

## Pharming announces enrolment of first patient in multinational clinical trial for the treatment of COVID-19 with RUCONEST®

### Highlights:

- Clinical trial follows encouraging results from five patients with confirmed COVID-19 infections administered RUCONEST® to treat the related severe pneumonia
- First patient at the University Hospital Basel, Basel, Switzerland, with confirmed COVID-19 infection has been enrolled in a clinical trial to investigate the use of RUCONEST® to prevent severe SARS-CoV-2 infection in hospitalised patients with COVID-19
- Study to be extended to additional clinical centres in Switzerland, Mexico and Brazil
- Additional study in multiple centres in the US in final stages of preparation

*Leiden, The Netherlands, 10 August 2020:* Pharming Group N.V. (“Pharming” or “the Company”) (Euronext Amsterdam: PHARM) today announced that the first patient has been enrolled in a randomized, controlled, investigator-initiated clinical trial in up to 150 patients for the treatment with RUCONEST® (recombinant human C1 inhibitor) of patients with confirmed COVID-19 (SARS-CoV-2) infections hospitalised with related severe pneumonia at the University Hospital Basel in Basel, Switzerland.

In April 2020, Pharming reported encouraging results from a compassionate use programme at the University Hospital Basel, Switzerland, in which four male patients and one female patient (between 53-82 years of age) with COVID-19, suffering from related severe pneumonia, who did not improve despite standard treatment, including hydroxychloroquine and lopinavir/ritonavir, had been administered RUCONEST®. Following treatment, fever resolved in four of the five patients within 48 hours, and laboratory markers of inflammation decreased significantly (CRP, IL-6). Soon thereafter, four of the five patients were discharged from the hospital as fully recovered. One patient had increased oxygen requirement and was eventually transferred to the ICU for intubation but has also since made a full recovery.

Following these encouraging results, the Company, in partnership with treating physician Dr Michael Osthoff from the University Hospital of Basel, Switzerland, saw potential for a larger investigator-initiated, multinational, multicentre study to investigate the full extent of the role of RUCONEST® in the treatment of severe pneumonia related to a COVID-19 infection. If successful, the clinical trial could also lead to additional studies in patients suffering from other diseases with severe respiratory or other organ failure complications driven by activation of the complement system as part of a systemic hyperinflammatory syndrome, also known as a ‘cytokine storm’.

### RUCONEST® AND COVID-19

RUCONEST® is a recombinant C1 esterase inhibitor (C1INH) approved for the treatment of hereditary angioedema (HAE) in the EU and US. C1INH is a protein that naturally occurs in the human body. It regulates several inflammatory pathways in the body by inhibiting certain proteins that are part of the

human immune system. In diseases like HAE, deficiency of functional C1 inhibitor leads to excessive activation of the complement system and other immunological and haemostatic pathways, giving cause to angioedema attacks. In HAE, these attacks are characterised by acute and painful swellings of soft tissues. Administration of C1 inhibitor can normalise the low C1 INH levels and stop angioedema attacks.

Systemic hyperinflammation is a hallmark of more severe stages of COVID-19 leading to acute respiratory distress syndrome, mechanical ventilation and ultimately death. Treatment with RUCONEST® may; 1) dampen uncontrolled complement activation and collateral lung damage and 2) reduce capillary leakage and subsequent pulmonary edema by direct inhibition of the kallikrein-kinin system and 3) reduce the generation of microthrombi by inhibiting MASP-1 induced clot formation and factor XII amplified thrombo-inflammation.

C1 inhibitor is an acute phase reactant, meaning that the body naturally increases production during inflammatory conditions, such as infections. Despite this, a relative deficiency may occur and complement activation continues unchecked, often leading to a cytokine storm, a dangerous biochemical process that worsens the complications of COVID-19 infection, such as organ failure and death.

This clinical study in hospitalised patients with COVID-19 seeks to identify if the administration of additional C1 INH can control or stop the systemic hyperinflammation syndrome or cytokine storm. Once results from either an interim analysis or after all patients have been treated, headline data will be made publicly available.

**Prof. Bruno Giannetti, Pharming's Chief Medical Officer commented:**

*"COVID-19 has proven that there is a significant need for better understanding of how the immune system fights infections. We have learned that cytokine storms caused by complement system activation cannot be controlled by targeted anti-inflammatory therapies. Instead, broad anti-inflammatory agents are required to stop the activation of multiple inflammation pathways. RUCONEST®'s multiple interactions with key inflammation pathways therefore make it a promising candidate to prevent the severe complications observed in COVID-19 patients. This investigator-initiated clinical trial in partnership with Dr Michael Osthoff, will be important not only for the treatment of pneumonia as a result of COVID-19 infection, but will also provide key insight into the future treatment of complement system influenced diseases."*

**Dr Michael Osthoff, University Hospital Basel, Switzerland and the treating physician, said:**

*"After the encouraging results observed in five patients treated with RUCONEST® in our clinic, it is justified to investigate this drug and its unique mode of action of targeting several inflammatory cascades in a clinical trial with a large number of patients. We will gather precious information about efficacy, safety and appropriate dosing of the drug in the treatment and prevention of the severe complications of COVID-19. After a short period of remission, we observe a worrisome increase of new COVID-19 cases in Europe, whilst in a number of other countries the disease still spreads almost uninhibited. The need for a treatment of COVID-19 associated complications is more urgent than ever."*

## 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 attacks of angio-edema in patients with hereditary angioedema (HAE) in Europe; for adults, adolescents and children from two years of age, in the US, for adults and adolescents and in Israel and South Korea. The product is available on a named-patient basis in other territories where it has not yet obtained marketing authorisation.

RUCONEST® is commercialised by Pharming in the US and in Europe, and the Company holds all other commercialisation rights in other countries not specified below. In some of these other countries distribution is made in association with the HAEi Global Access Program (GAP). 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 evaluated for various additional indications. Pharming's technology platform includes a unique production process that has proven capable of producing industrial quantities of pure high quality recombinant human proteins in a more economical and less immunogenic way compared with current cell-line based methods.

Leads for enzyme replacement therapy ("ERT") for Pompe and Fabry's diseases are also being produced and optimised respectively at present.

Pharming has recently in-licensed leniolisib from Novartis, a small molecule and selective PI3K $\delta$  inhibitor, which is in a registrational study for activated PI3K-delta syndrome (APDS), a rare form of Primary Immunodeficiency.

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. Preclinical development and manufacturing will take place to global standards at CSIPI and its affiliates 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.

## Forward-looking Statements

*This press release of Pharming Group N.V. and its subsidiaries ("Pharming", the "Company") 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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