24
    - Diplopia improvement at Week 24
    - Change in GO-QOL through Week 24

- **Safety profile consistent with Phase 2**

---

\(^{(1)}\) Percent of participants with ≥2 point reduction in Clinical Activity Score (CAS) and ≥2 mm reduction in proptosis from baseline, provided there is no corresponding deterioration (≥2-point/mm increase) in CAS or proptosis in the fellow eye.

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

Go-QOL: Graves' Ophthalmopathy Quality of Life.

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

BLA submission targeted for mid-2019
Phase 3 Trial Design: 24-Week Randomized, Double-Masked, Placebo-Controlled Trial of Teprotumumab

**Patient Criteria**
- Active TED
- 18 to 75 years
- <9 months since active TED onset with no prior treatment
- CAS ≥4
- FT4 and FT3 <50 percent above or below normal limits

**Screening**

**Randomization**

**Teprotumumab**
- 8 infusions: 1 every three weeks

**Placebo**
- 8 infusions: 1 every three weeks

**Off-Treatment Follow-Up Period**

**Primary endpoint at Week 24**
Percentage of participants with >2 mm reduction in proptosis

CAS: Clinical Activity Score, a 7-point scale that measures change in orbital inflammation and pain; a score of >3 indicates active TED.
FT4: Free thyroxine.
FT3: Free triiodothyronine.
Teprotumumab is an investigational candidate, and safety and efficacy have not been established.
Subject Disposition

83 underwent randomization
83 received study drug (ITT population)

42 randomized to receive placebo
2 subjects discontinued early
• Adverse event (1)
• Withdrew consent (1)
40 completed double-masked treatment period

41 randomized to receive teprotumumab
2 subjects discontinued early
• Adverse event (1)
• Withdrew consent (1)
39 completed double-masked treatment period

ITT: Intent to treat.
### Key Demographics

<table>
<thead>
<tr>
<th></th>
<th>Placebo (N=42)</th>
<th>Teprotumumab (N=41)</th>
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</thead>
<tbody>
<tr>
<td><strong>Age (years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean (SD)</td>
<td>48.9 (12.96)</td>
<td>51.6 (12.63)</td>
</tr>
<tr>
<td><strong>Gender, %</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>26.2%</td>
<td>29.3%</td>
</tr>
<tr>
<td>Female</td>
<td>73.8%</td>
<td>70.7%</td>
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<tr>
<td><strong>Race, %</strong></td>
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<td></td>
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<tr>
<td>White</td>
<td>88.1%</td>
<td>85.4%</td>
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<tr>
<td>Black</td>
<td>4.8%</td>
<td>9.8%</td>
</tr>
<tr>
<td>Asian</td>
<td>2.4%</td>
<td>4.90%</td>
</tr>
<tr>
<td>Other</td>
<td>4.8%</td>
<td>0%</td>
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<tr>
<td><strong>Years Since Diagnosis of Graves’ Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>0.820 (0.05 - 14.76)</td>
<td>0.970 (0.18 - 28.20)</td>
</tr>
<tr>
<td><strong>Months Since Diagnosis of Thyroid Eye Disease</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>5.920 (0.59 - 9.08)</td>
<td>5.860 (0.46 - 8.72)</td>
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<tr>
<td><strong>Smoking Status</strong></td>
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<tr>
<td>Non-smoker</td>
<td>81.0%</td>
<td>78.0%</td>
</tr>
<tr>
<td>Smoker</td>
<td>19.0%</td>
<td>22.0%</td>
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Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
Proptosis Response (Reduction of ≥2 mm) Over Time

Teprotumumab (N=41) vs Placebo (N=42)

Proptosis Responders (%)

Baseline | Week 6 | Week 12 | Week 18 | Week 24
--- | --- | --- | --- | ---
Teprotumumab | 7.1 | 56.1 | 75.6 | 82.9
Placebo | 9.5 | 14.3 | 14.3 | 82.9

Primary Endpoint

Difference: 73.45
(95%CI 58.89, 88.01)

Proptosis Response (Reduction of ≥2 mm) Over Time

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

- Overall responder rate at Week 24 (primary endpoint of Phase 2)\(^{(1)}\)
- Percent of patients with a CAS value of 0 or 1 at Week 24 in the study eye
- Mean change in proptosis measurement from baseline to Week 24 in the study eye
- Percent of patients with a change from baseline of at least one grade in diplopia (double vision)
- Mean change in Graves’ Ophthalmopathy Quality of Life from baseline to Week 24

All secondary endpoints met statistical significance (p≤0.001)

\(^{(1)}\) Percent of participants with ≥2 point reduction in Clinical Activity Score (CAS) and ≥2 mm reduction in proptosis from baseline, provided there is no corresponding deterioration (≥2-point/mm increase) in CAS or proptosis in the fellow eye.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
Phase 3 Safety Overview

- Safety profile similar to Phase 2 with no new safety observations
- Drop-out rate was low (<5%) and balanced across arms
- No deaths

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<td>1 (2.4%)(^{(1)})</td>
<td>2 (4.9%)(^{(2)})</td>
</tr>
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(1) Placebo: visual field defect requiring orbital decompression surgery (patient discontinued study)
(2) Teprotumumab: pneumothorax (considered not related to study drug; patient had history of throat cancer with radiation treatment), infusion reaction (patient discontinued study)

- Vast majority of treatment-emergent adverse events were mild to moderate in intensity and no non-serious events led to discontinuation

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

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

• All secondary endpoints also met statistical significance (p≤0.001)
  – Overall responder rate at Week 24 (primary endpoint of Phase 2)\(^{(1)}\)
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• Safety profile consistent with Phase 2

(1) Percent of participants with ≥2 point reduction in Clinical Activity Score (CAS) and ≥2 mm reduction in proptosis from baseline, provided there is no corresponding deterioration (≥2-point/mm increase) in CAS or proptosis in the fellow eye.

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

Go-QOL: Graves’ Ophthalmopathy Quality of Life.

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

BLA submission targeted for mid-2019
Conclusion

Timothy P. Walbert
Chairman, President and Chief Executive Officer
Horizon Pharma
Key Takeaways for Today’s Call

- Teprotumumab Phase 3 OPTIC trial achieved its primary endpoint, confirming Phase 2 and demonstrating that teprotumumab has the potential to be a disease-modifying therapy\(^{(1)}\)

- No FDA-approved therapies exist for TED; currently used therapies are not disease-modifying

- Active thyroid eye disease (TED) is a rare and debilitating inflammatory autoimmune disease of the eye; active TED impacts 15,000 to 20,000 U.S. patients annually\(^{(2)}\)

- Expect mid-2019 BLA submission and potential 2020 approval; fast-track and breakthrough designations
  - Estimated U.S. peak net sales potential of >$750M\(^{(3)}\)
  - Pre-launch planning underway

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\(^{(2)}\) Company analysis of claims data and market research.
\(^{(3)}\) Horizon Pharma estimate.

Teprotumumab is an investigational candidate and its safety and efficacy have not been established.
An Overview of Thyroid Eye Disease (TED), Teprotumumab and OPTIC Phase 3 Trial Topline Results

February 28, 2019