

Pharming announces initiation of clinical phase I/II pre-eclampsia study

Leiden, The Netherlands, 11 June 2019: Pharming Group N.V. (“Pharming” or “the Company”) (Euronext Amsterdam: PHARM) today announces that, following receipt of the Dutch investigating centre’s ethics committee approval, it is commencing a clinical study of the effects of its recombinant human C1 esterase inhibitor (rhC1INH), RUCONEST®, in patients with pre-eclampsia.

Sijmen de Vries, Chief Executive Officer of Pharming, commented:

“Our strong performance in 2018 and the first quarter of 2019 has enabled us to invest in future growth through the development of our pipeline. Today, following ethics committee approval, we are initiating our first pre-eclampsia study with RUCONEST®.”

The first part of the study will assess safety and tolerability in a small number of patients to confirm the safety profile of RUCONEST® before proceeding to a larger patient sample. The second part of the study will involve a wider group to assess preliminary efficacy parameters as well. The results will be combined and are expected to be available in the third quarter of 2020.

With no current approved therapies to treat pre-eclampsia, we look forward to treating the first patients in this study as we seek to address the very serious unmet patient need and improve the safety and outcomes of pregnant women and their unborn babies with this condition in the future.”

About pre-eclampsia

Pre-eclampsia (PE) is a life-threatening multisystem condition in pregnancies leading to increased maternal and neonatal mortality and morbidity. 50,000 maternal deaths during pregnancy per year around the world are recorded for patients who proceed to eclampsia, while many more are caused by long-term irreversible damage to organs caused by PE. Treatments include termination of pregnancy or premature birth. Even if born safely, over half of these newborns will suffer from growth restrictions, learning difficulties or moderate to severe disabilities. Almost 2.5 million cases of PE are reported annually, with rates running at between 1% and 17% of all pregnancies in various communities and countries. Premature delivery is presently the only solution for PE, and there are no approved therapies. This is not a viable option for early PE (from week 20 of pregnancy). The main goal of therapy is therefore to prolong a safe pregnancy for PE patients as long as possible to improve the chances of a good outcome from delivery.

Clinical trial design

In September 2018, Pharming filed a clinical trial application with the European Medicines Agency (EMA) to initiate the clinical development of RUCONEST® to treat and prevent pre-eclampsia (PE). As part of this process, the study was submitted to and has just been cleared by the first investigating centre’s ethics committee. A similar clinical trial application has been filed with the Therapeutic Goods Administration (TGA) in Australia where it is still subject to ethics committee clearance.

The first part of the study is an open label trial to investigate tolerability and safety of treatment with RUCONEST®. Very soon, Pharming will begin recruiting a small number of patients in this part of the study in mid- to late-stage symptomatic pre-eclampsia, where women at 27 weeks’ term or later may receive RUCONEST® from their first clear symptoms of PE for the remainder of their pregnancy. Patients will be constantly monitored to ensure their safety and that of the fetus.

To date, RUCONEST® has been used to treat HAE in approximately 50 pregnant HAE patients (up to 40 times during a single pregnancy), including during delivery, with no safety issue for either mother or baby detected at the time or since.

The second (open label, proof of concept) part of the study (following approval by the ethics committees) is planned to include 30 patients in total recruited between two centres, of which one is in the Netherlands and one in Australia. Patients with mild to moderate pre-eclamptic symptoms at 27 to 34 weeks of pregnancy will be selected. Patients will receive only those doses of RUCONEST® already known to be safe from the first part of the study. The second part of the study will also test RUCONEST® against (historical) documented standard-of-care results in similar patients. According to key opinion leaders in pre-eclampsia, every extra day closer to an on-term delivery can make an important difference for both mother and baby. The entire study is expected to last approximately one year, depending on the rate of recruitment and the early stage safety performance.

Scientific Rationale

The precise causes of pre-eclampsia are not known, but abnormal or impaired spiral artery modifications between the mother and the fetus are believed to be involved, as is the complement system which is triggered when these spiral arteries come under stress, especially oxidative stress because of poor blood flow. Emerging evidence has shown that activation of the complement system following such poor placentation is implicated in the pathological processes of PE.

C1 esterase inhibitor (C1INH) is a key component of the complement system and the only natural inhibitory mechanism of the system. Pregnant women and pre-eclamptic women have reduced circulating C1INH levels. Severely affected PE patients have significantly-reduced C1INH levels. It is therefore postulated that by supplying additional rhC1INH to such patients, it may be possible to slow the rate of progress of the condition and thereby reduce the level of damage that it can cause to mother and the unborn baby. The main goal of therapy is to prolong a safe pregnancy for PE patients as long as possible to improve the chances of a good outcome from delivery.

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 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 a clinical Phase I/II trial has been initiated for the treatment and prevention of pre-eclampsia.

RUCONEST® is also evaluated for various additional 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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