Pharming announces positive interim analysis data from open-label extension study of leniolisib in presentation at the 64th American Society of Hematology (ASH) Annual Meeting and Exposition

V. Koneti Rao, MD, shared new evidence of long-term safety and hematologic response in patients who received leniolisib to treat APDS, a rare primary immunodeficiency

Interim analysis demonstrated leniolisib to be well tolerated and indicated the durability of the efficacy results seen in the Phase II/III randomized, controlled trial

Leiden, The Netherlands, December 15, 2022: Pharming Group N.V. ("Pharming" or "the Company") (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces data, including new evidence, from an interim analysis of its open-label extension study evaluating the investigational drug leniolisib, an oral, selective phosphoinositide 3-kinase delta (PI3Kδ) inhibitor, to treat adult and adolescent patients with activated phosphoinositide 3-kinase delta syndrome (APDS), a rare primary immunodeficiency. Principal investigator V. Koneti Rao, M.D., a staff physician in the Primary Immune Deficiency Clinic at the National Institutes of Health in Bethesda, Maryland, U.S., shared the positive findings in an oral presentation at the 2022 Annual Meeting of the American Society of Hematology (ASH).

Dr. Virgil Dalm, Principal Investigator, Consultant Clinical Immunology, Erasmus MC, Rotterdam, the Netherlands, commented:

"I'm excited about Pharming's findings that further support leniolisib as a well-tolerated investigational treatment benefitting patients with APDS. The results demonstrate the long-term tolerability of leniolisib, with a median duration on study therapy of just over 2 years (102 weeks) and 5 subjects being treated for 5 years or more. Individuals with APDS frequently suffer from recurrent infections and lifelong Immunoglobulin Replacement Therapy (IRT) is required to reduce this burden. Notably, leniolisib treatment demonstrated a significant reduction in the annualized infection rate, while 37% of study patients on IRT were able to either reduce or altogether stop their IRT regimens. This is a remarkable outcome for any study of inborn errors of immunity and through the continued study of leniolisib, I look forward to contributing to the knowledge of an improved treatment option for individuals with APDS."

The ongoing extension study includes 37 patients with APDS aged 12 years or older who, at the time of data cutoff for the interim analysis, had received 70 mg of the selective PI3Kδ inhibitor leniolisib twice a day for up to six years and three months, with a median duration on study therapy of 102 weeks. The study was primarily designed to assess the safety and tolerability of long-term leniolisib treatment in adolescent and adult patients with APDS who previously participated in a

Phase II/III leniolisib study. The extension study's secondary endpoints are intended to evaluate the efficacy and pharmacokinetics of long-term leniolisib treatment in these patients.

The interim analysis found that leniolisib was well tolerated to this point in the study. It also indicated the durability of the efficacy results seen in the randomized, controlled trial, which showed significant improvement over placebo in the co-primary endpoints of reduction in lymph node size and increase in naïve B cells. The interim results indicate a favorable long-term impact on the immune dysregulation and deficiency often seen in patients with APDS, with clinical manifestations including infections, lymphoproliferation, autoimmunity, enteropathy, bronchiectasis, increased risk of lymphoma, and early mortality.

The majority of adverse events (AEs) reported in the interim analysis were grades 1 and 2, and included upper respiratory tract infection, headache and pyrexia. Grade 1 AEs are the least severe and grade 5 the most severe. Overall, 13.5% of AEs were study drug-related; these affected five patients and included weight gain, arthralgia, hyperglycemia, and decreased neutrophil count. Of all AEs assessed in the analysis, 16.2% were classified as serious, but none of these were identified as related to study treatment. There was one death among study participants which was identified as not related to study treatment.

Among study participants, some experienced reductions in APDS disease markers, with levels of response varying between individuals. Responses included:

- reduced lymphadenopathy, splenomegaly, and IgM levels;
- improved or resolved anemia, thrombocytopenia, and lymphopenia; and
- resolved neutropenia in all affected patients.

Importantly, 37% of participants who were on immunoglobulin replacement therapy (IRT) were able to reduce their IRT use while taking leniolisib. Six patients became IRT-independent, with four of those patients having been IRT-independent for 1 to 2.5 years at the data cutoff. As of the data cut-off for the interim analysis, among three patients who had a history of lymphoma prior to the trial, none had a recurrence or new lymphoma while participating in the study.

Anurag Relan, MD, MPH, Chief Medical Officer of Pharming, commented:

"Pharming is pleased to share positive interim findings on the long-term safety and efficacy of leniolisib. The results announced at the 2022 ASH Annual Meeting build on the Phase II/III study findings announced earlier this year and published in Blood[1] in November 2022, which highlighted leniolisib's potential to control the development of immune-related symptoms of APDS. We're proud to help fill an unmet need by developing what could become the first approved drug to target the cause of APDS."

The interim analysis findings are consistent with the data, first reported on February 2, 2022, for the Phase II/III clinical trial investigating leniolisib as a treatment for adult and adolescent patients with APDS. Compared with placebo, patients in the Phase II/III clinical trial achieved significant reductions in index lymph node size and increases in the percentage of naïve B cells in peripheral blood.

Based on the results of Phase II/III clinical trial and the long-term, open-label extension data, the U.S. Food and Drug Administration (FDA) is conducting a priority review of Pharming's New Drug Application for leniolisib as a treatment for adolescents and adults with APDS and has an assigned Prescription Drug User Fee Act (PDUFA) goal date of March 29, 2023. In addition, Pharming's Marketing Authorisation Application (MAA) for leniolisib in the same patient population has been validated for evaluation under an accelerated assessment by the European Medicines Agency's (EMA) Committee for Medicinal Products for Human Use (CHMP). Marketing authorization for leniolisib in the European Union is anticipated in H1 2023.

