



## **ViroPharma and Halozyme Announce Positive Data of Subcutaneous Cinryze® (C1 esterase inhibitor [human]) with Recombinant Human Hyaluronidase (rHuPH20)**

### **- Data Presented at the 2012 Annual Meeting of the American Academy of Allergy Asthma & Immunology (AAAAI) -**

ORLANDO, Fla., March 6, 2012 /PRNewswire/ -- ViroPharma Incorporated (NASDAQ: VPHM) and Halozyme Therapeutics (Nasdaq: HALO) today announced the presentation of positive data from ViroPharma's Phase 2 subcutaneous trial of Cinryze® (C1 esterase inhibitor [human]) in combination with Halozyme's Enhance™ technology, a proprietary drug delivery platform using Halozyme's recombinant human hyaluronidase enzyme (rHuPH20), in patients with hereditary angioedema (HAE), a rare, debilitating and potentially fatal genetic disease. The presentation occurred as part of the late-breaker session at the 2012 annual meeting of the American Academy of Allergy Asthma & Immunology (AAAAI), held March 2 to 6, 2012 in Orlando, Fla. According to the presenters, these data demonstrate that subcutaneous co-administration of Cinryze with rHuPH20 was easy to administer, well tolerated and resulted in sustained physiologically relevant C1 INH functional concentrations. The presenters concluded that this innovative combination administered subcutaneously as a single injection will be further evaluated for the prevention of HAE attacks.

Cinryze is approved in the United States as intravenous (IV) administration for routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE, and in Europe for routine prevention, pre-procedure prevention and acute treatment of angioedema attacks in adolescent and adult patients with HAE.

In poster #5208 entitled, 'Safety, Pharmacokinetics (PK), and Pharmacodynamics (PD) of Subcutaneous (SC) Cinryze® (C1 inhibitor (C1 INH) with Recombinant Human Hyaluronidase (rHuPH20) in Subjects with Hereditary Angioedema (HAE),' Jennifer Schranz, M.D., ViroPharma's vice president of clinical research, and colleagues discussed key study results.

- Cinryze with rHuPH20 was well tolerated with no serious adverse events (SAEs), and no adverse events (AEs) led to study drug discontinuation:
  - No subjects experienced an HAE attack during the study;
  - Mild to moderate injection site reactions were the most frequently reported AEs.
- Cinryze with rHuPH20 delivered physiologically relevant C1 INH functional concentrations
  - Cinryze 2000U with rHuPH20 resulted in mean C1 INH functional concentrations greater than or equal to 0.4U/mL for 92 percent of the 72 hour post dosing period as compared to 73 percent for 1000U IV.
- Addition of rHuPH20 to Cinryze 2000U resulted in a statistically significant increase in bioavailability of C1 INH antigen relative to Cinryze 2000U alone;
- The addition of rHuPH20 to Cinryze resulted in a dose proportional increase of C1 INH function for C<sub>max</sub>, C<sub>avg</sub>, and AUC<sub>tau</sub> over the 1000 to 2000U dose range;
- No C1 INH antibodies were detected during the 30 day post treatment follow up after the last dose of Cinryze.

"Cinryze administered intravenously has been shown to be a safe and effective option in the management of HAE," said Dr. Schranz. "But HAE is not a disease for which there is a 'one size fits all' therapy; there are still unmet medical needs for novel therapeutic options to help patients manage their disease in a manner that best suits their lives. ViroPharma is developing subcutaneous delivery of Cinryze in combination with rHuPH20 to provide patients with broader options to help control their disease. The results of this study support further clinical development of the combination, and move us closer to potentially enabling prevention-minded patients living with HAE to self administer the drug subcutaneously with a single injection per dose."

Halozyme's Enhance™ technology, a proprietary drug delivery platform using recombinant human hyaluronidase enzyme (rHuPH20) facilitates the absorption and dispersion of drugs or fluids that are injected under the skin. Recombinant HuPH20 transiently generates channels in subcutaneous tissues to increase the absorption and spread of injected drugs.

