



## **Pivotal Data Demonstrating Efficacy of Plenadren® (Hydrocortisone, Modified Release Tablet) in Adrenal Insufficiency Published in the Journal of Clinical Endocrinology and Metabolism**

### **- Improved Cortisol Exposure-Time Profile with Plenadren Associated with Improved Outcomes -**

EXTON, Pa., Feb. 16, 2012 /PRNewswire/ -- ViroPharma Incorporated (NASDAQ: VPHM) today announced that data from the pivotal study for their orphan drug Plenadren® (hydrocortisone, modified release tablet) were published in the Journal of Clinical Endocrinology and Metabolism (JCEM), a leading scientific journal for endocrinology. Plenadren was recently granted European Marketing Authorization for treatment of adrenal insufficiency in adults.

The authors described results showing that the once daily dual-release tablet provided a more circadian-based serum cortisol profile, and that reduced body weight, reduced blood pressure, and improved glucose metabolism were observed during once daily treatment, compared to treatment with immediate release hydrocortisone three times per day. In particular, the authors noted glucose metabolism improved in patients with concomitant diabetes mellitus. In addition, the preference of once daily versus three times per day treatment was assessed to be large or very large by 85 percent of patients at 12 weeks.

Professor Gudmundur Johannsson of the Department of Endocrinology, Sahlgrenska University Hospital, Gothenburg, Sweden, and primary author of the publication, commented, "These data indicate that patients with Addison's Disease now have an important therapeutic option with once daily Plenadren. The time-exposure of Plenadren may be important in improving the outcome of patients suffering with adrenal insufficiency."

Replacement therapy for the treatment of the rare disease adrenal insufficiency has been available for more than 50 years. Oral hydrocortisone is the most widely used replacement therapy for treatment, but no formal studies of its efficacy and safety have been performed in patients suffering from adrenal insufficiency. The JCEM publication entitled, '*Improved Cortisol Exposure-Time Profile and Outcome in Patients with Adrenal insufficiency: A Prospective Randomized Trial of a Novel Hydrocortisone Dual-Release Formulation*,' described the data from the prospective study on glucocorticoid replacement therapy in adrenal insufficiency. The pivotal study was an open label, randomized, two-period, 12-wk crossover multicenter trial with a 24-wk extension at five university hospital centers in 64 patients with primary adrenal insufficiency, also called Addison's disease. The trial compared the efficacy and safety of the same daily doses of once daily Plenadren with conventional immediate release hydrocortisone given three times per day (TID). The most commonly reported adverse events on Plenadren during the crossover phase of the study were nasopharyngitis, fatigue, gastroenteritis and influenza with infections reported in 43.8% of patients on Plenadren and 39.1% on TID treatment. Six serious adverse events were reported during Plenadren treatment and two during TID treatment, all caused by infectious disorders. No deaths occurred during the study and no withdrawals due to adverse events were reported. Fifty-nine of 64 randomized patients (92%) chose to continue into the extension phase of the study.

Patients with adrenal insufficiency are dependent on exogenous glucocorticoid replacement therapy, such as hydrocortisone. While standard formulations of hydrocortisone require multiple daily doses that result in sizeable variations in cortisol levels, Plenadren is a once daily dual-release oral glucocorticoid tablet with a release profile designed to more closely mimic the body's natural secretion pattern of cortisol. These differences may explain the reductions in body weight and blood pressure and the improved glucose metabolism observed with Plenadren.

On November 3, 2011, the European Commission (EC) granted European Marketing Authorization for Plenadren® (hydrocortisone, modified release tablet), an orphan drug for treatment of adrenal insufficiency in adults, which will bring these patients their first pharmaceutical innovation in over 50 years. ViroPharma anticipates commercial launch of Plenadren in the EU in the fourth quarter of 2012. A named patient program is currently available to patients in the EU, which ViroPharma expects to continue until commercial launch. Plenadren is not approved in the United States. However, it has received orphan drug designation status in the United States and has maintained orphan status in Europe upon approval.

