

## Pharming reports favourable conclusion from first investigator-initiated direct comparative real-world study of acute hereditary angioedema therapies

**Treatment with recombinant therapy RUCONEST® and plasma-derived C1 treatments requires significantly less re-dosing than icatibant (Firazyr®) to resolve HAE attacks**

**Leiden, The Netherlands, 7 December 2018:** Pharming Group N.V. (“Pharming” or “the Company”) (Euronext Amsterdam: PHARM) today acknowledged presentation of the results from an investigator-initiated comparative study of therapies in acute attacks of hereditary angioedema (“HAE”). The study examined and compared re-dosing rates *inter alia* for human C1 esterase inhibitor in recombinant form (Ruconest®) and plasma-derived forms (Berinert®, Cinryze®) to icatibant (Firazyr®) in seven individual patients at risk of HAE attacks. A total of 69 attacks were recorded. The study was led by Professor Dr Marcus Magerl of the Department of Dermatology and Allergy at the Charité Universitätsmedizin Berlin, Berlin, Germany. The main outcome of the study was that treatment with recombinant therapy RUCONEST® and plasma-derived C1 treatments requires significantly less re-dosing than icatibant (Firazyr®) to resolve HAE attacks.

There were 69 initial attacks in total across all seven patients. In this real-world study, the patients were able to choose the treatment for their attack. Following initial intervention, some patients needed to treat their attacks with a second dose or subsequent treatments to try to resolve the attack. The choice of the subsequent re-treatments was also decided by the patient. The majority of the attacks were classified as mild (67%), with 27% moderate and 6% severe.

Patients treated their attack initially with either *Berinert®* (five attacks) or *Cinryze®* (17 attacks), both plasma-derived C1 esterase inhibitors (“pdC1INH”), or *Firazyr®* (25 attacks) (icatibant, a small molecule bradykinin inhibitor, “icatibant”), or Pharming’s *RUCONEST®* (20 attacks), a recombinant human C1 esterase inhibitor (“rhC1INH”).

### Results

In the study, RUCONEST® showed 100% efficacy with first dose at appropriate clinical levels. In two cases, additional therapy was applied because of initial underdosing of the first treatment. Cinryze® and Berinert® also showed good results.

The main difference, however, was shown in those patients who selected Firazyr® as their first line therapy. These patients recorded re-dosing rates that were higher than controlled clinical studies have indicated before..

Of the 25 attacks treated with Firazyr® as a first line therapy, 11 (44%) failed on the first dose. In eight of those 11 failed therapy situations (72%), the patient took a second dose of Firazyr® to try to end the attack. In the other three cases, the patients took a C1 esterase inhibitor (two taking Berinert®, and one RUCONEST®).

All of the patients who took a C1 esterase inhibitor reported the attack resolved, whereas in a further five of the eight Firazyr® treatments patients had to take a third dose of medication to try to resolve the attack. Where either Ruconest® (two) or Berinert® (one) were used as the third treatment of the

attack, it was again resolved, whereas one out of two attacks re-treated with Firazyr® required a fourth dose of Firazyr® for the attack to be resolved.

Initial Treatment	Resolved on first dose	%	Failed (required second treatment)	%	Failed (required third treatment)	%	Failed (required fourth treatment)	%
Beriner <sup>®</sup> (6)	6	100.0	-	-			-	
Cinryze <sup>®</sup> (18)	17	94.4	1	11.1			-	
Firazyr <sup>®</sup> (25)	14	56.0	11	44.0	5 (of 8)	62.5	1 (of 2)	50.0
Ruconest <sup>®</sup> (20)	18	90.0	2*	10.0*			-	
<b>Total</b>	<b>55</b>		<b>14</b>		<b>5</b>		<b>1</b>	

\*Underdosed: Only one vial administered and not the prescribed dose of 50U/kg

Note: The percentages show the failure rate within the drug noted, so that for example 5 out of 8 patients who sought to resolve their attacks with a second dose of Firazyr® needed a third treatment.

Further data regarding reasons for drug selection and subjective observations on the performance of the drugs in each attack are being analysed and the full results of the study will be published by the investigators in due course.

#### Dr Bruno Giannetti, Chief Operations Officer of Pharming, said:

“This was a well-run independent investigator-led comparative study under real world conditions, which gives a clear signal confirming reports from patients: Treatment with adequate doses of C1 esterase inhibitor is an excellent therapy to minimize and end an acute HAE attack. It also confirms that re-dosing with icatibant is often needed to successfully treat an attack. In fact, this study reports failure rates for treatment with icatibant of 44% for the first dose and 62% for the second dose, with one of the patients needing to take four doses to stop one attack.”

#### About HAE

Hereditary Angioedema (HAE) is a rare genetic disorder. It is characterized 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 diarrhea caused by swelling of the intestinal wall.

Edema of the throat, nose or tongue can be particularly dangerous as this can lead to obstruction of the airway passages and be potentially life threatening. Although there is currently no known cure for HAE, it is possible to treat the symptoms associated with edema 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 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 Cytobiotech, 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](http://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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