May 5, 2015

Ardelyx Reports Results from Phase 2a Clinical Trial Evaluating Tenapanor in Chronic Kidney Disease Patients with Type 2 Diabetes Mellitus and Albuminuria

-- Conference Call and Webcast Today at 5:00 p.m. ET --

FREMONT, Calif., May 5, 2015 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage biopharmaceutical company focused on cardio-renal, gastrointestinal, and metabolic diseases, today announced that a 154-patient Phase 2a clinical trial evaluating tenapanor in Stage 3 chronic kidney disease patients with type 2 diabetes mellitus and albuminuria did not meet the primary endpoint of decreasing the urinary albumin-creatinine ratio in tenapanor-treated patients compared to patients receiving placebo.

Ardelyx formed a partnership with AstraZeneca in October 2012 to develop and commercialize tenapanor. Tenapanor has been evaluated in over 1,000 subjects as part of 14 clinical trials in healthy volunteers and in patients with constipation-predominant irritable bowel syndrome (IBS-C), hyperphosphatemia and chronic kidney disease (CKD). With the completion of the CKD trial, Ardelyx and AstraZeneca are assessing the data from all the trials. Under the terms of the agreement, AstraZeneca is obligated to communicate to Ardelyx, on or before June 29, 2015, whether it will continue the development of tenapanor. Should AstraZeneca decide to pursue the development of only the IBS-C indication, Ardelyx will be entitled to a milestone payment of $10 million. Should AstraZeneca decide to pursue the development of any other indication or multiple indications, Ardelyx will be entitled to receive a $20 million milestone payment.

"We continue to work with AstraZeneca as they evaluate the data, and we are preparing for the continuation of the development of tenapanor under a variety of different scenarios," said Mike Raab, President and CEO. "We are preparing for an end of phase 2 meeting for IBS-C with the FDA scheduled to occur in June. Should AstraZeneca decide to return the program to us, we seek to be in a position to initiate a Phase 3 clinical program for tenapanor in IBS-C in the fourth quarter of 2015. Additionally, we intend to be prepared to continue the development of tenapanor for the treatment of hyperphosphatemia in CKD patients on dialysis. We believe that tenapanor can be a best-in-class treatment for IBS-C and hyperphosphatemia and we hope to accelerate the development for these underserved conditions either independently or with AstraZeneca."

About the CKD Study

The CKD study was a 154-patient Phase 2a clinical trial evaluating tenapanor in Stage 3 chronic kidney disease patients with type 2 diabetes mellitus and albuminuria. In this study, patients who received tenapanor all started at 15 mg twice daily and had their dose escalated, stepwise, to 30 mg and 60 mg twice daily until they could no longer tolerate the gastrointestinal side effects (e.g., diarrhea), following which time the patient could elect to down-titrate the dose in a stepwise manner to as low as 5 mg twice daily. Approximately one-third of those patients treated with tenapanor had no incidence of diarrhea.

This study did not meet the primary endpoint of a statistically significant decrease of urinary albumin-creatinine ratio from baseline to week 12 for tenapanor-treated patients compared to patients receiving placebo with a 16% reduction in the tenapanor group versus 11% on placebo. No significant effect was observed on mean systolic or diastolic blood pressure or eGFR. No significant effect was detected on mean urinary sodium excretion: a decrease compared to baseline of 1.5 mmol/day in the placebo group was observed versus 9.6 mmol/day in the tenapanor group. A pharmacodynamic effect was observed in terms of increased stool frequency and softer stool in the tenapanor group and these effects returned to baseline after stopping drug. Tenapanor also produced a mean decrease compared to baseline in urinary phosphorus as compared to placebo, with an increase of 53.1 mg/day in placebo versus a decrease of 118.6 mg/day in tenapanor.

The overall safety profile remains consistent with that observed in previous tenapanor trials, with no significant differences observed between placebo and tenapanor, except with respect to diarrhea and loose stools. No other tolerability issues were observed.

"The pharmacodynamic effects of tenapanor in both reducing the absorption of dietary phosphorus as measured by decreased

urinary phosphorous excretion and softer stool form and increased stool frequency were confirmed in the Phase 2a CKD trial and continue to support the use of tenapanor in IBS-C and in patients with hyperphosphatemia on dialysis," said David Rosenbaum, Ph.D., Senior Vice President of Drug Development for Ardelyx. "We are enthusiastic about tenapanor in these other indications and we anticipate further confirmation of its effects in these patient populations as the clinical program advances."

Tenapanor's Clinical Development

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. Fourteen clinical trials of tenapanor have been completed, and over 1,000 subjects have been administered tenapanor to date.

Ardelyx reported positive Phase 2b data in October 2014 for the use of tenapanor in patients with IBS-C. At the twice-daily 50 mg dose of tenapanor, the study met the primary efficacy endpoint of an increase in the complete spontaneous bowel movement (CSBM) responder rate ($p < 0.001$). Most secondary endpoints, including abdominal pain, the overall responder rate and other abdominal and IBS-C symptoms, demonstrated statistically significant and clinically meaningful improvements.

In February 2015, Ardelyx announced results from a Phase 2b clinical study evaluating tenapanor to manage hyperphosphatemia in patients on dialysis with end stage renal disease, or CKD-5D, demonstrating that tenapanor caused 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 and the rate of discontinuations due to diarrhea were higher than expected based on previous clinical trials. Higher discontinuation rates due to diarrhea were observed primarily in the 30 mg once daily and 30 mg twice daily dose groups. The overall safety profile was consistent with that observed in previous tenapanor trials.

Conference Call & Webcast Information

Ardelyx management will host a live conference call and webcast today at 5:00 p.m. Eastern Time. The live webcast and a replay may be accessed by visiting Ardelyx's website on the investor page of the Company's website at http://ir.ardelyx.com/

Please connect to the Company's website at least 15 minutes prior to the live webcast to ensure adequate time for any software download that may be needed to access the webcast. Alternatively, please call 1-855-296-9612 (US) or 920-663-6277 (International) to listen to the live conference call. The conference ID number for the live call is 41903488. Please dial in approximately 10 minutes prior to the call. An archived webcast replay will be available on the Company's website for two weeks.

About Ardelyx, Inc.

Ardelyx is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-systemic, small molecule therapeutics that work exclusively in the gastrointestinal tract to treat cardio-renal, gastrointestinal and metabolic diseases. Ardelyx 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, the Company has discovered and designed tenapanor. Ardelyx formed a partnership with AstraZeneca in October 2012 to develop and commercialize tenapanor. In addition to tenapanor, Ardelyx has discovered small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in patients on dialysis, 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 hyperphosphatemia in CKD patients on dialysis, the timing of AstraZeneca's decisions regarding its future plans for tenapanor, the potential receipt and timing of milestone payments from AstraZeneca in connection with any decision by it to continue the development of tenapanor and our future development plans and the timing thereof, if the rights to tenapanor are returned to us. 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, AstraZeneca's right under the license agreement to choose which indication or indications for which tenapanor will be developed, and AstraZeneca's right under the license agreement to terminate the agreement upon written notice to Ardelyx. 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 annual report filed on Form 10-K filed with the Securities and Exchange Commission on March 5, 2015.

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