



# PHARMING

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## **SANTARUS AND PHARMING ANNOUNCE POSITIVE TOP-LINE PHASE III RESULTS FOR RUCONEST IN ACUTE HEREDITARY ANGIOEDEMA**

### **Statistically significant results for primary endpoint of time to beginning of symptom relief**

**SAN DIEGO and LEIDEN, The Netherlands (November 7, 2012)** – [Santarus, Inc.](#) (NASDAQ: SNTS) and [Pharming Group NV](#) (NYSE Euronext: PHARM) today announced that their pivotal Phase III clinical study to evaluate the safety and efficacy of the investigational drug RUCONEST® (recombinant human C1 esterase inhibitor) 50 U/kg for the treatment of acute attacks of angioedema in patients with Hereditary Angioedema (HAE) met the primary endpoint of time to beginning of symptom relief.

A statistically significant difference in the time to beginning of symptom relief was observed in the intent-to-treat population (n=75) between RUCONEST and placebo (p=0.031, log-rank test); the median time to beginning of symptom relief was 90 minutes for RUCONEST patients (n=44) and 152 minutes for placebo patients (n=31). The time to beginning of symptom relief was defined as the time from the beginning of infusion of study medication (RUCONEST or placebo) until the beginning of a persistent beneficial effect, based on the patient's responses to a Treatment Effect Questionnaire for the primary attack location.

RUCONEST was generally well tolerated in this Phase III clinical study and the frequency of patients experiencing at least one treatment emergent adverse event in the RUCONEST treated group was less than in the placebo group. Within 72 hours of the completion of infusion of study medication, four RUCONEST patients (7%) experienced six adverse events: sneezing, procedural headache, back pain, skin burning sensation, an increase in fibrin D-dimer and lipoma. Within the 72 hour period four placebo patients (22%) experienced four adverse events: sinus congestion, vasomotor rhinitis, diarrhea and dyspepsia. Thromboembolic events, anaphylaxis, or neutralizing antibodies to C1 inhibitor were not observed in any patient. There was one patient in the RUCONEST group that experienced a serious adverse event (abdominal hernia at Day 79) that was assessed by the investigator as not related to the study drug.

“These positive results are consistent with the efficacy data previously reported from two smaller randomized, controlled clinical studies with RUCONEST in patients with HAE, and we believe the results provide strong

support for our proposed dosing regimen of 50 U/kg in treating acute attacks of HAE,” said Wendell Wierenga, Ph.D., executive vice president of research and development of Santarus.

“We are very pleased with these pivotal study results and look forward to working with our colleagues at Santarus to prepare and submit the Biologics License Application (BLA) for RUCONEST to the FDA in the first half of 2013,” said Bruno Giannetti, M.D., Ph.D., chief operations officer of Pharming. “We anticipate that additional data from this Phase III study will be presented at an appropriate medical meeting in 2013.”

Santarus licensed exclusive rights to commercialize RUCONEST in North America for the treatment of acute attacks of HAE as well as other potential future indications from Pharming. Under the terms of the license agreement, a \$10 million milestone is now payable to Pharming as a result of the successful achievement of the primary endpoint of the Phase III clinical study. An additional \$5 million milestone will be payable to Pharming upon U.S. Food and Drug Administration (FDA) acceptance of the BLA for review.

#### RUCONEST Phase III Clinical Study (Study 1310)

Pharming conducted Study 1310 with RUCONEST under a Special Protocol Assessment (SPA) agreement with the FDA, and the study is intended to support the submission of a BLA in the U.S.

- In Study 1310, RUCONEST was evaluated for the treatment of acute attacks of angioedema in patients with HAE in an international, multicenter, randomized, placebo-controlled Phase III study comparing a single IV infusion of 50 U/kg of RUCONEST to a saline control with a primary endpoint of time to beginning of symptom relief.
- The time to beginning of symptom relief was defined as the time lapsed from the beginning of the infusion of study medication to the beginning of a persistent beneficial effect based on the patient’s responses to a Treatment Effect Questionnaire for the primary attack location.
- A 90 day follow-up period was required for each patient enrolled, or until such time that the patient required open-label treatment for a subsequent attack during the 90 day period. The data from the open-label extension are being collected for additional efficacy and safety analyses.
- The study enrolled a total of 75 patients who were randomized 3:2 to receive either RUCONEST or saline.

