



## Pharming Announces Positive Data from Phase II/III Leniolisib Trial Presented at Clinical Immunology Society 2022 Annual Meeting

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LEIDEN, Netherlands, April 1, 2022 /PRNewswire/ -- Pharming Group N.V. ("Pharming" or "the Company") (EURONEXT Amsterdam: PHARM/Nasdaq: PHAR) announces new data from the pivotal Phase II/III trial of leniolisib for the treatment of activated phosphoinositide 3-kinase delta (PI3K $\delta$ ) syndrome (APDS), a 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, shared the findings in a presentation at the [Clinical Immunology Society \(CIS\) 2022 Annual Meeting](#).



As announced on February 2, 2022, the multinational, triple-blind, placebo-controlled, randomized, Phase III portion of the clinical trial, conducted by Novartis, met its co-primary endpoints, which evaluated reduction in lymph node size and correction of immunodeficiency. The shrinking of lymphadenopathy lesions and increased proportion of naïve B cells are important in this population, as they indicate a reduction in APDS disease markers. Presented for the first time at CIS, the co-primary endpoints at day 85 after baseline demonstrated:

- In the index lymphadenopathy lesions, a statistically significant adjusted mean change in the log<sub>10</sub> transformed sum of product of diameters (SPD) of -0.30 among patients who received leniolisib compared with -0.06 among patients who received placebo (95% CI: -0.37, -0.11; p=0.0012).
- From a baseline level of <48%, an increase of 34.76% in the proportion of naïve B cells in patients who received leniolisib versus a -5.37% decrease in patients who received placebo (95% CI: 28.51, 51.75; p<0.0001).

The study drug was well-tolerated. 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 in the placebo group. None of the SAEs were suspected to be related to study treatment.

**Charlotte Cunningham-Rundles, M.D., Ph.D., David S. Gottesman Professor of Immunology at the Mount Sinai School of Medicine in New York, said:**

*"It is great news that leniolisib has achieved such positive results in this Phase III study in APDS. It is extremely encouraging to see that this medication is capable of targeting the cause of this difficult disease, both improving care and reducing patients' symptoms. Progress toward a treatment that is tailor-made for our patients with APDS is a milestone we have long awaited."*

Pharming plans to begin submitting global regulatory filings for leniolisib in the second quarter of 2022 and, subject to approval, launching the treatment in the U.S. in the first quarter of 2023 and starting a series of European launches in the second half of 2023.

**Anurag Relan, Chief Medical Officer of Pharming, commented:**

*"Pharming is delighted that leniolisib achieved significance in both co-primary endpoints and was well tolerated in these APDS patients, as the product's approval would address an unmet need for those with this rare disease, who currently rely on supportive therapies such as antibiotics and immunoglobulin replacement therapy. In addition to working closely with regulatory authorities across the globe to make leniolisib available to immunologists, hematologists, and their patients, we will continue to develop this treatment through our open-label extension study and two additional studies that will enroll children under the age of 12, as well as potentially extending the geographic reach of the product."*

### About Activated Phosphoinositide 3-Kinase $\delta$ Syndrome (APDS)

APDS is a rare primary immunodeficiency that affects approximately one to two people per million. Also known as PASLI, it 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 PI3K $\delta$  (phosphoinositide 3-kinase delta) pathway.<sup>1,2</sup> Balanced signaling in the PI3K $\delta$  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.<sup>1,3</sup> APDS is characterized by severe, recurrent sinopulmonary infections, lymphoproliferation, autoimmunity, and enteropathy.<sup>4,5</sup> 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.<sup>6</sup> As APDS is a progressive disease, this delay may lead to an accumulation of damage over time, including permanent lung damage and lymphoma.<sup>4-7</sup> 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 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 PI3K $\alpha$  and PI3K $\beta$ , which are ubiquitously expressed, PI3K $\delta$  and PI3K $\gamma$  are expressed primarily in cells of hematopoietic origin. The central role of PI3K $\delta$  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 PI3K $\delta$  is a valid and potentially effective therapeutic target for several immune diseases.

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.

#### **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. These 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.*

#### **References:**

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#### **For further public information, contact:**

Pharming Group, Leiden, The Netherlands

Sijmen de Vries, CEO: T: +31 71 524 7400

Susanne Embleton, Investor Relations Manager: T: +31 71 524 7400 E: [investor@pharming.com](mailto:investor@pharming.com)

FTI Consulting, London, UK

Victoria Foster Mitchell/Alex Shaw

T: +44 203 727 1000

FTI Consulting, USA

Jim Polson

T: +1 (312) 553-6730

LifeSpring Life Sciences Communication, Amsterdam, The Netherlands

Leon Melens

T: +31 6 53 81 64 27

E: [pharming@lifespring.nl](mailto:pharming@lifespring.nl)

