Pharming announces positive results of Phase II/III pivotal clinical study of leniolisib for the treatment of activated PI3K delta syndrome

Study meets both co-primary endpoints

Global regulatory filings planned to begin in Q2-22

The company will hold an analyst conference call tomorrow, Thursday 3 February, at 14:00CET/08:00ET details for the call can be found on page 5 of this release

Leiden, The Netherlands, 02 February 2022: Pharming Group N.V. ("Pharming" or "the Company") (Euronext Amsterdam: PHARM/NASDAQ: PHAR) announces positive results from the pivotal Phase II/III blinded randomized, placebo-controlled registration-enabling study of leniolisib for the treatment of activated phosphoinositide 3-kinase delta (PI3Kδ) syndrome (APDS) also known as PASLI (p110δ-activating mutation causing senescent T cells, lymphadenopathy, and immunodeficiency).

APDS is an ultra-rare primary immunodeficiency disease caused by genetic mutations affecting approximately 1-2 people per million. Clinical hallmarks of the disease are significant lymphoproliferation and immune dysfunction, as well as increased risk of malignant lymphoma. Current treatment is generally limited to supportive therapies, such as antibiotics and the use of immunoglobulin replacement therapy, and there is no approved therapy for the treatment of the disease.

Leniolisib is a small molecule PI3Kδ inhibitor that was discovered and developed by Novartis and was licensed to Pharming in 2019. The study, sponsored by Novartis, is a Phase II/III registration-enabling study composed of two sequential parts, the first part was an open-label dose escalation study (results previously reported in Blood. 2017;130(21):2307-2316)

Part 2 of the study was a randomized, subject, investigator, and sponsor-blinded, placebo-controlled study, that enrolled 31 patients with APDS who were 12 years or older. Patients were randomized 2:1 to receive either leniolisib 70mg twice daily or placebo for 12 weeks. Following this, patients were permitted to rollover to an open-label extension study to evaluate long-term safety, tolerability, and efficacy. The co-primary endpoints of the randomized study were designed to evaluate reduction in lymph node size and correction of immunodeficiency.

The primary efficacy results demonstrated clinical efficacy of leniolisib over placebo with a statistically significant reduction from baseline in the log10 transformed sum of product of diameters (SPD) in the index lymphadenopathy lesions ($p=0.0012$) and normalization of immune dysfunction, as evidenced by increased proportion of naïve B cells from baseline ($p<0.0001$).

In the study, leniolisib was generally well-tolerated. The majority of reported adverse events in both treatment groups were classified as mild. There were no adverse events that led to discontinuation of study treatment, there were no deaths, and the incidence of serious adverse

events (SAEs) was lower in the leniolisib group than the placebo group. None of the SAEs were suspected to be related to study treatment.

Full results will be presented at upcoming medical conferences and published in a peer-reviewed journal.

Dr. Virgil Dalm, Principal Investigator, Erasmus University Medical Center Rotterdam, the Netherlands commented:

"These study results demonstrate the tremendous power of collaborative clinical research with scientists, clinicians, and patients working together with the pharmaceutical industry. Less than 10 years ago, researchers at the University of Cambridge and National Institutes of Health (NIH) described a genetic variant in the PIK3CD gene in patients leading to immune dysfunction and dysregulation due to overactive PI3Kinase pathway, giving the name APDS/PASLI to the condition.

These patients have limited treatment options including symptomatic therapies, such as antibiotics, antivirals and immunoglobulin replacement therapy (IgRT). Unapproved empirical therapies such as mTOR inhibitors, can have serious side effects, and the only potentially curative treatment, stem cell transplant, is also associated with high morbidity and mortality. Novartis working with doctors across the world studied leniolisib in APDS patients, which showed these positive results today.

I look forward to working with Pharming to bring leniolisib to APDS patients and studying it further in younger children, as well as other patient populations that may benefit from this precisely targeted therapy."

Global regulatory filings for approval of leniolisib for APDS are targeted for submission beginning in the second quarter of this year.

