FDA Approval

January 21, 2020
Forward-Looking Statements

This presentation contains forward-looking statements, including, but not limited to, statements related to expected financial performance and operating results in future periods, including expected net sales of TEPEZZA; expected timing of clinical trials and regulatory submissions and decisions; potential market opportunity for and benefits of TEPEZZA; Horizon’s commercialization plans and strategy for TEPEZZA; 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 successfully launch TEPEZZA and grow net sales; 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 and launching 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.
Agenda

Introduction

Thyroid Eye Disease (TED) and Clinical Review

Commercial Strategy

Q&A
TEPEZZA: First and Only FDA-Approved Medicine for Patients with Thyroid Eye Disease

Received early U.S. FDA approval on Jan. 21, 2020 for patients with Thyroid Eye Disease
• Impressive Phase 3 results show 82.9 percent of TEPEZZA patients with ≥2mm proptosis reduction

Thyroid Eye Disease is a debilitating, vision-threatening, rare 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 TEPEZZA

Significant pre-launch market education efforts completed; U.S. commercial launch now underway
• Multi-functional, highly experienced team has been working with stakeholders since July 2019

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

(1) Horizon estimate.
Note: For additional TEPEZZA safety information, please see end of presentation.
### Indication

**TEPEZZA** is indicated for the treatment of Thyroid Eye Disease

### Dosing & Administration

**Dosing:**
- Initiate dosing with 10 mg/kg, followed by 20 mg/kg 3 weeks later and every 3 weeks for 7 additional infusions
- Administer **TEPEZZA** by intravenous infusion over 60 to 90 minutes

### Safety

No contraindications

**Warnings and Precautions:**
- Infusion reactions
- Exacerbation of preexisting Inflammatory Bowel Disease
- Hyperglycemia

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Note: For additional TEPEZZA safety information, please see end of presentation.
Thyroid Eye Disease and Clinical Review
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
Active TED Progresses to Inactive TED; Permanent Damage May Require Surgery

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

Disease Activity

- Efficacious therapy
- Untreated
- Surgery

Up to 3 years  Beyond 3 years

- Active
- Inactive

Complex and Multiple Surgeries, Including Decompression Surgery

Exposing Orbit

Removing Bone

Removing Tissue and Bone

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: 7.1%
- Week 6: 56.1%
- Week 12: 75.6%
- Week 18: 82.9%
- Week 24: 82.9%

**Difference:** 73.45%
(95%CI 58.89, 88.01)

Proptosis Reduction of 3.32 mm at Week 24

Proptosis Reduction (mm)

- Baseline: -4.00 mm
- Week 6: -3.62 mm
- Week 12: -3.26 mm
- Week 18: -3.05 mm
- Week 24: -2.79 mm

**Difference:** -2.79 mm
(95%CI -3.40, -2.17)

**Note:** Throughout the 24-week treatment period, patients treated with TEPEZZA had an average proptosis reduction of 2.82 mm compared with 0.54 mm for those who received placebo (p<0.001).

**Note:** For additional TEPEZZA safety information, please see end of presentation.

(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.
Phase 3 Trial: All Secondary Endpoints Met with Statistical Significance

### Diplopia (double vision)
- Percentage of participants with improvement from baseline of at least one grade in diplopia
- Data from Diplopia: Double vision. Note: Only participants who had baseline diplopia (diplopia score >0) were included in the diplopia analysis.

### Quality of Life
- Mean change from baseline in GO-QoL questionnaire overall score
- Data from GO-QoL: Graves’ Ophthalmopathy Quality of Life.

### Clinical Activity Score
- Percentage of participants with a CAS value of 0 or 1 in the study eye
- Data from 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.

Note: For additional TEPEZZA safety information, please see end of presentation.
Example of Patients in TEPEZZA Clinical Program

Proptosis Reduction Seen at Week 24 in TEPEZZA Clinical Trial

Note: Patient photos provided with permission from patients of Raymond Douglas, M.D.
Note: For additional TEPEZZA safety information, please see end of presentation.
Source: Horizon Therapeutics FDA Advisory Committee Presentation.
MRI Demonstrates Improved Effects on Orbital Muscle and Fat after TEPEZZA Treatment

MRI: Magnetic resonance imaging.
Note: For additional TEPEZZA safety information, please see end of presentation.
Source: Horizon Therapeutics FDA Advisory Committee Presentation.
Positive Benefit/Risk Profile for TEPEZZA in Thyroid Eye Disease

