# PHARMING AND SALIX ANNOUNCE FIRST PATIENT TREATED IN CLINICAL STUDY OF RUCONEST® FOR PROPHYLAXIS OF HEREDITARY ANGIOEDEMA

**LEIDEN, THE NETHERLANDS, RALEIGH, NC, 08 January 2015** - Pharming Group NV (EURONEXT: PHARM) and Salix Pharmaceuticals, Ltd. (NASDAQ:SLXP) today announced that the first patient was treated in their Phase 2 clinical study of Ruconest®, (C1 Esterase Inhibitor [Recombinant]) 50 IU/kg, for prophylaxis in patients with hereditary angioedema (HAE).

HAE patients deficient in C1 inhibitor and with a history of at least four attacks per month are being enrolled in the randomized, double-blind study, in which 30 patients will receive Ruconest® either once or twice weekly, or placebo in each of 3 treatment periods. With the crossover design, all patients will receive each of the dosing regimens. The study will evaluate the safety and efficacy of Ruconest® when used for prophylaxis of angioedema attacks in patients with HAE.

The study will be conducted at sites in Canada, Europe, Israel, and the United States. The trial is being coordinated by principal investigators, Dr. Marco Cicardi, Professor at the University of Milan, and Dr. Marc Riedl, Associate Professor and Clinical Director of the US HAEA Angioedema Center at the University of California, San Diego.

"We are pleased to have quickly initiated the treatment phase of this important study, and look forward to its completion later in 2015," said Bruno Giannetti, MD PhD, Chief Operating Officer of Pharming.

Under the terms of the Pharming-Salix license agreement, the companies will equally share the development costs for Ruconest® for HAE prophylaxis. Pharming will receive an undisclosed milestone payment from Salix as and when FDA approval for this additional indication is given.

#### Important Safety Information for RUCONEST

#### Indication:

RUCONEST® is a C1 esterase inhibitor [recombinant] indicated for the treatment of acute attacks in adult and adolescent patients with hereditary angioedema (HAE). Effectiveness in clinical studies was not established in HAE patients with laryngeal attacks.

RUCONEST® (C1 esterase inhibitor [recombinant]) is contraindicated in patients with a history of allergy to rabbits or rabbit-derived products, and patients with a history of life-threatening immediate hypersensitivity reactions to C1 esterase inhibitor preparations, including anaphylaxis.

Severe hypersensitivity reactions may occur. The signs and symptoms of hypersensitivity reactions may include hives, generalized urticaria, tightness of the chest, wheezing, hypotension, and/or anaphylaxis during or after injection of RUCONEST. Should symptoms occur, discontinue RUCONEST and administer appropriate treatment. Because hypersensitivity reactions may have symptoms similar to HAE attacks, treatment methods should be carefully considered.

Serious arterial and venous thromboembolic (TE) events have been reported at the recommended dose of plasma derived C1 esterase inhibitor products in patients with risk factors. Risk factors may include the presence of an indwelling venous catheter/access device, prior history of thrombosis, underlying atherosclerosis, use of oral contraceptives or certain androgens, morbid obesity, and immobility. Monitor patients with known risk factors for TE events during and after RUCONEST administration.



RUCONEST has not been studied in pregnant women; therefore, it should only be used during pregnancy if clearly needed.

The most common adverse reactions (incidence ≥2%) were headache, nausea, and diarrhea. The serious adverse reaction in clinical studies of RUCONEST was anaphylaxis.

Please see complete Prescribing Information for RUCONEST.

#### **About RUCONEST®**

RUCONEST® (C1 Esterase Inhibitor [Recombinant]) 50 IU/kg is an injectable medicine that is used to treat acute angioedema attacks in adult and adolescent patients with hereditary angioedema (HAE). HAE is caused by a deficiency of the C1 esterase inhibitor protein, which is present in blood and helps control inflammation (swelling) and parts of the immune system. A shortage of C1 esterase inhibitor can lead to repeated attacks of swelling, pain in the abdomen, difficulty breathing and other symptoms. RUCONEST® contains C1 esterase inhibitor at 50 IU/kg.

When administered at the onset of HAE attack symptoms at the recommended dose, RUCONEST works to return a patient's C1-INH levels to normal range and quickly begins to relieve the symptoms of an HAE attack with a low recurrence of symptoms.

RUCONEST is the first and only plasma-free, recombinant C1-INH approval from the U.S. Food and Drug Administration (FDA) and was approved in July 2014.

RUCONEST has been granted Orphan Drug designation by the FDA for the treatment of acute angioedema attacks in patients with hereditary angioedema (HAE). With RUCONEST now approved by the FDA, Salix believes this designation should provide seven years of marketing exclusivity in the United States.

#### **About HAE**

Hereditary angioedema (HAE) is a genetic condition occurring between 1 in 10,000 to 1 in 50,000 people. Those with HAE experience episodes of swelling in their extremities, face and abdomen, with potentially life-threatening swelling of the airway. When it occurs in the abdomen, this swelling can be accompanied by bouts of nausea, vomiting and severe pain. Swelling in the face or extremities can be painful, disfiguring, and disabling.

