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Ardelyx's Tenapanor Reduces Phosphorus Absorption and Protects against Vascular Calcification in Preclinical In Vivo Model of Chronic Kidney Disease

-- Data Published Online in the Journal of the American Society of Nephrology --

FREMONT, Calif., Nov. 17, 2014 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage biopharmaceutical company focused on cardio-renal, gastrointestinal and metabolic diseases, today announced publication of data in the *Journal of the American Society of Nephrology* (JASN) showing that in a preclinical *in vivo* model of chronic kidney disease (CKD), tenapanor reduced phosphorus absorption and protected against vascular calcification. The article was published online at http://jasn.asnjournals.org/content/early/recent. Tenapanor, a minimally-systemic inhibitor of the intestinal sodium transporter NHE3, has demonstrated the ability to reduce the absorption of dietary sodium and phosphorus in human and animal studies.

"Elevated levels of phosphate and sodium are key factors in the progression of kidney disease. We have known that tenapanor administration reduces the absorption of sodium in animals and humans, so it was exciting to see such a strong effect of phosphate in these animal models of human disease," said Mike Raab Ardelyx's President and Chief Executive Officer. "In addition, the study demonstrated the ability of tenapanor to protect against vascular calcification, one of the most common complications in end-stage renal disease (ESRD) and CKD patients. The results further deepen our understanding of tenapanor and its potential in treating hyperphosphatemia in ESRD. We look forward to seeing the results of our ongoing Phase 2b clinical trial in hyperphosphatemic ESRD patients in the first quarter of 2015."

According to the research findings reported in JASN, tenapanor decreased phosphorous absorption in rats, both in a setting of normal renal function and in a model of CKD. In the normal renal function group, tenapanor administration resulted in significantly decreased urinary phosphate excretion. In a model of CKD (5/6th nephrectomized (NPX), fed a high-salt diet), administration of tenapanor consistently lowered urinary phosphorus excretion over the course of 28 days compared with untreated controls. Additionally, in a CKD model of vascular calcification, tenapanor reduced serum phosphorus and serum creatinine as well as soft tissue calcification, as shown by significantly reduced phosphorous and calcium content of the aortic arch and stomach compared with vehicle treatment. Tenapanor-treated animals also demonstrated significant attenuation of renal and cardiac hypertrophy, signs of a compromised kidney and heart. Tenapanor in this model also reduced the expression of FGF-23, an important hormone suspected to aggravate vascular calcification and heart hypertrophy in CKD.

"The ability to stop vascular calcification over the long-term may be one of the most important goals in the management of kidney disease," said Orson Moe, MD, Professor of Internal Medicine, University of Texas Southwestern Medical Center. "I am impressed with the results reported in this paper, and look forward to the results from studies in humans to determine if tenapanor can demonstrate similar effects." Dr. Moe is a leading researcher in mineral metabolism. Dr. Moe is an advisor to Ardelyx, but was not involved in the study reported in JASN.

About CKD and ESRD

CKD is marked by a progressive loss in renal function, resulting in less efficient blood filtration and phosphorus elimination, ultimately leading to hyperphosphatemia. CKD can lead to the nearly total loss of kidney function. When this occurs, it is called end-stage renal disease (ESRD), and the patient must receive a kidney transplant, undergo frequent dialysis or risk death. In ESRD patients on hemodialysis, buildup of excess levels of phosphorus in the blood have been shown to lead to an increase in cardiovascular disease risk, as well as increases in serum FGF-23, an important serum endocrine hormone that regulates phosphorus metabolism. Elevated levels of FGF-23 are strongly associated with an increased risk of cardiovascular mortality. With concurrent elevated calcium levels common in these patients, particularly when calcium is used as a means of controlling phosphorus, deposits containing calcium and phosphate, called vascular calcification, develop in arteries, joints, skin, soft tissue and other organs. Increased coronary artery calcification is associated with an increased risk of heart disease, stroke and death. Intestinal phosphate binders are currently used in this market to control phosphorus accumulation in the body. The Company estimates, based on phosphate binder utilization, the only approved therapies for hyperphosphatemia, that there are approximately 270,000, 215,000 and 220,000 ESRD patients with hyperphosphatemia in the United States, Europe and Japan, respectively.

About Tenapanor

Tenapanor (also known as RDX5791 and AZD1722) is a minimally-systemic small molecule inhibitor of NHE3, a transporter of sodium in the gastrointestinal tract. Orally administered tenapanor has been shown in clinical trials to reduce the intestinal absorption of both dietary sodium and phosphorus. Ardelyx licensed tenapanor to AstraZeneca in October 2012. Under this license agreement, Ardelyx and AstraZeneca are evaluating tenapanor for the treatment of hyperphosphatemia in patients with ESRD in an ongoing Phase 2b study. In October 2014, Ardelyx announced positive results from its Phase 2b clinical trial evaluating tenapanor in patients with constipation-predominant irritable bowel syndrome (IBS-C). Ardelyx and AstraZeneca are also evaluating tenapanor in an ongoing Phase 2a study for its effect on kidney function and fluid overload in patients with CKD with type 2 diabetes mellitus.

About Ardelyx, Inc.

Ardelyx is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the gastrointestinal tract to treat cardio-renal, gastrointestinal and metabolic diseases. The Company has developed a proprietary drug discovery and design platform enabling it, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing this platform, Ardelyx has discovered and designed tenapanor.

Ardelyx formed a collaborative partnership with AstraZeneca in October 2012 to develop and commercialize tenapanor. In addition to tenapanor, the Company has discovered small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in ESRD, a program licensed to Sanofi, and independently is advancing several additional research programs focused in cardio-renal, gastrointestinal and metabolic diseases. Ardelyx is located in Fremont, California. For more information, please visit Ardelyx's website at www.ardelyx.com.

Forward Looking Statements

To the extent that statements contained in this press release are not descriptions of historical facts regarding Ardelyx, they are forward-looking statements reflecting the current beliefs and expectations of management made pursuant to the safe harbor of the Private Securities Reform Act of 1995, including statements regarding the potential of tenapanor in treating IBS-C patients, the potential of tenapanor in treating the renal indications for which it is currently being evaluated, the potential of tenapanor to demonstrate similar results in a human clinical study as seen in the *in vivo* model, estimates of the number of ESRD patients with hyperphosphatemia and the potential of our drug discovery and design platform. Such forward-looking statements involve substantial risks and uncertainties that could cause the development of tenapanor, or Ardelyx's future results, performance or achievements to differ significantly from those expressed or implied by the forward-looking statements. Such risks and uncertainties include, among others, the uncertainties inherent in the clinical development process, Ardelyx's reliance upon AstraZeneca for the development of tenapanor, and AstraZeneca's right under the license agreement to choose which indication or indications for which tenapanor will be developed. Ardelyx undertakes no obligation to update or revise any forward-looking statements. For a further description of the risks and uncertainties that could cause actual results to differ from those expressed in these forward-looking statements, as well as risks relating to Ardelyx's business in general, please refer to Ardelyx's third quarter report on Form 10-Q filed with the Securities and Exchange Commission on November 7, 2014.

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