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# Ardelyx Reports Results from Phase 2b Clinical Trial Evaluating Tenapanor in Treating Hyperphosphatemia in Chronic Kidney Disease Patients on Hemodialysis

FREMONT, Calif., Feb. 2, 2015 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage biopharmaceutical company focused on cardio-renal, gastrointestinal, and metabolic diseases, today announced that AstraZeneca's 161-patient Phase 2b clinical trial evaluating tenapanor in hyperphosphatemic patients with chronic kidney disease on hemodialysis met its primary endpoint by demonstrating a statistically significant dose-related decrease in serum phosphate levels for tenapanor-treated patients compared to patients receiving placebo (p=0.012). It was noted, however, that the rate of diarrhea was distinctly higher than expected. The overall safety profile remains consistent with that observed in previous tenapanor trials. In October 2012, Ardelyx entered into a partnership with AstraZeneca for the worldwide development and commercialization of tenapanor.

"We are encouraged by tenapanor's ability to significantly decrease elevated serum phosphate levels, although we did not anticipate the high incidence of diarrhea," said Mike Raab, President and Chief Executive Officer of Ardelyx. "We look forward to working with our partner, AstraZeneca, to evaluate the future development plans for tenapanor in conjunction with the ongoing CKD trial and the positive Phase 2b results from IBS-C."

**The Phase 2b Hyperphosphatemia Clinical Trial**

This Phase 2b trial (ClinicalTrials.gov identifier NCT02081534) was a randomized, double blind, placebo-controlled, multi-center, international study evaluating the safety and efficacy of six dose levels of tenapanor (3 and 30 mg once daily, and 1, 3, 10, and 30 mg twice daily) in 161 hyperphosphatemic patients with chronic kidney disease on hemodialysis (CKD-5D, also referred to as end-stage renal disease, or ESRD). The primary efficacy endpoint was the change from baseline of S-phosphate levels to the end of treatment and the endpoint was analyzed using an analysis of covariance model (ANCOVA). The results are reported on an intent-to-treat basis. A dose-response relationship was observed in the primary endpoint and twice daily dosing had better pharmacodynamic activity than once daily dosing.

As expected, due to its pharmacological actions, the most frequent adverse event was diarrhea; however, the rate was distinctly higher than previously observed. The overall safety profile remains consistent with that observed in previous tenapanor trials in this patient population. The findings of the clinical study are expected to be presented in an appropriate peer-reviewed forum.

**Hyperphosphatemia in CKD-5D (ESRD)**

As kidney function declines in patients with CKD, phosphorus begins to accumulate to dangerous levels in the blood. Left untreated, hyperphosphatemia can lead to vascular and tissue calcifications, bone pain, fractures and worsening secondary hyperparathyroidism and is associated with increased cardiovascular morbidity and mortality. In CKD-5D patients, phosphorus is not readily removed by the dialysis procedure and other means of managing phosphorus levels must be employed. Commercially available phosphate binders are commonly used. While being severely restricted in fluid intake, CKD-5D patients take on average 10-14 oral medications each day, including 9 or more phosphate binder pills. Based on the most recent data available from the U.S. Renal Data System and percentages of patients prescribed phosphate binders, there are approximately 280,000 CKD-5D patients in the US who currently receive phosphate binders. Based on similar data from Europe and Japan, there are about 220,000 hyperphosphatemic CKD-5D patients in Europe and about 220,000 in Japan.

**About Tenapanor**

Tenapanor is a minimally-absorbed 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.

A total of 14 clinical trials of tenapanor have been completed or are ongoing, and over 1,000 subjects have been administered tenapanor to date. In addition to the hyperphosphatemia Phase 2b clinical trial in CKD-5D patients, Ardelyx and AstraZeneca

are evaluating tenapanor in two other indications:

- IBS-C : A phase 2b randomized, double-blind, placebo-controlled 12-week clinical trial in 371 IBS-C patients met its primary endpoint of an increase in complete spontaneous bowel movement (CSBM) responders with tenapanor 50 mg twice daily as compared to placebo. Ardelyx announced positive results of this trial in October 2014.
- Stage 3 CKD patients with type 2 diabetes mellitus, the presence of the protein albumin in the urine, or albuminuria, and high blood pressure: this Phase 2a clinical trial is ongoing and the results are expected in the second quarter of 2015, earlier than the second half of 2015, as was previously reported.

**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 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 CKD-5D, 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 for tenapanor in treating IBS-C patients, the potential of tenapanor in treating the renal indications for which it is currently being evaluated, and the availability and timing of data from the ongoing CKD clinical trial. 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 filed on Form 10-Q filed with the Securities and Exchange Commission on November 7, 2014.

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