



Horizon Pharma plc Increases Peak Net Sales Guidance for Key Growth Drivers and Announces Rheumatology and Orphan Pipeline Developments

- Increases KRYSTEXXA® (pegloticase injection) Estimated Peak Annual Net Sales to more than \$750 Million --*
- Increases Teprotumumab Estimated Peak Annual Net Sales to more than \$750 Million --*
- Confirms Expectation of More Than 50 Percent Year-Over-Year Net Sales Growth for KRYSTEXXA in 2018 --*
- Announces Licensing Agreement with MedImmune for Potential Next-Generation Biologic for Uncontrolled Gout --*

DUBLIN, IRELAND – Jan. 8, 2018 – Horizon Pharma plc (NASDAQ: HZNP), today provided updates on the potential performance of key growth drivers and its research and development (R&D) pipeline.

“The increase in our sales expectations for our key growth drivers, KRYSTEXXA and teprotumumab, reflect our confidence in the significant potential they have for patients,” said Timothy P. Walbert, chairman, president and chief executive officer, Horizon Pharma plc. “Based on our commercial expansion for KRYSTEXXA and a larger anticipated addressable patient population for both KRYSTEXXA and teprotumumab, we see significant opportunity ahead.

“We are also announcing several additions to our rheumatology development pipeline, including MEDI4945, a potential next-generation gout biologic to support and sustain our leadership of the uncontrolled gout market,” continued Walbert. “We are expanding the investment now to advance the next phase of our Company’s strategy, which is to build a robust development-stage pipeline to generate long-term value for shareholders.”

Updated Peak Net Sales Expectations and Market Opportunities for KRYSTEXXA and Teprotumumab

Following additional analysis of the addressable patient population and market opportunities for both KRYSTEXXA and teprotumumab in the United States, as well as a significant commercial expansion for KRYSTEXXA, the Company is increasing its estimated peak annual net sales expectations for each medicine to more than \$750 million. Previously, peak net sales expectations for KRYSTEXXA were more than \$400 million and peak net sales expectations for teprotumumab were more than \$250 million.

KRYSTEXXA is the only medicine approved by the U.S. Food and Drug Administration (FDA) for adults living with uncontrolled gout, chronic gout that is refractory (not responsive) to conventional gout therapies. In the fourth quarter of 2017, the Company completed its second expansion of its KRYSTEXXA commercial organization, approximately doubling it in size. In addition, through new outreach efforts to nephrologists, the Company’s estimated addressable patient population for KRYSTEXXA has doubled from 50,000 to 100,000 patients. Nephrologists treat chronic kidney disease (CKD) patients of whom 25 to 50 percent have concurrent gout. Additionally, approximately half of people living with gout also have CKD. The Company continues to expect 2018 net sales growth for KRYSTEXXA of more than 50 percent.

Teprotumumab is a fully human monoclonal antibody IGF-IR-inhibitor being studied in a confirmatory Phase 3 clinical trial for the treatment of a rare eye disease, thyroid eye disease (TED). If approved, it would be the only FDA-approved medicine available to treat TED. Following additional market research and analysis of the treatable TED patient population, the Company now assumes a larger addressable



patient population exists. It estimates that the annual U.S. incidence of moderate-to-severe active TED is between 15,000 and 20,000 patients.

Pipeline Developments: Rheumatology Candidates and Programs

The Company announced several developments today to its growing pipeline related to its Rheumatology products, including KRYSTEXXA. KRYSTEXXA is a recombinant protein of uricase, an enzyme not found in humans, and PEGylation, a synthetic technology used to extend the half-life of uricase. As with many biologic medicines, some people treated with KRYSTEXXA may develop antidrug antibodies as part of an immune response to the medicine, a reaction known as immunogenicity, and lose response to therapy.

HZN-003 (Potential Next-Generation Biologic for Uncontrolled Gout Using Optimized Uricase and Optimized PEGylation Technology)

Earlier today, the Company announced that has licensed HZN-003 (formerly MEDI4945), a potential next-generation biologic for uncontrolled gout, from MedImmune, the global biologics research and development arm of AstraZeneca. HZN-003 is a pre-clinical, genetically engineered uricase derivative with optimized uricase and optimized PEGylation technology that has the potential to improve the response rate to the biologic as well as the potential for subcutaneous dosing.

