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Horizon Pharma Announces FDA Approval of RAYOS® (prednisone) Delayed-Release Tablets for Rheumatoid Arthritis and Multiple Additional Indications

RAYOS approved for key rheumatology indications such as Rheumatoid Arthritis, Polymyalgia Rheumatica, Psoriatic Arthritis and Ankylosing Spondylitis.

DEERFIELD, Ill., July 26, 2012 /PRNewswire/ -- Horizon Pharma, Inc., (NASDAQ: HZNP) announced today that the U.S. Food and Drug Administration (FDA) has approved **RAYOS®** (prednisone) delayed-release tablets (1 mg, 2 mg and 5 mg) to treat a broad range of diseases including rheumatoid arthritis (RA), polymyalgia rheumatica (PMR), psoriatic arthritis (PsA), ankylosing spondylitis (AS), asthma and chronic obstructive pulmonary disease (COPD) (**see full prescribing information at www.RAYOSrx.com**). The FDA approval was supported by data bridging the pharmacokinetics of RAYOS to immediate-release prednisone and data from the Circadian Administration of Prednisone in RA (CAPRA-1 and 2) trials. The CAPRA-2 trial demonstrated that people with moderate to severe RA treated with RAYOS experienced a statistically significant improvement in ACR20 response criteria compared to placebo. The CAPRA-1 trial supported the overall safety of RAYOS.

"We are extremely pleased the FDA has approved RAYOS for a broad range of indications, including RA and polymyalgia rheumatica," said Timothy P. Walbert, chairman, president and chief executive officer, Horizon Pharma. "Our initial focus will be on the launch of RAYOS in rheumatologic diseases such as RA and polymyalgia rheumatica in the fourth quarter of this year. Based on the extent of the approved indications, we will be developing a broader commercial strategy to expand the opportunity for RAYOS in key IL-6 mediated diseases, including asthma and COPD."

RAYOS Clinical Data

U.S. New Drug Application

The efficacy of RAYOS in the treatment of RA was assessed in the CAPRA-2 trial, a double-blind, placebo-controlled, randomized, 12-week trial in patients with active rheumatoid arthritis diagnosed according to American College of Rheumatology (ACR) criteria. Enrolled patients were not currently being treated with corticosteroids but had received non-biologic disease-modifying antirheumatic drug (DMARD) therapy for at least 6 months prior to receipt of study medication, with an incomplete response to DMARD therapy alone. Patients were randomized in a 2:1 ratio to treatment with RAYOS 5 mg (n=231) or placebo (n=119) administered at 10 p.m. in addition to their DMARD therapy. A total of 350 patients were enrolled and ranged in age from 27 to 80 years (median age 57 years). Patients were predominantly Caucasian and 84% were female.

Results from CAPRA-2 demonstrated:

- A statistically significant improvement in ACR20 response criteria, the primary study endpoint, for patients who were treated with RAYOS compared to the placebo group (47% vs. 29%; p-value = 0.001).
- A statistically significant improvement in ACR50 response compared to placebo (22% vs. 10%; p-value = 0.007) and an improvement in the more stringent ACR70 response criteria (7% vs. 3%; p-value = 0.0984). Both ACR50 and ACR70 were pre-specified secondary endpoints.

The relative change from baseline in the duration of morning stiffness at 12 weeks was assessed as a pre-specified secondary endpoint. Patients treated with RAYOS had a median decrease in the duration of morning stiffness of 55 minutes compared to 33 minutes in placebo-treated patients (20 minute estimated median difference between treatment groups with 95% confidence interval [7, 32; p-value = 0.001]).

Results from CAPRA-2 are published in *Annals of the Rheumatic Diseases*.¹

"Prednisone is a common therapy for patients with various inflammatory diseases, including RA, and the delayed-release enhancement offered with RAYOS is an important treatment advance," said Michael Schiff, M.D., Clinical Professor of Medicine at the University of Colorado School of Medicine, Rheumatology Division. "RAYOS is engineered to benefit the underlying patterns of inflammatory diseases. RAYOS, as studied in its clinical trials with ten p.m. dosing, reduces the overnight rise of inflammatory mediators, which results in less pain and stiffness for patients as they begin their day."

The safety of RAYOS was based on the evaluation of 375 RA patients in two controlled trials. Patients treated with RAYOS ranged in age from 20 to 80 years (median age 56 years). Patients were predominantly Caucasian and 85% were female.

Included in these safety results were data from the CAPRA-1 trial, a 12 week, double-blind, placebo-controlled study that evaluated 288 RA patients. CAPRA-1 compared 10 p.m. administration of RAYOS with the morning administration of immediate-release prednisone at the same individual dose (average dose of 6.7 mg). Following the 12-week CAPRA-1 study, patients were followed in a 9-month, open-label extension study, which included 249 RA patients, 219 of whom completed the extension study. Patients received RAYOS 3 mg to 10 mg once daily at 10 p.m.; the majority (84%) received 5 mg or less.

The clinical trial experience did not raise any safety concerns beyond those already established for immediate-release prednisone.