#### **About the Study**

This open-label, multiple-dose Phase 2 study was conducted in 12 subjects with HAE who previously participated in the ViroPharma trial evaluating the pharmacokinetics of subcutaneous injections of Cinryze when given alone relative to intravenous infusion. Qualified subjects participated in a single 18-day study period, followed by a 30-day post-treatment follow-up. A 1000U or 2000U dose of Cinryze in combination with rHuPH20 was administered as a single subcutaneous

injection, twice weekly, allowing within-subject comparison across the different methods of administration. Plasma C1 INH functional activity was assessed by chromogenic assay and plasma C1 inhibitor antigenic concentration and C4 complement levels were assessed by ELISA.

Additional information about this subcutaneous Cinryze clinical trial can be found at [clinicaltrials.gov](http://clinicaltrials.gov).

#### **About Cinryze® (C1 esterase inhibitor [human])**

Cinryze is a highly purified, pasteurized and nanofiltered plasma-derived C1 esterase inhibitor product. In the U.S., Cinryze is approved by the FDA for routine prophylaxis against angioedema attacks in adolescent and adult patients with HAE. In the E.U., the product is approved by the EMA for the treatment and pre-procedure prevention of angioedema attacks in adults and adolescents with hereditary angioedema (HAE), and routine prevention of angioedema attacks in adults and adolescents with severe and recurrent attacks of hereditary angioedema (HAE), who are intolerant to or insufficiently protected by oral prevention treatments or patients who are inadequately managed with repeated acute treatment. Cinryze is for intravenous use only.

Severe hypersensitivity reactions to Cinryze may occur. Thrombotic events have occurred in patients receiving Cinryze, and in patients receiving off-label high dose C1 inhibitor therapy. Monitor patients with known risk factors for thrombotic events. With any blood or plasma derived product, there may be a risk of transmission of infectious agents, e.g. viruses and, theoretically, the CJD agent. The risk has been reduced by screening donors for prior exposure to certain virus infections and by manufacturing steps to reduce the risk of viral transmission including pasteurization and nanofiltration.

The most common adverse reactions in clinical trials associated with Cinryze were rash, headache, nausea, erythema, phlebitis and local reactions at the injection site. Adverse events of sinusitis and upper respiratory infection also were observed in clinical trials. No drug-related serious adverse events (SAEs) were reported in clinical trials.

Please visit <http://www.viopharma.com/products/cinryze.aspx> for the full U.S. Prescribing Information; the prescribing information for other countries can be found at [www.viopharma.com](http://www.viopharma.com).

#### **About Enhanze™ Technology**

Enhanze™ technology is a proprietary drug delivery platform using Halozyme's first approved enzyme, recombinant human hyaluronidase or rHuPH20. When formulated with other injectable drugs, Enhanze technology can facilitate the subcutaneous dispersion and absorption of these drugs. Molecules as large as 200 nanometers may pass freely through the extracellular matrix, which recovers its normal density within approximately 24 hours, leading to a drug delivery platform which does not permanently alter the architecture of the skin. The principal focus of Halozyme's Enhanze technology platform is the use of rHuPH20 to facilitate subcutaneous administration for large molecule biological therapeutics, some of which currently require intravenous administration.

#### **About Hereditary Angioedema (HAE)**

HAE is a rare, severely debilitating, life-threatening genetic disorder caused by a deficiency of C1 inhibitor, a human plasma protein. This condition is the result of a defect in the gene controlling the synthesis of C1 inhibitor. C1 inhibitor maintains the natural regulation of the contact, complement, and fibrinolytic systems, that when left unregulated, can initiate or perpetuate an attack by consuming the already low levels of endogenous C1 inhibitor in HAE patients. Patients with C1 inhibitor deficiency experience recurrent, unpredictable, debilitating, and potentially life threatening attacks of inflammation affecting the larynx, abdomen, face, extremities and urogenital tract. Patients with HAE experience approximately 20 to 100 days of incapacitation per year. There are estimated to be at least 6,500 people with HAE in the United States and at least 10,000 people in the European Union.

For more information on HAE, visit the HAEi's (International Patient Organization for C1 Inhibitor Deficiencies) website at [www.haei.org](http://www.haei.org) and the U.S. HAE Association's website at: [www.haea.org](http://www.haea.org).

