CHMP adopts positive opinion for treatment of acute angioedema attacks in children with hereditary angioedema with RUCONEST®

Pharming announces the Committee for Medicinal Products for Human Use (CHMP), an advisory committee of the European Medicine Agency (EMA), has adopted a positive opinion recommending an extension of the indication for RUCONEST® to the European Commission.

Highlights:

- Symptoms of HAE often present in childhood, and while attacks can occur at any age, early onset may predict a more severe disease course, which affects their development and ability to participate in daily life.
- Recommendation is based on a paediatric investigation plan (PIP) that includes a study in children.
- Pharming awaits the formal European Commission (EC) decision on the approval of this new RUCONEST® license extension in the European Union.

Leiden, the Netherlands, 27 March 2020: Pharming Group N.V. (Euronext Amsterdam: PHARM) today announced that the Committee for Medicinal Products for Human Use (CHMP) of the European Medicine Agency (EMA) has recommended approval of RUCONEST® (conestat alfa) for the treatment of acute angioedema attacks in children with hereditary angioedema (HAE). This marketing authorisation would expand the age range of Pharming's lead product, RUCONEST®, a recombinant analogue of the human C1 esterase inhibitor produced by recombinant DNA technology in the milk of transgenic rabbits. RUCONEST® was previously approved for adults and adolescents in Europe.

The positive opinion is based on the data from a Phase II clinical trial in 20 children. This recommendation will allow children aged 2 years and older to be treated with RUCONEST® for acute angioedema attacks. The European Commission's (EC) approval decision is expected in June 2020. In the European Union (EU), RUCONEST® has been approved for this indication in adults since 2010 and in adolescents since 2016.

HAE is a rare disease caused by a deficiency of the C1 esterase inhibitor protein and is characterised by spontaneous and recurrent episodes of swelling (edema attacks) of the skin in different parts of the body, as well as in the airways and internal organs. Edema of the throat, nose or tongue is particularly dangerous and potentially life-threatening and can lead to obstruction of the airway passages.

The C1 esterase inhibitor protein is required to control the 'complement' and 'contact' systems, collections of proteins in the blood that fight against infection and cause inflammation. Patients with low levels of this protein have excessive activity of these two systems, which leads to the symptoms of angioedema. The active substance in RUCONEST®, conestat alfa, is a copy of the C1 esterase inhibitor protein and works in the same way as the natural human protein. When it is given during an angioedema attack, RUCONEST® stops this excessive activity, helping to relieve the patient's symptoms.

Earlier in January 2020 Pharming already received the European Medicines Agency (EMA) approval for a new facility. Together with this extension of the indication, Pharming believes that supply of RUCONEST® to the market is now further strengthened. RUCONEST® will be available for use in

children patients later in 2020 throughout Member States of the EU, as well the European Economic Area (EEA) in which Pharming currently has a license in the adult and adolescent population.

Sijmen de Vries, Chief Executive of Pharming, said:
"As we continue to see increasing demand for RUCONEST® in the treatment of hereditary angioedema, we are pleased to announce this step forward in this paediatric label expansion. This will enable us to treat attacks of patients of all ages living with HAE in the EU. In addition, as a result of our recent re-acquisition of RUCONEST® 's European distribution rights from Sobi, this extension of the indication will allow us to reach an even greater number of EU patients."

Paediatric study results

The open-label, single arm, Phase II clinical trial was designed in agreement with the EMA as part of a Paediatric Investigation Plan (PIP) to assess the pharmacokinetic, safety and efficacy profiles of RUCONEST® at a dose of 50 U/kg in HAE patients aged 2-13 years in support of the indication for treatment of HAE attacks in children.

A total of 20 children with HAE were treated for 73 HAE attacks at a dose of 50 U/kg (up to a maximum of 4200 U). The study reported clinically meaningful relief of symptoms assessed using a visual analogue scale (VAS) completed by the patient (assisted by their parent). The median time to onset of relief was 60 minutes (95% confidence interval: 60-653), and the median time to minimal symptoms was 123 minutes (95% confidence interval: 120-126). Only 3/73 (4%) attacks were treated with a second dose of RUCONEST®.

RUCONEST® was generally safe and well-tolerated in the study. No patients withdrew from the study due to adverse events. There were no related serious adverse events, hypersensitivity reactions, or neutralising antibodies detected.

About HAE

Hereditary Angioedema (HAE) is a rare genetic disorder. The condition is caused by a deficiency of the C1 esterase inhibitor protein, which is normally present in blood and helps control inflammation (swelling) and parts of the immune system. Because defective C1-Inhibitor does not adequately perform its regulatory function, a biochemical imbalance can occur and produce unwanted peptides that induce the capillaries to release fluids into surrounding tissue, thereby causing swelling or edema.

HAE is characterised by spontaneous and recurrent episodes of swelling (edema attacks) of the skin in different parts of the body, as well as in the airways and internal organs. Edema of the skin usually affects the extremities, the face, and the genitals. Patients suffering from this kind of edema often withdraw from their social lives because of the disfiguration, discomfort and pain these symptoms may cause. Almost all HAE patients suffer from bouts of severe abdominal pain, nausea, vomiting and diarrhoea caused by swelling of the intestinal wall.

Edema of the throat, nose or tongue is particularly dangerous and potentially life-threatening and can lead to obstruction of the airway passages. Although there is currently no known cure for HAE, it is possible to treat the symptoms associated with angioedema attacks. HAE affects about 1 in 10,000 to 1 in 50,000 people worldwide. Experts believe that a lot of patients are still seeking the right diagnosis: although HAE is (in principle) easy to diagnose, it is frequently identified very late or not discovered at all. The reason HAE is often misdiagnosed is because the symptoms are similar to those

of many other common conditions such as allergies or appendicitis. By the time it is diagnosed correctly, the patient has often been through a long-lasting ordeal.

About RUCONEST®

RUCONEST® (recombinant C1 esterase inhibitor) is indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE).

RUCONEST® contains C1 esterase inhibitor at 50 U/kg. When administered at the onset of HAE attack symptoms at the recommended dose, RUCONEST® may help to return a patient's C1 esterase inhibitor levels to normal range and relieve the symptoms of an HAE attack with a low recurrence of symptoms within 24 hours.

The most common side effect of RUCONEST® (seen in between 1 and 10 patients in 100) is headache. For the full list of all side effects reported with RUCONEST®, see the package leaflet. RUCONEST® must not be used in patients with known or suspected allergy to rabbits. For the full list of restrictions, see the package leaflet.

RUCONEST® is the only recombinant C1 esterase inhibitor worldwide. RUCONEST® is approved by the US Food and Drug Administration (FDA) for the treatment of acute attacks in adult and adolescent patients with HAE since July 2014.

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 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 PI3Kδ 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.

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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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