#### About RUCONEST and Hereditary Angioedema

RUCONEST (INN conestat alfa) is a recombinant version of the human protein C1 esterase inhibitor, and is produced with Pharming’s proprietary technology which uses milk from transgenic rabbits. RUCONEST is approved in Europe for the treatment of acute angioedema attacks in patients with HAE, a genetic disorder in which the patient is deficient in or lacks a functional plasma protein C1 esterase inhibitor, resulting in unpredictable and debilitating episodes of intense swelling. The swelling may occur in one or more anatomical areas, including the extremities, face, trunk, genitals, abdomen and upper airway. The frequency and severity of HAE attacks vary and are most serious when they involve laryngeal edema, which can close the upper airway and cause death by asphyxiation. According to the U.S. Hereditary Angioedema Association, epidemiological estimates for HAE range from one in 10,000 to one in 50,000 individuals. RUCONEST is an investigational drug in the U.S. and has been granted orphan drug designation by the FDA both for the treatment of acute attacks of HAE and for prophylactic treatment of HAE.

#### About Pharming Group NV

Pharming Group NV develops innovative products for the treatment of unmet medical needs. RUCONEST® is a recombinant human C1 esterase inhibitor approved for the treatment of angioedema attacks in patients with HAE in all 27 EU countries plus Norway, Iceland and Liechtenstein, and is distributed in the EU by Swedish Orphan Biovitrum (OMX: SOBI). The product is also being evaluated for various follow-on indications. Pharming's advanced technologies include innovative and validated platforms for the production of protein therapeutics, technology and processes for the purification and formulation of these products. A feasibility study, using the validated transgenic rabbit platform, aimed at the development of recombinant Factor VIII for the treatment of Haemophilia A is underway with partner, Renova Life, Inc. Additional information is available on the Pharming website, [www.pharming.com](http://www.pharming.com).

## About Santarus

Santarus, Inc. is a specialty biopharmaceutical company focused on acquiring, developing and commercializing proprietary products that address the needs of patients treated by physician specialists. The company's current commercial efforts are focused on [GLUMETZA®](#) (metformin hydrochloride extended release tablets) and [CYCLOSET®](#) (bromocriptine mesylate) tablets, which are indicated as adjuncts to diet and exercise to improve glycemic control in adults with type 2 diabetes, and on [FENOGLIDE®](#) (fenofibrate) tablets, which is indicated as an adjunct to diet to reduce high cholesterol. Santarus also sells ZEGERID® (omeprazole/sodium bicarbonate), which is indicated for the treatment of certain gastrointestinal diseases and disorders.

Santarus has a diverse product development pipeline. A New Drug Application for UCERIS™ (budesonide) for induction of remission of active mild to moderate ulcerative colitis is under review by the U.S. Food and Drug Administration with a response expected in January 2013. The pipeline also includes two late-stage investigational drugs in Phase III clinical studies: RUCONEST® (recombinant human C1 esterase inhibitor) for treatment of acute attacks of hereditary angioedema and rifamycin SV MMX® for treatment of travelers' diarrhea. In addition, the company's investigational monoclonal antibody, SAN-300, is being evaluated in a Phase I clinical program. More information about Santarus is available at [www.santarus.com](http://www.santarus.com).

*Santarus and Pharming caution you that statements included in this press release that are not a description of historical facts are forward-looking statements. The inclusion of forward-looking statements should not be regarded as a representation by Santarus or Pharming that any of its plans or objectives will be achieved. Actual results may differ materially from those set forth in this release due to the risks and uncertainties inherent in Santarus and Pharming's businesses, including, without limitation: risks related to the timing for submission of the BLA and whether the FDA will accept the BLA for review following submission and ultimately approve it; whether the FDA will concur with the clinical interpretation of the Phase III study results or the conduct of the study; whether the FDA ultimately will require additional clinical studies or other development programs before accepting the RUCONEST BLA or approving RUCONEST; risks related to Santarus' dependence on Pharming for many functions related to RUCONEST, and Pharming's ability to continue to perform these functions based on its limited financial resources; risks related to the license and supply arrangements between Santarus and Pharming, including the potential for termination of the arrangements; other difficulties or delays in development, testing, manufacturing and marketing of, and obtaining and maintaining regulatory approvals for, Santarus' and Pharming's products; and other risks detailed in prior press releases as well as in public periodic filings with the Securities and Exchange Commission.*

*You are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof. All forward-looking statements are qualified in their entirety by this cautionary statement and neither Santarus nor Pharming undertakes any obligation to revise or update this news release to reflect events or circumstances after the date hereof. This caution is made under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995.*

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