HAE patients have a defect in the gene that controls production of a protein found in the blood vessels, called C1 inhibitor or C1-INH. When a person's C1-INH levels are low, fluid from blood vessels can leak into nearby connective tissues, causing severe pain and swelling and, in rare cases, death from asphyxiation from airway swelling.

#### **About Pharming Group NV**

Pharming Group NV is developing innovative products for the treatment of unmet medical needs. Ruconest® (conestat alfa) is a recombinant human C1 esterase inhibitor approved for the treatment of angioedema attacks in patients with HAE in the USA, Israel, all 27 EU countries plus Norway, Iceland and Liechtenstein.

Ruconest is commercialized by Pharming in Austria, Germany and Netherlands.

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 partnered with Salix Pharmaceuticals Inc. (NASDAQ: SLXP) in North America.

## **PHARMING**

Ruconest is also being investigated in a randomized Phase II clinical trial for prophylaxis of HAE and evaluated for various additional follow-on indications.

Pharming has a unique GMP compliant, validated platform for the production of recombinant human proteins that has proven capable of producing industrial volumes of high quality recombinant human protein in a more economical way compared to current cell based technologies. Leads for enzyme replacement therapy in Pompe's, Fabry's and Gaucher's diseases are under early evaluation. The platform is partnered with Shanghai Institute for Pharmaceutical Industry (SIPI), a Sinopharm Company, for joint global development of new products. Pre- clinical development and manufacturing will take place at SIPI and are funded by SIPI. Pharming and SIPI initially plan to utilize this platform for the development of rh-FVIII for the treatment of Haemophilia-A. Additional information is available on the Pharming website; www.pharming.com.

#### **About Salix Pharmaceuticals**

Salix Pharmaceuticals, Ltd., headquartered in Raleigh, North Carolina, develops and markets prescription pharmaceutical products and medical devices for the prevention and treatment of gastrointestinal diseases. Salix's strategy is to in-license late-stage or marketed proprietary therapeutic products, complete any required development and regulatory submission of these products, and commercialize them through the Company's 500-member specialty sales force.

Salix trades on the NASDAQ Global Select Market under the ticker symbol "SLXP". For more information, please visit our website at <a href="https://www.salix.com">www.salix.com</a> or contact Salix at 919-862-1000. Follow us on Twitter (@SalixPharma) and Facebook (<a href="https://www.facebook.com/SalixPharma">www.salix.com</a> or contact Salix at 919-862-1000. Follow us on Twitter feed, Facebook page and website is not incorporated in our filings with the SEC.

#### Salix Disclosure Notice

Please Note: The statements provided herein that are not historical facts are or might constitute projections and other forward-looking statements regarding future events. Although we believe the expectations reflected in such forward-looking statements are based on reasonable assumptions, our expectations might not be attained. Forward-looking statements are just predictions and are subject to known and unknown risks and uncertainties that could cause actual events or results to differ materially from expected results. Factors that could cause actual events or results to differ materially from those described herein include, among others: uncertainty that Ruconest will be commercially successful; market acceptance for approved products; generic and other competition in an increasingly global industry; litigation and the possible impairment of, or inability to obtain, intellectual property rights and the costs of obtaining such rights from third parties in an increasingly global industry; the unpredictability of the duration and results of regulatory review of New Drug Applications, Biologics License Agreements and Investigational NDAs, including risk that XIFAXAN (rifaximin) 550 mg will not receive the necessary regulatory approvals for Irritable Bowel Syndrome with Diarrhea; the cost, timing and results of clinical trials and other development activities involving pharmaceutical products; post-marketing approval regulation, including the ongoing Department of Justice investigation of Salix's marketing practices; revenue recognition and other critical accounting policies; the need to acquire new products; changes in tax laws or interpretations thereof; general economic and business conditions; and other factors. Readers are cautioned not to place undue reliance on the forward-looking statements included herein, which speak only as of the date hereof. Salix does not undertake to update any of these statements in light of new information or future events, except as required by law. The reader is referred to the documents that Salix files from time to time with the SEC.

# **PHARMING**

### Pharming Disclosure Notice

This press release contains forward looking statements that involve known and unknown risks, uncertainties and other factors, which may cause the actual results, performance or achievements of the Company to be materially different from the results, performance or achievements expressed or implied by these forward looking statements.

#### **Contacts:**

## **Pharming Group NV**

Sijmen de Vries Chief Executive Officer +31 71 5247400 Julia Phillips/ Victoria Foster Mitchell FTI Consulting +44 203 727 1136

#### Salix Pharmaceuticals

Timothy J. Creech Senior Vice President Finance & Administrative Services and Acting Chief Financial Officer +1 919-862-1000 G. Michael Freeman Associate Vice President, Investor Relations and Corporate Communications

+1 919-862-1000