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Ardelyx Announces Successful Phase 3 Trial of Tenapanor for Hyperphosphatemia in Patients with End-Stage Renal Disease

Tenapanor Represents First Small Molecule, Non-Binder Treatment to Demonstrate Statistically Significant Effect in Hyperphosphatemia
Tenapanor Exhibits Favorable Tolerability Profile; Company Plans to Initiate Second Phase 3 Trial
Company to Host Conference Call Today at 8:30 a.m. ET

FREMONT, Calif., Feb. 15, 2017 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage company focused on enhancing the treatment of patients with cardiorenal and gastrointestinal (GI) diseases, today reported that the Phase 3 clinical trial evaluating the efficacy and safety of tenapanor as a treatment for hyperphosphatemia in patients with end-stage renal disease (ESRD) who are on dialysis met its primary endpoint and was generally well-tolerated.

Key Trial Results
The responder population (n=80 out of 164) had a mean reduction in serum phosphorus from baseline to the end of the eight-week treatment period of 2.56 mg/dL, with a reduction of up to 5.7 mg/dL. Notably, in this group, 33 percent of patients had a reduction in serum phosphorus of greater than 3 mg/dL. The study demonstrated a statistically significant difference in serum phosphorus levels from the end of the eight-week treatment period to the end of the four-week randomized withdrawal period between the tenapanor-treated group and the placebo-treated group in the responder patient population (mean -1.01 mg/dL, median of -1.3 mg/dL) and met its primary endpoint (95% CI -1.44, -0.21; LSmean -0.82 mg/dL; p=0.01). Only 7.8 percent of patients discontinued treatment due to GI side effects.

Hyperphosphatemia is a condition of higher than normal levels of serum phosphorus in the blood that is estimated to affect more than 745,000 people with ESRD who are on dialysis in major developed countries[1].

"The reduction in serum phosphorus in many patients treated with tenapanor is remarkable. These data validate tenapanor's unique mechanism of action and its potential to be the first non-phosphate binder treatment for this difficult-to-manage disorder," said Geoff Block M.D., director, clinical research at Colorado Kidney Care, and a Phase 3 investigator. "My patients are often required to take more than 19 pills per day, of which, nearly half are phosphate binders. The efficacy of tenapanor with only a few small pills, combined with its GI tolerability, has the potential to change the way in which we treat our patients in the future. I look forward to participating in the next Phase 3 study and evaluating the full potential of this novel agent."

"We are very pleased with the overall efficacy and improved tolerability profile of tenapanor in this study. The magnitude of the reduction of serum phosphorus in a large percentage of patients treated with tenapanor in this trial surpassed our expectations," said Mike Raab, president and chief executive officer of Ardelyx. "We are highly confident in tenapanor and look forward to further establishing its clinical and commercial value in the next Phase 3 trial."

Top-line Tolerability
Tenapanor was well-tolerated in the trial. In the eight-week treatment period, the only adverse event that affected more than five percent of patients treated with tenapanor was diarrhea (39 percent), a patient-reported side effect of loosened stool or increased frequency in bowel movements regardless of magnitude. In the four-week randomized withdrawal period, there was a diarrhea rate of 1.2 percent for patients treated with tenapanor compared with 2.4 percent on placebo. Treatment discontinuations due to diarrhea for patients treated with tenapanor was 7.8 percent (n=17). There were no discontinuations due to diarrhea in the randomized withdrawal period.

In order to fully assess GI tolerability, patients used an eDiary to record the frequency of daily bowel habits, as well as stool form using the Bristol Stool Form Scale (BSFS). During the eight-week treatment period, there was a 0.4 per day increase in bowel movement frequency from baseline, and during the four-week randomized withdrawal period, there was a 0.29 per

day increase as compared to placebo. Bowel movement frequency was within the normal range in all groups.

During the eight-week treatment period, there was a 0.87 point increase in BSFS from a baseline score of 4.2, out of a maximum of seven, where seven is liquid stool. During the four-week randomized withdrawal period, there was a 0.7 point difference in BSFS between placebo (4.4) and tenapanor treatment (5.1).

Second Phase 3 Trial
The results from this trial support Ardelyx's plans to initiate the second Phase 3 study of tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis in mid-2017. This Phase 3 study will include a 26-week open-label treatment period, with a randomized withdrawal period followed by an additional 26-week long-term safety extension. Full details of the final trial design are under consultation with advisors and will be disclosed upon study initiation.

"What is particularly exciting about these data is the innovation that we are bringing to patients on dialysis who have relied on the available binder treatments for decades," said Dr. Reg Seeto, chief operating officer of Ardelyx. "These positive data from our first Phase 3 study are an important milestone for Ardelyx. They are essential to our ability to achieve our goal of establishing leading, revenue-generating cardiorenal and GI business units over the next five years, and bringing important new medicines to underserved patients."