**Benefits**

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

**Manageable Safety Profile**

- Warnings and Precautions
  - Infusion reactions
  - Exacerbation of preexisting Inflammatory Bowel Disease
  - Hyperglycemia
- Post-marketing study to evaluate safety in a larger patient population and retreatment rates relative to how long patients receive medicine

Note: For additional TEPEZZA safety information, please see end of presentation.
TEPEZZA Commercial Strategy and Launch
Driving TEPEZZA Adoption: Our Commercialization Strategy

**Establish**
- Market structure and patient journey

**Educate**
- All stakeholders about Thyroid Eye Disease and TEPEZZA

**Support**
- TEPEZZA launch with our high-touch, patient-centric model

**Facilitate**
- Access to medicine and infusion referral process

Note: For additional TEPEZZA safety information, please see end of presentation.
With No Approved Treatment, the Patient Journey Is Long and Ill-Defined

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
- Optic nerve compromised
- Steroids fail → Surgery

Inactive Stage

“Watch and Wait” Approach

Primary Care
Ophthalmologist
Allergist or Optometrist
Endocrinologist

Surgery
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

Endocrinologist
Recognizes TED symptoms and refers to ophthalmologist

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

TEPEZZA Infused at Site of Care

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

“In Watch and Wait” Approach

Inactive Stage

Surgeries

Note: For additional TEPEZZA safety information, please see end of presentation.
We Have Established 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

Note: For additional TEPEZZA safety information, please see end of presentation.
Ready for the **TEPEZZA** Commercial Launch

*Executed on Significant Pre-Launch Activities; Expected Peak U.S. Annual Net Sales of >$1B\(^{(1)}\)*

### Pre-Launch Efforts Drove Awareness and Excitement; Paved 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** (150,000 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 **TEPEZZA** clinical results and TED education sessions at >**10 medical meetings** since Phase 3 data readout
- **Significant engagement** with advocacy and patient communities

### Launch and Post-Launch

- **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
- **Anticipating 2020 Net Sales Expectations:** $30M-$40M\(^{(1)}\)

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

Note: For additional TEPEZZA safety information, please see end of presentation.

Approval Date: January 21, 2020
Compelling TEPEZZA Value Proposition

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

Rare Disease
U.S. addressable incidence of 15K to 20K patients (2)

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

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

Safety
Significant benefits outweigh manageable risks

Expected average net realized price: ~$200,000
Assumptions:
• 75% to 80% adherence for six-month course of treatment
• Typical rebates and discounts required by various stakeholders, as well as financial assistance Horizon provides to eligible patients

(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

(2) Horizon estimate of patients eligible for TEPEZZA each year. Note: For additional TEPEZZA safety information, please see end of presentation.
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Q&A
**TEPEZZA Important Safety Information**

**INDICATION**
**TEPEZZA** is indicated for the treatment of Thyroid Eye Disease.

**IMPORTANT SAFETY INFORMATION**

**Warnings and Precautions**

**Infusion Reactions:** **TEPEZZA** may cause infusion reactions. Infusion reactions have been reported in approximately 4% of patients treated with **TEPEZZA**. Reported infusion reactions have usually been mild or moderate in severity. Signs and symptoms may include transient increases in blood pressure, feeling hot, tachycardia, dyspnea, headache and muscular pain. Infusion reactions may occur during an infusion or within 1.5 hours after an infusion. In patients who experience an infusion reaction, consideration should be given to pre-medicating with an antihistamine, antipyretic or corticosteroid and/or administering all subsequent infusions at a slower infusion rate.

**Preexisting inflammatory bowel disease:** **TEPEZZA** may cause an exacerbation of preexisting inflammatory bowel disease (IBD). Monitor patients with IBD for flare of disease. If IBD exacerbation is suspected, consider discontinuation of **TEPEZZA**.

**Hyperglycemia:** Increased blood glucose or hyperglycemia may occur in patients treated with **TEPEZZA**. In clinical trials, 10% of patients (two-thirds of whom had pre-existing diabetes or impaired glucose tolerance) experienced hyperglycemia. Hyperglycemic events should be managed with medications for glycemic control, if necessary. Monitor patients for elevated blood glucose and symptoms of hyperglycemia while on treatment with **TEPEZZA**. Patients with pre-existing diabetes should be under appropriate glycemic control before receiving **TEPEZZA**.

**Adverse Reactions**
The most common adverse reactions (incidence ≥5% and greater than placebo) are muscle spasm, nausea, alopecia, diarrhea, fatigue, hyperglycemia, hearing impairment, dysgeusia, headache and dry skin.

For additional information on **TEPEZZA**, please see Full Prescribing Information at TEPEZZAhcp.com.