About Activated Phosphoinositide 3-Kinase δ Syndrome (APDS)

APDS is a rare primary immunodeficiency that affects approximately 1 to 2 people per million. APDS is caused by variants in either of two genes, *PIK3CD* or *PIK3R1*, that regulate maturation of white blood cells. Variants of these genes lead to hyperactivity of the PI3Kδ (phosphoinositide 3-kinase delta) pathway.[2,3] Balanced signaling in the PI3Kδ pathway is essential for physiological immune function. When this pathway is hyperactive, immune cells fail to mature and function properly, leading to immunodeficiency and dysregulation.[2,4] APDS is characterized by severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy.[5,6] Because these symptoms can be associated with a variety of conditions, including other primary immunodeficiencies, people with APDS are frequently misdiagnosed and suffer a median 7-year diagnostic delay.[7] As APDS is a progressive disease, this delay may lead to an accumulation of damage over time, including permanent lung damage and lymphoma.[5-8] The only way to definitively diagnose this condition is through genetic testing.

About leniolisib

Leniolisib is a small-molecule inhibitor of the delta isoform of the 110 kDa catalytic subunit of class IA PI3K. PI3Kδ is expressed predominately in hematopoietic cells and is essential to normal immune system function through conversion of phosphatidylinositol-4-5-trisphosphate (PIP2) to phosphatidylinositol-3-4-5-trisphosphate (PIP3). Leniolisib inhibits the production of PIP3 and PIP3 serves as an important cellular messenger activating AKT (via PDK1) and regulates a multitude of cell functions such as proliferation, differentiation, cytokine production, cell survival, angiogenesis, and metabolism. Unlike PI3Kα and PI3Kβ, which are ubiquitously expressed, PI3Kδ and PI3Kγ are expressed primarily in cells of hematopoietic origin. The central role of PI3Kδ in regulating numerous cellular functions of the adaptive immune system (B-cells and, to a lesser extent, T cells) as well as the innate immune system (neutrophils, mast cells, and macrophages) strongly indicates that PI3Kδ is a valid and potentially effective therapeutic target for immune diseases such as APDS. To date, leniolisib has been well tolerated during both the Phase 1 first-in-human trial in healthy subjects and the Phase II/III registration-enabling study in patients with APDS.

About Pharming Group N.V.

Pharming Group N.V. (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) is a global biopharmaceutical company dedicated to transforming the lives of patients with rare, debilitating, and life-threatening diseases. Pharming is commercializing and developing an innovative portfolio

of protein replacement therapies and precision medicines, including small molecules, biologics, and gene therapies that are in early to late-stage development. Pharming is headquartered in Leiden, Netherlands, and has employees around the globe who serve patients in over 30 markets in North America, Europe, the Middle East, Africa, and Asia-Pacific.

For more information, visit www.pharming.com and find us on LinkedIn.

Forward-Looking Statements

This press release may contain forward-looking statements. Forward-looking statements are statements of future expectations that are based on management's current expectations and assumptions and involve known and unknown risks and uncertainties that could cause actual results, performance, or events to differ materially from those expressed or implied in these statements. These forward-looking statements are identified by their use of terms and phrases such as "aim", "ambition", "anticipate", "believe", "could", "estimate", "expect", "goals", "intend", "may", "milestones", "objectives", "outlook", "plan", "probably", "project", "risks", "schedule", "seek", "should", "target", "will" and similar terms and phrases. Examples of forward-looking statements may include statements with respect to timing and progress of Pharming's preclinical studies and clinical trials of its product candidates, Pharming's clinical and commercial prospects, and Pharming's expectations regarding its projected working capital requirements and cash resources, which statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to the scope, progress and expansion of Pharming's clinical trials and ramifications for the cost thereof; and clinical, scientific, regulatory and technical developments. In light of these risks and uncertainties, and other risks and uncertainties that are described in Pharming's 2021 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2021, filed with the U.S. Securities and Exchange Commission, the events and circumstances discussed in such forward-looking statements may not occur, and Pharming's actual results could differ materially and adversely from those anticipated or implied thereby. All forward-looking statements contained in this press release are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. Readers should not place undue reliance on forward-looking statements. Any forward-looking statements speak only as of the date of this press release and are based on information available to Pharming as of the date of this release. Pharming does not undertake any obligation to publicly update or revise any.

Inside Information

This press release relates to the disclosure of information that qualifies, or may have qualified, as inside information within the meaning of Article 7(1) of the EU Market Abuse Regulation.

References

1. Rao VK, et al. Blood. 2022. https://doi.org/10.1182/blood.2022018546.
2. Lucas CL, et al. Nat Immunol. 2014;15:88-97.
3. Elkaim E, et al. J Allergy Clin Immunol. 2016;138(1):210-218.
4. Nunes-Santos C, Uzel G, Rosenzweig SD. J Allergy Clin Immunol. 2019;143(5):1676-1687.
5. Coulter TI, et al. J Allergy Clin Immunol. 2017;139(2):597-606.

6. Maccari ME, et al. Front Immunol. 2018;9:543.
7. Jamee M, et al. Clin Rev Allergy Immunol. 2019;May 21.
8. Condliffe AM, Chandra A. Front Immunol. 2018;9:338.

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