Potential Next-Generation Biologic for Uncontrolled Gout Using PASylation Technology

The Company also recently entered into a collaboration agreement with XL-protein GmbH to identify clinical-stage product candidates that could use PASylation technology to construct a next-generation gout biologic. PASylation technology is a biological alternative to synthetic PEGylation and is intended to extend both the half-life of uricase and the duration of treatment for people living with uncontrolled gout, and also has the potential for subcutaneous dosing. If the collaboration agreement identifies clinical-stage candidates, the Company will have the right to license the candidates.

KRYSTEXXA Investigator-Initiated Trials: RECIPE and TRIPLE

In addition to these new programs, two investigator-initiated trials will evaluate the use of immunomodulatory therapies to enhance the response rate for KRYSTEXXA. The studies will use different immunomodulators, both of which rheumatologists are very familiar with and comfortable prescribing.

The University of Alabama at Birmingham Division of Clinical Immunology and Rheumatology is expected to begin a clinical trial in the first quarter of 2018 evaluating the use of the immunomodulator mycophenolate mofetil (MMF) along with KRYSTEXXA to improve the response rate to the medicine.

REduCing Immunogenicity to PegloticasE (RECIPE) is a double-blind, placebo controlled trial is designed to evaluate if a 12-week course of immunomodulating therapy with daily MMF can safely and meaningfully prevent the incidence of an immune response to KRYSTEXXA. The study will also assess the incidence and types of adverse events and infusion reactions related to the medicine. More detailed information about the RECIPE study is available at ClinicalTrials.gov.

The second investigator-initiated trial is the **Tolerization Reduces Intolerance to Pegloticase and Prolongs the Urate Lowering Effect (TRIPLE)** study. An exploratory, open-label adaptive trial with multiple patient cohorts, TRIPLE will include a cohort to evaluate the impact of adding the immunomodulator azathioprine



for a 2-week run-in period, followed by daily azathioprine and KRYSTEXXA every 2 weeks for a total of 13 doses. The immunomodulation arm of the study is expected to begin in the first quarter of 2018. More detailed information about the TRIPLE study is available at ClinicalTrials.gov.

HZN-002 (Potential Targeted Novel Dexamethasone Conjugate for Inflammatory Diseases)

The Company has licensed an additional pipeline compound to augment its rheumatology portfolio: HZN-002, a preclinical, targeted novel dexamethasone conjugate with potential advantages over existing therapies for inflammatory diseases.

Pipeline: Teprotumumab (HZN-001)

In October 2017, the Company announced that the first patient had been enrolled in a confirmatory Phase 3 clinical trial evaluating Horizon Pharma's late-stage development candidate teprotumumab, a fully human monoclonal antibody IGF-1R-inhibitor, for moderate-to-severe active TED. The Company continues to anticipate enrollment to be completed by the end of 2018.

Titled "Treatment of Graves' Orbitopathy (Thyroid Eye Disease) to Reduce Proptosis with Teprotumumab Infusions in a Randomized, Placebo-Controlled, Clinical Study (OPTIC)," the Phase 3 trial is expected to enroll 76 patients across 11 centers in the United States, Germany and Italy. Those who meet OPTIC ([NCT03298867](https://clinicaltrials.gov/ct2/show/study/NCT03298867)) Phase 3 eligibility criteria will be randomized to receive eight infusions of teprotumumab or placebo every three weeks for 21 weeks.

The primary endpoint of the trial is the effect of teprotumumab versus placebo on the proptosis responder rate at Week 24, defined as the percentage of participants with a ≥ 2 mm reduction of proptosis in the study eye (without deterioration in the fellow eye). In addition, the OPTIC trial has several secondary endpoints at Week 24, including overall response rate, percentage of participants with a Clinical Activity Score value of 0 or 1, mean change in proptosis measurement and mean change in the overall score of the Graves' Ophthalmopathy Quality of Life questionnaire. The Clinical Activity Score is a well-established 7 point scale used to measure the stages of TED; a score of 3 or above indicates active thyroid eye disease. More detailed information about the study is available at ClinicalTrials.gov.

Teprotumumab demonstrated unprecedented clinical efficacy in patients with TED in the Phase 2 clinical trial. For the Phase 2 primary endpoint of proptosis reduction of ≥ 2 mm, which is the same primary endpoint as the Phase 3 trial, 71 percent of patients receiving teprotumumab responded to treatment at week 24 compared to 20 percent of patients receiving placebo ($p < 0.001$). Teprotumumab received Breakthrough Therapy, Orphan Drug and Fast Track designations from the FDA in 2016.