Adrenal insufficiency, or AI, is a result of insufficient cortisol production by the adrenal glands. Primary AI is caused by impairment of the adrenal glands, most often due to Addison's disease, a destruction of the adrenal cortex by an autoimmune disease, and Congenital Adrenal Hyperplasia, a gene mutation affecting cortisol production. Secondary AI is a result of breakdown of the hypothalamic-pituitary-adrenal (HPA) axis, most often due to a hypothalamic-pituitary tumor. AI is associated with potentially severe morbidities, including gastrointestinal distress, weight loss, kidney failure, muscle weakness, severe

fatigue, low blood pressure, and depression. If not treated, adrenal crisis may develop, which can be fatal if not properly treated.

Although glucocorticoid hormone replacement therapy for adrenal insufficiency has been available for decades, studies have recorded complications and comorbidities including premature death, impaired quality of life, increased cardiovascular risk, and decreased bone mineral density in treated patients, most likely because of lack of therapeutic options, and difficulties when using them to match the natural secretion pattern of cortisol.

**About Plenadren® (hydrocortisone, modified release tablet)**

Plenadren is the first true innovation in over 50 years in the treatment of adrenal insufficiency.

Hypersensitivity to the active substance of Plenadren or to any of the excipients may occur. During acute adrenal insufficiency, parenteral administration of hydrocortisone in high doses, together with physiological sodium chloride solution for injection, must be given. Use of Plenadren with potent CYP 3A4 inducers and inhibitors may merit an adjustment of hydrocortisone dosage. High (supra-physiological) dosages of cortisone can cause elevation of blood pressure, salt and water retention, and increased excretion of potassium. Long-term treatment with higher than physiological hydrocortisone doses can lead to clinical features resembling Cushing's syndrome with increased adiposity, abdominal obesity, hypertension and diabetes, and thus result in an increased risk of cardiovascular morbidity and mortality. All glucocorticoids increase calcium excretion and reduce the bone remodeling rate. Patients with adrenal insufficiency on long term glucocorticoid replacement therapy have been found to have reduced bone mineral density. Psychiatric adverse events may occur with systemic glucocorticoids.

The most common adverse reactions observed in clinical studies have been fatigue, gastroenteritis, upper respiratory tract infection, sedation, vertigo and dry eyes.

**About Adrenal Insufficiency**

Adrenal insufficiency (AI) is a disorder caused by dysfunction of the adrenal gland resulting in low levels of the hormone cortisol, which normally follows a circadian rhythm and regulates many critical body functions. To survive, AI patients need replacement therapy with glucocorticoids (usually hydrocortisone). Because it is a chronic condition, they require this life-saving therapy throughout their lives. Primary AI is referred to as Addison's disease, which affects up to 14 in every 100,000 people. Common symptoms of Addison's disease include fatigue, muscle weakness, fever, weight loss, difficulty in standing up, changes in personality, and gastrointestinal involvement. Severe adrenal insufficiency, which can manifest as shock (very low blood pressure with loss of consciousness), dehydration, and imbalance of sodium and potassium levels, can be life threatening. These cases of adrenal crisis (sometimes called 'adrenal or Addisonian crisis') can occur after a significant stress such as infection or trauma, and can be fatal if not promptly diagnosed and treated with glucocorticoid therapy.

**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, 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.viropharma.com/Products.aspx>; the prescribing information for other countries can be found at [www.viropharma.com](http://www.viropharma.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.viropharma.com](http://www.viropharma.com). The company encourages investors to consult these sections for more information on ViroPharma and our business.

**Disclosure Notice**

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. There can be no assurance that that the data presented in the JCEM publication regarding Plenadren is predictive of how Plenadren will perform in commercial usage. We cannot assure that current or future studies with Plenadren will demonstrate the same or similar safety and efficacy profile of Plenadren as described in the JCEM publication. 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, 2010 and 10-Q for the quarters ended March 31, 2011, June 30, 2011 and September 30, 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.

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