Results from the CAPRA-1 12-week study and the 9-month open-label extension are published in *The Lancet* and *Annals of the Rheumatic Diseases*, respectively.^{2,3}

About RAYOS

RAYOS, known as LODOTRA[®] in Europe, is a proprietary delayed-release formulation of low-dose prednisone. The pharmacokinetic profile of RAYOS is different with an approximately four-hour lag time from that of immediate-release prednisone formulations. In clinical trials studying use of RAYOS in RA, patients were administered RAYOS at 10 p.m. with food. Given RAYOS delayed-release profile, this helps to achieve therapeutic prednisone blood levels at a time point when cytokine levels start rising during the middle of the night. While the pharmacokinetic profile of RAYOS differs in terms of lag time from immediate-release prednisone, its absorption, distribution and elimination processes are comparable

RAYOS utilizes SkyePharma's proprietary Geoclock[™] technology.

Outside the United States, LODOTRA is approved for the treatment of moderate to severe active RA when accompanied by morning stiffness in 16 European countries and Israel. Horizon has granted commercialization rights for LODOTRA in Europe, Asia and Latin America to its distribution partner Mundipharma International Corporation Limited.

Important Safety Information

RAYOS[®] (prednisone) delayed - release tablets

Approved uses of RAYOS

RAYOS, a delayed - release form of prednisone, prevents the release of substances in the body that cause inflammation. RAYOS is approved to treat a broad range of diseases including rheumatoid arthritis (RA), polymyalgia rheumatica (PMR), psoriatic arthritis (PsA), ankylosing spondylitis (AS), asthma and chronic obstructive pulmonary disease (COPD). **For a full list of RAYOS indications, please see full prescribing information at www.RAYOSrx.com.**

RAYOS is contraindicated in patients who have known hypersensitivity to prednisone or to any of the excipients. Rare instances of anaphylaxis have occurred in patients receiving corticosteroids.

Important information about RAYOS

Do not use RAYOS if you are allergic to prednisone.

Long - term use of RAYOS can affect how your body responds to stress. Symptoms can include weight gain, severe fatigue, weak muscles, and high blood sugar.

RAYOS can weaken your immune system, making it easier for you to get an infection or worsening an infection you already have or have recently had.

RAYOS can cause high blood pressure, salt and water retention and low blood potassium.

There is an increased risk of developing holes in the stomach or intestines if you have certain stomach and intestinal disorders.

Behavior and mood changes can occur, including intense excitement or happiness, sleeplessness, mood swings, personality changes or severe depression.

Long - term use of RAYOS can cause decreases in bone density.

RAYOS can cause cataracts, eye infections and glaucoma.

Do not receive a "live" vaccine while taking RAYOS. The vaccine may not work as well during this time, and may not fully

protect you from disease.

Taking RAYOS during the first trimester of pregnancy can harm an unborn baby.

Long - term use of RAYOS can slow growth and development in children.

The most common side effects with RAYOS are water retention, high blood sugar, high blood pressure, unusual behavior and mood changes, increased appetite and weight gain.

Please see full prescribing information for RAYOS at www.RAYOSrx.com.

About Horizon Pharma

Horizon Pharma, Inc. (NASDAQ: HZNP) is a biopharmaceutical company that is developing and commercializing innovative medicines to target unmet therapeutic needs in arthritis, pain and inflammatory diseases. For more information, please visit www.horizonpharma.com.

Forward Looking Statements

This press release contains forward-looking statements, including statements regarding the timing of a potential commercial launch of RAYOS in the United States, the company's plans to develop a broader commercial strategy for RAYOS and the potential for RAYOS to provide a new treatment option for patients with inflammatory diseases. These forward-looking statements are based on management's expectations and assumptions as of the date of this press release, and actual results may differ materially from those in these forward-looking statements as a result of various factors, including, but not limited to, risks regarding the company's ability to commercialize products successfully, changes in the company's strategy as to when to launch RAYOS in the United States and on which approved indications it will focus its initial commercial efforts, whether physicians will prescribe and patients will use RAYOS, once available, and competition in the market for RAYOS. For a further description of these and other risks facing the company, please see the risk factors described in the company's filings with the United States Securities and Exchange Commission, including those factors discussed under the caption "Risk Factors" in those filings. Forward-looking statements speak only as of the date of this press release, and the company undertakes no obligation to update or revise these statements, except as may be required by law.

References

1. *Buttgereit F, Mehta D, Kirwan J, et al. Low-dose prednisone chronotherapy for rheumatoid arthritis: a randomised clinical trial (CAPRA-2). Ann Rheum Dis. 2012 May 5. [Epub ahead of print]*
2. *Buttgereit F, Doering G, Schaeffler A, et al. Efficacy of modified-release versus standard prednisone to reduce duration of morning stiffness of the joints in rheumatoid arthritis (CAPRA-1): a double-blind, randomised controlled trial. Lancet. 2008;371:205-214.*
3. *Buttgereit F, Doering G, Schaeffler A, et al. Targeting pathophysiological rhythms: prednisone chronotherapy shows sustained efficacy in rheumatoid arthritis. Ann Rheum Dis. 2010;69:1275-1280.*

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