#### **About ViroPharma Incorporated**

ViroPharma Incorporated is an international biopharmaceutical company committed to developing and commercializing novel solutions for physician specialists to address unmet medical needs of patients living with diseases that have few if any clinical therapeutic options, including C1 esterase inhibitor deficiency, treatment of seizures in children and adolescents, adrenal insufficiency (AI), and *C. difficile* infection (CDI). Our goal is to provide rewarding careers to employees, to create new standards of care in the way serious diseases are treated, and to build international partnerships with the patients, advocates, and health care professionals we serve. ViroPharma's commercial products address diseases including hereditary angioedema (HAE), seizures in children and adolescents, and CDI; for full U.S. prescribing information on our products, please download the package inserts at <http://www.viopharma.com/Products.aspx>; the prescribing information for other countries can be found at [www.viopharma.com](http://www.viopharma.com).

ViroPharma routinely posts information, including press releases, which may be important to investors in the investor relations and media sections of our company's web site, [www.viopharma.com](http://www.viopharma.com). The company encourages investors to consult these sections for more information on ViroPharma and our business.

### **About Halozyme**

Halozyme Therapeutics is a biopharmaceutical company dedicated to developing and commercializing innovative products that advance patient care. With a diversified portfolio of enzymes that target the extracellular matrix, the Company's research focuses primarily on a family of human enzymes, known as hyaluronidases, that increase the absorption and dispersion of biologics. Halozyme's pipeline addresses therapeutic areas, such as diabetes, oncology and dermatology that have significant unmet medical need. The Company markets HYLENEX® recombinant (hyaluronidase human injection) and has partnerships with Roche, Baxter, ViroPharma and Intrexon. Halozyme is headquartered in San Diego, CA. For more information on how we are innovating, please visit our corporate website at [www.halozyme.com](http://www.halozyme.com).

### **ViroPharma Forward Looking Statements**

Certain statements in this press release contain forward-looking statements that involve a number of risks and uncertainties. Forward-looking statements provide our current expectations or forecasts of future events, including the therapeutic indication and use, safety, efficacy, tolerability and potential of Cinryze and our focus, goals, strategy, research and development programs, and ability to develop pharmaceutical products, commercialize pharmaceutical products, and execute on our plans including clinical development activities with Cinryze related to subcutaneous administration in combination with rHuPH20. The safety, pharmacokinetics and pharmacodynamics data described in this press release are preliminary and additional review of the data may reveal additional findings which may not be consistent with this press release. The data described in this press release may not be predictive of the results of future studies and there can be no assurance that that future studies with Cinryze utilizing subcutaneous administration in combination with rHuPH20 will yield positive results or support further development of Cinryze for subcutaneous administration in combination with rHuPH20. The FDA or EMA may view the data regarding subcutaneous administration of Cinryze in combination with rHuPH20 as insufficient or inconclusive, request additional data, require additional clinical studies, delay any decision past the time frames anticipated by us, limit any approved indications, or deny the approval of Cinryze for subcutaneous administration in combination with rHuPH20. These factors, and other factors, including, but not limited to those described in our annual report on Form 10-K for the year ended December 31, 2011 filed with the Securities and Exchange Commission, could cause future results to differ materially from the expectations expressed in this press release. The forward-looking statements contained in this press release are made as of the date hereof and may become outdated over time. ViroPharma does not assume any responsibility for updating any forward-looking statements. These forward looking statements should not be relied upon as representing our assessments as of any date subsequent to the date of this press release.

### **Halozyme Safe Harbor Statement**

In addition to historical information, the statements set forth above regarding the subcutaneous Cinryze with rHuPH20 product candidate, its possible advantages and attributes, future development and clinical trials plans, possible indications and other statements regarding Halozyme's product candidates and potential attributes of these product candidates, involve risk and uncertainties that could cause actual results to differ materially from those in the forward-looking statements. The forward-looking statements are also identified through use of the words "expect," "believe," "enable," "may," "will," "could," "intends," "estimate," "anticipate," "plan," "predict," "probable," "potential," "possible," "should," "continue," and other words of similar meaning. Actual results could differ materially from the expectations contained in forward-looking statements as a result of several factors, including clinical trial results, delays in development, possible adverse events associated with the use of the product candidate, regulatory delays and competitive conditions. These and other factors that may result in differences are discussed in greater detail in the company's reports on Forms 10-K, 10-Q, and other filings with the Securities and Exchange.

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