Ardelyx plans to submit detailed results from its first Phase 3 trial for presentation during the American Society of Nephrology Kidney Week taking place in New Orleans from October 31 to November 5, 2017.

About the Trial
The Phase 3 trial was an eight-week, double-blind, randomized trial, with a four-week placebo-controlled randomized withdrawal period. Ardelyx enrolled a total of 219 ESRD patients with hyperphosphatemia who are on dialysis. Enrolled patients were randomized evenly into three arms, in which all groups received tenapanor for eight weeks. Tenapanor was administered at doses of 3 mg or 10 mg twice-daily and in a dose-titration arm starting at 30 mg twice-daily with the option to down-titrate once a week during the first four weeks to 20, 15, 10 and 3 mg twice-daily, based on GI tolerability. After the end of the eight-week treatment period, patients were re-randomized 1:1 to either remain on their current tenapanor dose or switch to placebo for a four-week, placebo-controlled, randomized withdrawal period.

The primary endpoint of the trial is the difference in change in serum phosphorus between the pooled tenapanor-treated patients and placebo-treated patients from the end of the eight-week treatment period to the end of the four-week randomized withdrawal period, in the responder population. The responder population, which was reviewed by the U.S. Food and Drug Administration, is defined as patients who demonstrate a greater than or equal to 1.2 mg/dL decrease in serum phosphorus from baseline during the initial eight-week treatment period.

Tolerability endpoints included stool consistency as measured by the Bristol Stool Form Scale and frequency.

About Tenapanor for Hyperphosphatemia
Tenapanor is a first-in-class, proprietary, oral, experimental medication in late-stage clinical development. It has a unique mechanism of action that works exclusively in the gut. In hyperphosphatemia, tenapanor blocks the NHE3 sodium transporter in the GI tract, reducing the absorption of dietary sodium and resulting in increased protons within the cells. The increase in protons causes a selective reduction in phosphate uptake by tightening junctions or pores that regulate phosphate absorption in the GI tract. These effects are selective without impacting transport of other ions, nutrients or macromolecules, and consistent with our observations in clinical trials. Tenapanor is minimally absorbed and has been specifically designed to work exclusively within the GI tract, thereby significantly reducing the potential side effects that could occur.

About Hyperphosphatemia
Hyperphosphatemia is a condition resulting in an abnormally elevated level of phosphorus in the blood that is estimated to affect more than 745,000 people in major developed countries[1]. Phosphorus is one of the most abundant and essential elements in the body and plays an important role in multiple biological processes. The kidney is the major organ involved in regulating phosphorus levels in the body, but when kidney function is impaired, phosphorus is not excreted adequately from the body. As such, hyperphosphatemia is a common condition associated with end-stage renal disease in people receiving dialysis. There are currently no treatments approved for hyperphosphatemia that are not phosphate binders.

Conference Call Information
The company will host a conference call today, February 15, 2017 at 8:30 a.m. ET, to discuss the Phase 3 findings. To participate in the conference call, please call (855) 296-9612 (toll-free) or (920) 663-6277 (toll) and reference call ID number 73336444. The call will also be webcast, which can be accessed by visiting the investor page of the company's website www.ardelyx.com, and will be available on the website for 60 days following the call.

About Ardelyx, Inc.

Ardelyx is focused on enhancing the way patients with cardiorenal and gastrointestinal (GI) diseases are treated by using the gut as the gateway to delivering medicines that matter. The company has established unique cardiorenal and GI business units aimed at bringing new, effective medicines with distinct safety and dosing advantages to underserved patients. Ardelyx's cardiorenal portfolio includes the Phase 3 development of tenapanor for the treatment of hyperphosphatemia in people with end-stage renal disease who are on dialysis and the Phase 3 development of RDX7675 for the treatment of people with hyperkalemia. The company's GI portfolio includes the Phase 3 development of tenapanor for the treatment of people with irritable bowel syndrome with constipation (IBS-C), and RDX8940, a TGR5 agonist approaching Phase 1 development. Leveraging the company's platform and unique gut-restriction chemistry, Ardelyx intends to build a fully integrated, revenue-generating biopharmaceutical company with leading cardiorenal and GI business units. For more information, please visit www.ardelyx.com and connect with us on Twitter @Ardelyx.

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 the potential of tenapanor in the treatment of hyperphosphatemia in ESRD patients on dialysis, the expected timing of the initiation of the second Phase 3 clinical trial evaluating tenapanor for the treatment of hyperphosphatemia in ESRD patients on dialysis. 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 research and the clinical development process. 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 Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission on November 7, 2016, and its subsequent current and periodic reports filed and to be filed with the Securities and Exchange Commission.

[1] USRDS 2014; European ERA-EDTA Registry Annual report 2012; Nakai S, et al, 2008