

Pharming acquires exclusive license to CDZ173, a late stage drug for the treatment of APDS

- CDZ173 is in a registration-enabling study for the treatment of APDS, an ultra-rare, debilitating disease with no approved treatment
- APDS is treated by immunologists; the main physicians treating HAE and therefore already addressed by Pharming
- Upfront payment will be \$20 million (€17.9 million)
- If approved, the drug is expected to reach the market in 2H 2021 or 1H 2022
- Pharming will hold a conference call at 15.00 CET/ 09.00 EST today: dial-in details can be found at the end of this announcement

Leiden, The Netherlands, 13 August 2019: Pharming Group N.V. (Euronext Amsterdam: PHARM) today announced it has entered into a development collaboration and license agreement with Novartis to develop and commercialize CDZ173, a small molecule phosphoinositide 3-kinase delta (PI3K δ) inhibitor being developed by Novartis to treat patients with Activated Phosphoinositide 3-kinase Delta Syndrome (“APDS”).

APDS is a primary immune deficiency caused by a mutation in the PIK3CD gene that increases activity of PI3K δ , a promoter of activity in the immune system. As a result of this over-activity, the cells involved in immune response can fail to be differentiated properly, which means that sufferers are unable to react well to infections, and can suffer early cell death. Patients frequently suffer a functional inability to fight off infections, as well as developing airway and other lesions and certain cancers. It is an ultra-rare disease with incidence rates across the world of approximately 1-2 per million. Importantly, there is a commercially available genetic test that can identify the patients who will benefit from CDZ173 making this program personalized medicine for these APDS patients and their family members who also have the mutation.

Novartis has completed all the preclinical and clinical work to date and will continue to run the ongoing registration-enabling trial and the ongoing open label extension study. Pharming will work alongside Novartis to complete enrollment of the ongoing trial. Upon approval, Pharming will commercialize CDZ173 through its existing commercial infrastructure in the US and Europe and look for ways to make the drug available in other markets worldwide.

Sijmen de Vries, Chief Executive of Pharming, said:

“This transaction represents a great milestone for Pharming. The license of CDZ173 is our first step towards building off the commercial success of Ruconest in HAE to grow and diversify our portfolio. We are very excited by the profile of this drug and the match between its mechanism of action and the disease pathology, and it is a perfect strategic fit for our existing medical and commercial infrastructure. This is a great example of solid science and deep disease understanding coming together to create a real and personalised treatment option for patients with no prospect of treatment. We are pleased to be joining Novartis in its commitment to these patients and we look forward to working alongside them to finish the development work on this drug.”

Under the terms of the agreement, Pharming will pay an upfront payment of \$20 million. Novartis is eligible to receive regulatory and commercial milestones and will also earn tiered, double digit royalties on net sales.

About CDZ173 (leniolisib)

CDZ173 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. CDZ173 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 α and PI3K β which are ubiquitously expressed, PI3K δ and PI3K γ are expressed primarily in cells that are hematopoietic origin. The central role of PI3K δ in regulating numerous function of cells 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 the PI3K δ is a valid and potentially effective therapeutic target for several immune diseases

CDZ173 is being studied in a registration-enabling Phase II/III trial which is currently enrolling patients in clinical sites in the US and Europe. To date, CDZ173 has proven to be safe and well tolerated in healthy subjects as well as the APDS patients during the P1, first in human trial and the ongoing open label extension trial.

About Activated Phosphoinositide 3-kinase Delta Syndrome (APDS)

Activated PI3K-delta syndrome is a disorder that impairs the immune system. Individuals with this condition often have low numbers of white blood cells (lymphopenia), particularly B cells and T cells. Normally, these cells recognize and attack foreign invaders, such as viruses and bacteria, to prevent infection. Beginning in childhood, people with APDS develop recurrent infections, particularly in the lungs, sinuses, and ears. Over time, recurrent respiratory tract infections can lead to a condition called bronchiectasis, which damages the passages leading from the windpipe to the lungs (bronchi) and can cause breathing problems. People with activated PI3K-delta syndrome may also have chronic active viral infections, commonly Epstein-Barr virus or cytomegalovirus infections. Sufferers also frequently develop lymphomas and other cancers.

