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News Release

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For Immediate Release

FDA APPROVES ASTELLAS' VAPRISOL® FOR THE TREATMENT OF HYPERVOLEMIC HYPONATREMIA

Arginine vasopressin (AVP) receptor antagonist now approved for the management of the two most common forms of potentially life-threatening sodium/water imbalance

DEERFIELD, Illinois, March 2, 2007 — Astellas Pharma US, Inc. today announced that the U.S. Food and Drug Administration (FDA) has approved Vaprisol® (conivaptan hydrochloride injection), an arginine vasopressin (AVP) receptor antagonist, for the intravenous treatment of hypervolemic hyponatremia in hospitalized patients. Vaprisol, discovered and developed by Astellas, is the first drug specifically indicated for the treatment of both euvolemic and hypervolemic hyponatremia, potentially life-threatening conditions that occur when the body's blood sodium level falls significantly below normal. Vaprisol was approved by the FDA as a treatment for euvolemic hyponatremia in December 2005, and has been marketed by Astellas since April 2006.

Hyponatremia is estimated to affect up to four percent of hospitalized patients in the United States each year.[1] While many patients with hyponatremia have no symptoms, severe cases are medical emergencies that can result in swelling of the brain, respiratory arrest and death. Hypervolemic hyponatremia, which occurs when the total body water increase is greater than the body's serum sodium levels, resulting in edema (swelling of body tissues) and is often associated with congestive heart failure, severe liver disease and kidney failure.

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In the treatment of hyponatremia associated with congestive heart failure, Vaprisol is indicated only for those patients for whom the expected benefit of raising serum sodium outweighs the increased risk of adverse events. Caution should be used when administering Vaprisol to patients with liver or kidney impairment.

“With this additional indication, Vaprisol will provide physicians with an important new treatment option for patients with this often serious condition,” said Yoshihiko Hatanaka, Chief Executive Officer at Astellas Pharma US, Inc. "Astellas is committed to developing novel treatments and providing innovative products such as Vaprisol in order to solidify its presence in the critical care market.”

In a randomized, double-blind, placebo-controlled study, intravenous administration of Vaprisol 40 mg/day for four days achieved a clinically meaningful aquaresis which resulted in increased serum sodium levels in hospitalized patients with hypervolemic hyponatremia. Aquaresis is defined as the excretion of electrolyte-free water. Significant increases in serum sodium levels were observed within the first day of treatment with Vaprisol (mean increase of 6.4 mEq/L at 24 hours) and continued throughout the remainder of the treatment period. The most common adverse events associated with Vaprisol were infusion-site reactions. Some serious infusion-site reactions did occur, however, these were the most common types of adverse events leading to the discontinuation of Vaprisol.

“Vaprisol is the first dual V_{1a} and V_2 vasopressin receptor antagonist approved by the FDA for the treatment of hypervolemic and euvolemic hyponatremia,” said Steven R. Goldsmith, M.D., Professor of Medicine at the University of Minnesota Medical School. “Vaprisol is a novel treatment option that effectively increases serum sodium levels and will help physicians to manage these potentially very serious conditions.”

About Hyponatremia

Hyponatremia often results from elevated levels of the hormone arginine vasopressin (AVP), which regulates water and salt balance in the body. It is the most common electrolyte disorder in clinical medicine and one of the most difficult to treat. Syndrome of inappropriate antidiuretic hormone (SIADH), advanced kidney failure, hypothyroidism, cancer and chronic high blood pressure are common causes of

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hyponatremia. Dilutional hyponatremia, which includes euvolemic and hypervolemic hyponatremia, is the most common form of the condition, and occurs when retained water dilutes serum sodium content. Patients with hyponatremia are classified as *hypervolemic* if swelling of body tissues (edema) is present or *euvolemic* if there is an increase in total body water content without edema.[2,3]

About Vaprisol

Discovered and developed by Astellas Pharma Inc. headquartered in Tokyo, Japan, Vaprisol is a novel drug that blocks the activity of AVP, resulting in increased urine output without loss of valuable electrolytes such as sodium and potassium. This effect, known as “aquaresis,” helps to increase serum sodium levels in patients with hyponatremia, a condition of low serum sodium concentration, due to increased body water (dilutional hyponatremia). Vaprisol is the first AVP receptor antagonist with a demonstrated safety profile and that effectively promotes aquaresis in order to help restore salt and water balance in patients with euvolemic and hypervolemic hyponatremia.

Vaprisol is indicated for the treatment of euvolemic and hypervolemic hyponatremia in hospitalized patients. Vaprisol is not indicated for the treatment of congestive heart failure. It should only be used for the treatment of hyponatremia in patients with underlying heart failure when the expected benefit of raising serum sodium outweighs the increased risk of adverse events. Vaprisol is contraindicated in patients with hypovolemic hyponatremia. In addition, coadministration of Vaprisol with potent CYP3A4 inhibitors, such as ketoconazole, itraconazole, clarithrmyin, ritanovir, and indinavir, is contraindicated. Serum sodium, volume, and neurological status must be monitored frequently because Vaprisol potentially can cause overly rapid correction of sodium leading to serious sequelae. The use of Vaprisol in patients with hepatic impairment (including ascites, cirrhosis, or portal hypertension) or renal impairment has not been systematically evaluated. Use caution when administering Vaprisol to these patients. The most common adverse reactions reported were infusion site reactions (incidence of 73% and 63% for 20 mg/day and 40 mg/day respectively) which were also the most common type of adverse reaction leading to discontinuation of Vaprisol. Discontinuations from treatment due to infusion site reactions were more common among Vaprisol-treated patients (3%) than among placebo-treated patients (0%). Other common adverse reactions were headaches (8%, 10%), hypokalemia (22%, 10%), orthostatic hypotension (14%, 6%), and pyrexia (11%, 5%) for Vaprisol 20mg/day and 40mg/day, respectively.

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About Astellas

Astellas Pharma US, Inc., located in Deerfield, Illinois, is a US affiliate of Tokyo-based Astellas Pharma Inc., Astellas is a pharmaceutical company dedicated to improving the health of people around the world through the provision of innovative and reliable pharmaceutical products. The organization is committed to becoming a global pharmaceutical company by combining outstanding R&D and marketing capabilities and continuing to grow in the world pharmaceutical market. For more information about Astellas Pharma US, Inc., please visit our website at www.astellas.com/us.

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