"The key tenet to our R&D strategy is to provide patients with the maximum benefit of our medicines and address unmet needs," said Shao-Lee Lin, M.D., Ph.D., executive vice president, head of research and development and chief scientific officer, Horizon Pharma plc. "We are effecting this by enhancing our commercialized medicines and building a pipeline of candidates focused primarily on rare and rheumatic diseases. We are committed to establishing Horizon as a leader in the rare disease space, and our pipeline programs are moving us toward that goal. These development programs will enable us to make an even greater impact on the lives of patients suffering from diseases that affect more limited populations."



Impact of the Tax Cut and Jobs Act

The Company anticipates the recently enacted Tax Cut and Jobs Act to have a marginally positive impact on its non-GAAP adjusted tax expense. Guidance on the impact of the Tax Cut and Jobs Act to the Company's GAAP tax expense has not been provided due to the inherent difficulty of forecasting the timing or amount of items that would be included in GAAP tax expenses and impacted by the Tax Cut and Jobs Act. The Company expects to record a one-time tax provision benefit in 2017 to reflect a reduction in net deferred tax liabilities, which would be included as an adjustment to the Company's non-GAAP adjusted tax expense.

About Horizon Pharma plc

Horizon Pharma plc is focused on researching, developing and commercializing innovative medicines that address unmet treatment needs for rare and rheumatic diseases. By fostering a growing pipeline of medicines in development and exploring all potential uses for currently marketed medicines, we strive to make a powerful difference for patients, their caregivers and physicians. For us, it's personal: by living up to our own potential, we are helping others live up to theirs. For more information, please visit www.horizonpharma.com. Follow [@HZNPplc](https://twitter.com/HZNPplc) on Twitter, like us on [Facebook](https://www.facebook.com/horizonpharma) or explore career opportunities on [LinkedIn](https://www.linkedin.com/company/horizonpharma).

Forward-Looking Statements

This press release contains forward-looking statements, including, but not limited to, statements related to Horizon Pharma's business strategy and development plans, expected net sales growth of KRYSTEXXA, expected financial performance in future periods, expected timing of clinical, regulatory and commercial events, including those relating to the Phase 3 clinical trial of teprotumumab and investigator-sponsored clinical trials of KRYSTEXXA, potential market opportunity and estimated peak sales for Horizon Pharma's approved medicines and pipeline candidates, potential growth of Horizon Pharma's medicines, expected impact of the Tax Cut and Jobs Act, 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 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 and risks relating to Horizon Pharma's ability to successfully implement its business strategies; risks associated with drug development and regulatory approvals; potential delays in clinical trials, including due to enrollment rates or adverse events; risks that results from on-going or future clinical trials may be inconsistent with results from prior pre-clinical studies or clinical trials; 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 SEC. Horizon Pharma undertakes no duty or obligation to update any forward-looking statements contained in this press release as a result of new information.



About KRYSTEXXA®

INDICATIONS AND USAGE

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

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

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

IMPORTANT SAFETY INFORMATION

WARNING: ANAPHYLAXIS AND INFUSION REACTIONS

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

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

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

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

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

CONTRAINDICATIONS: G6PD DEFICIENCY ASSOCIATED HEMOLYSIS AND METHEMOGLOBINEMIA

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

GOUT FLARES

An increase in gout flares is frequently observed upon initiation of anti-hyperuricemic therapy, including treatment with KRYSTEXXA. If a gout flare occurs during treatment, KRYSTEXXA need not be discontinued. Gout flare prophylaxis with a non-steroidal anti-inflammatory drug (NSAID) or colchicine is recommended



starting at least 1 week before initiation of KRYSTEXXA therapy and lasting at least 6 months, unless medically contraindicated or not tolerated.

CONGESTIVE HEART FAILURE

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

ADVERSE REACTIONS

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

Contacts:

Tina Ventura
Senior Vice President, Investor Relations
Investor-relations@horizonpharma.com

Ruth Venning
Executive Director, Investor Relations
Investor-relations@horizonpharma.com

U.S. Media Contact:
Geoffrey Curtis
Senior Vice President, Corporate Affairs and Chief Communications Officer
media@horizonpharma.com

Ireland Media Contact:
Ray Gordon
Gordon MRM
ray@gordonmrm.ie

Source: Horizon Pharma plc