About Activated phosphoinositide 3-kinase δ syndrome (APDS)

APDS is an ultra-rare primary immunodeficiency disease that is caused by variants in either of two genes, PIK3CD or PIK3R1. Variants of these genes lead to hyperactivity of the PI3Kδ (phosphoinositide 3-kinase delta) pathway.[1,2] 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.[1,3] APDS is characterized by severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy.[4,5] Patients with APDS suffer a median 7-year diagnostic delay.[6] Because APDS is a progressive disease, this delay may lead to an accumulation of damage over time, including permanent lung damage and lymphoma.[4-7]

About leniolisib

Leniolisib is a small molecule inhibitor of the delta isoform of the 110 kDa catalytic subunit of class IA PI3K with immunomodulating and potentially anti-neoplastic activities. Leniolisib inhibits the production of phosphatidylinositol-3-4-5-trisphosphate (PIP3). PIP3 serves as an important cellular messenger specifically 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 (neutrophil, mast cells, and macrophages) strongly indicates that PI3Kδ is a valid and potentially effective therapeutic target for several immune diseases.

To date, leniolisib has proven to be safe and well tolerated during the Phase 1 first-in-human trial in healthy subjects, and in the 12-week dose-escalation study in APDS patients

About Pharming Group N.V.

Pharming Group N.V. is a global, commercial stage biopharmaceutical company developing innovative protein replacement therapies and precision medicines for the treatment of rare diseases and unmet medical needs.

The flagship of our portfolio is our recombinant human C1 esterase inhibitor (rhC1INH) franchise. C1INH is a naturally occurring protein that down regulates the complement and contact cascades in order to control inflammation in affected tissues.

Our lead product, RUCONEST®, is the first and only plasma-free rhC1INH protein replacement therapy. It is approved for the treatment of acute hereditary angioedema (HAE) attacks. We are commercializing RUCONEST® in the United States, the European Union and the United Kingdom through our own sales and marketing organization, and the rest of the world through our distribution network.

In addition, we are investigating the clinical efficacy of rhC1INH in the treatment of further indications, including pre-eclampsia, acute kidney injury and severe pneumonia as a result of COVID-19 infections.

We are also studying our oral precision medicine, leniolisib (a phosphoinositide 3-kinase delta, or PI3K delta, inhibitor), for the treatment of activated PI3K delta syndrome, or APDS. World-wide rights for leniolisib were licensed from Novartis AG in 2019. Leniolisib met both of its primary end points in a registration enabling Phase 2/3 study in the United States and Europe. We are targeting global regulatory filings for leniolisib from Q2 2022 onwards.

Additionally, we entered into a strategic collaboration with Orchard Therapeutics to research, develop, manufacture and commercialize OTL-105, a newly disclosed investigational ex-vivo autologous hematopoietic stem cell (HSC) gene therapy for the treatment of HAE.

Furthermore, we are leveraging our transgenic manufacturing technology to develop next-generation protein replacement therapies, most notably for Pompe disease, which is currently in preclinical development.

Forward-looking Statements

This press release contains forward-looking statements, including with respect to timing and progress of Pharming's preclinical studies and clinical trials of its product candidates, Pharming's clinical and commercial prospects, Pharming's ability to overcome the challenges posed by the COVID-19 pandemic to the conduct of its business, 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 2020 Annual Report and the Annual Report on Form 20-F for the year ended December 31, 2020 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. 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.

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.

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References:

1. Lucas CL, et al. Nat Immunol. 2014;15:88-97.
2. Elkaim E, et al. J Allergy Clin Immunol. 2016;138(1):210-218.
3. Nunes-Santos C, Uzel G, Rosenzweig SD. J Allergy Clin Immunol. 2019;143(5):1676-1687.
4. Coulter TI, et al. J Allergy Clin Immunol. 2017;139(2):597-606.
5. Maccari ME, et al. Front Immunol. 2018;9:543.
6. Jamee M, et al. Clin Rev Allergy Immunol. 2019;May 21.
7. Condliffe AM, Chandra A. Front Immunol. 2018;9:338.

Conference call dial in information

Thursday February 3, 2022 14:00CET/08:00ET

Please note, the company will only take questions from dial-in attendees.

Dial in details:

United Kingdom	0800 640 6441
United Kingdom (Local)	020 3936 2999
Netherlands (Local)	085 888 7233
United States	1 855 9796 654
United States (Local)	1 646 664 1960

Access code: 871929

Webcast link:

https://webcast.openbriefing.com/pharming-22/