APDS is a primary immune deficiency caused by a mutation in the PIK3CD gene that increases activity of phosphoinositide-3-kinase delta, a promoter of activity in the immune system. Such a mutation which increases the activity of a molecule rather than suppressing it is called a gain-of-function mutation. As a result of this over-activity, the B and T cells involved in immune response can fail to be differentiated properly, which means that sufferers are unable to recruit them to help react to infections, and can suffer early cell death. The effect can be seen in epithelial cells and nervous system cells as well as those regulating cell adhesion (such as airway mucosal layer cells). By selectively inhibiting the enzyme p110 δ which activates the gain-of-function mutation causing APDS, CDZ173 specifically targets the causative factor of APDS. For this reason, APDS is sometimes called “p110 delta activating mutation causing senescent T cells, lymphadenopathy, and immunodeficiency”, or PASLI.

Another possible feature of activated PI3K-delta syndrome is abnormal clumping of white blood cells. These clumps can lead to enlarged lymph nodes (lymphadenopathy), or the white blood cells can build up to form solid masses (nodular lymphoid hyperplasia), usually in the moist lining of the airways or intestines. While lymphadenopathy and nodular lymphoid hyperplasia are noncancerous (benign), activated PI3K-delta syndrome also increases the risk of developing a form of cancer called B-cell lymphoma.

About Pharming Group N.V.

Pharming is a specialty pharmaceutical company developing innovative products for the safe, effective treatment of rare diseases and unmet medical needs. Pharming's lead product, RUCONEST® (conestat alfa) is a recombinant human C1 esterase inhibitor approved for the treatment of acute Hereditary Angioedema ("HAE") attacks in patients in Europe, the US, Israel and South Korea. The product is available on a named-patient basis in other territories where it has not yet obtained marketing authorization.

RUCONEST® is distributed by Pharming in Austria, France, Germany, Luxembourg, the Netherlands, the United Kingdom and the United States of America. Pharming holds commercialisation rights in Algeria, Andorra, Bahrain, Belgium, Ireland, Jordan, Kuwait, Lebanon, Morocco, Oman, Portugal, Qatar, Syria, Spain, Switzerland, Tunisia, United Arab Emirates and Yemen. In some of these countries distribution is made in association with the HAEi Global Access Program (GAP).

RUCONEST® is distributed by Swedish Orphan Biovitrum AB (publ) (SS: SOBI) in the other EU countries, and in Azerbaijan, Belarus, Georgia, Iceland, Kazakhstan, Liechtenstein, Norway, Russia, Serbia and Ukraine.

RUCONEST® is distributed in Argentina, Colombia, Costa Rica, the Dominican Republic, Panama, and Venezuela by Cytobioteck, in South Korea by HyupJin Corporation and in Israel by Kamada.

RUCONEST® is also being examined for approval for the treatment of HAE in young children (2-13 years of age) and evaluated for various additional follow-on indications.

Pharming's technology platform includes a unique, GMP-compliant, validated process for the production of pure recombinant human proteins that has proven capable of producing industrial quantities of high quality recombinant human proteins in a more economical and less immunogenetic way compared with current cell-line based methods. Leads for enzyme replacement therapy ("ERT") for Pompe and Fabry's diseases are being optimized at present, with additional programs not involving ERT also being explored at an early stage at present.

Pharming has a long-term partnership with the China State Institute of Pharmaceutical Industry ("CSIPI"), a Sinopharm company, for joint global development of new products, starting with recombinant human Factor VIII for the treatment of Haemophilia A. Pre-clinical development and manufacturing will take place to global standards at CSIPI and are funded by CSIPI. Clinical development will be shared between the partners with each partner taking the costs for their territories under the partnership.

Additional information is available on the Pharming website: www.pharming.com

Forward-looking Statements

This press release of Pharming Group N.V. and its subsidiaries ("Pharming", the "Company" or the "Group") may contain forward-looking statements including without limitation those regarding Pharming's financial projections, market expectations, developments, partnerships, plans, strategies and capital expenditures.

The Company cautions that such forward-looking statements may involve certain risks and uncertainties, and actual results may differ. Risks and uncertainties include without limitation the effect of competitive, political and economic factors, legal claims, the Company's ability to protect intellectual property, fluctuations in exchange and interest rates, changes in taxation laws or rates, changes in legislation or accountancy practices and the Company's ability to identify, develop and successfully commercialise new products, markets or technologies.

As a result, the Company's actual performance, position and financial results and statements may differ materially from the plans, goals and expectations set forth in such forward-looking statements. The Company assumes no obligation to update any forward-looking statements or information, which should be taken as of their respective dates of issue, unless required by laws or regulations.

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