Ardelyx Announces Presentations at ERA-EDTA Virtual Congress 2021

June 7, 2021

The OPTIMIZE Presentation Highlights Data Showing Tenapanor Allows a Greater Percentage of Previously Uncontrolled Patients to Achieve Targeted Serum Phosphorus Levels
The PHREEDOM Presentation Shows Positive Long Term Safety Data for Tenapanor Compared to Sevelamer

FREMONT, Calif. and WALTHAM, June 7, 2021 /PRNewswire/ -- Ardelyx, Inc. (Nasdaq: ARDX), a biopharmaceutical company focused on developing innovative first-in-class medicines to improve treatment for people with kidney and cardiorenal diseases, today announced two presentations highlighting new tenapanor data at the European Renal Association – European Dialysis and Transplant Association (ERA-EDTA) Virtual Congress 2021, taking place June 5-8, 2021.

Interim data from the company's ongoing OPTIMIZE study shows that tenapanor can play a central role across the hyperphosphatemia treatment paradigm in adult patients with chronic kidney disease on dialysis, enabling greater achievement of phosphorus targets in binder-treated patients with phosphorus >5.5 and control of serum phosphorus in binder-naïve patients.

In a separate presentation, the company reported that patients who were on tenapanor had a smaller percentage of deaths and hospitalizations than those on the phosphate binder, sevelamer, in the long-term Phase 3 PHREEDOM study.

"Our OPTIMIZE study was designed to evaluate multiple methods for integrating the novel blocking mechanism of tenapanor into the hyperphosphatemia treatment paradigm with the goal of increasing the proportion of patients able to achieve target phosphorus levels," said David Rosenbaum, Ph.D. chief development officer. "We are extremely pleased with the interim results demonstrating that tenapanor use resulted in approximately 50% of previously uncontrolled patients achieving target phosphorus levels when either switched to tenapanor monotherapy or with the addition of tenapanor with a concurrent reduction in binder dose. The interim results also demonstrated that two-thirds of binder-naïve patients who started on tenapanor monotherapy were able to achieve and/or maintain target phosphorus levels."

Dr. Steven Fishbane, Chief of Nephrology, Northwell Health and Professor of Medicine, Zucker School of Medicine, commented "I am excited by these results that demonstrate both binder-treated and binder-naïve patients may be better able to achieve target phosphorus levels by applying a blocking mechanism approach as an integral component to hyperphosphatemia management, reflecting the important role of tenapanor across a broad range of patients and treatment regimen scenarios."

Ardelyx Presentations at ERA-EDTA

Abstract Title: A Randomized, Open-Label Study to Evaluate Potential Real-World Use of Tenapanor as the Core Therapy in the Treatment of Hyperphosphatemia in Patients with Chronic Kidney Disease on Dialysis (OPTIMIZE)

Authors: Steven Fishbane**,** David P. Rosenbaum, Yang Yang, Stuart Sprague, Robert I Lynn, Geoff Block, Arnold Silva, Daniel Weiner, George Fadda, Pablo Pergola

Session Title: Late Breaking Clinical Trials

Format: Mini Oral Presentation (available June 5th, 8:00AM CET)

OPTIMIZE Oral Presentation
As of the interim analysis, 232 patients had been randomized in the OPTIMIZE study to Cohort 1 (straight switch to tenapanor from binder, n=116) or Cohort 2 (start tenapanor and reduce binder dose by 50%, n=116) and 27 binder naïve individuals had been enrolled into Cohort 3 and started on tenapanor. Among participants that had completed 8 weeks of treatment, 47.7% in Cohort 1, 47.8% in Cohort 2 achieved, and 66.7% in Cohort 3 achieved and/or maintained recommended serum phosphorus (s-P) levels ≤ 5.5 mg/dL at week 8. Furthermore, subgroup analyses on randomized participants in Cohort 1 and Cohort 2 demonstrated that 53.3% of participants with a baseline s-P > 5.5 and ≤ 6.5 mg/dL, 51.7% of participants with a baseline s-P > 6.5 and ≤ 7.5, and 38.7% of participants with a baseline s-P > 7.5 mg/dL achieved an s-P ≤ 5.5 mg/dL at week 8. Diarrhea, the most common adverse event in this study, was reported with an incidence rate of 29.3% in Cohort 1, 36.2% in Cohort 2, and 14.8% in Cohort 3. Five participants (1.9%), none from Cohort 3, experienced diarrhea that led to study drug discontinuation.

Abstract Title: Long-Term Safety of Tenapanor for the Control of Serum Phosphorus in Patients with CKD on Dialysis

Authors: Daniel Weiner, Robert I Lynn, Steven Fishbane**,** Yang Yang, David P. Rosenbaum,

Session Title: Bones & Outcomes in CKD

Format: Oral Presentation (June 7th, 12:00-12:15PM CET)

PHREEDOM Oral Presentation
The 52-week PHREEDOM study consisted of a 26-week, open-label, randomized treatment period with a 12-week placebo-controlled randomized withdrawal period, followed by a 14-week open label safety extension period.

Maintenance dialysis patients with serum phosphorus ≥ 6.0 mg/dL and a 1.5 mg/dL increase in serum phosphorus following phosphate binder washout were randomized 3:1 to receive tenapanor 30 mg twice daily or sevelamer carbonate, dosed per package insert. Sevelamer was used as a safety control for comparisons of serious adverse events/hospitalizations. Comparing patients who only received tenapanor versus those who only received sevelamer, the data demonstrated a lower overall incidence of death (3.1% versus 3.6%) as well as serious adverse events leading to hospitalization (22.5% versus 35.8%) and a shorter mean duration of hospitalization (11.5 days versus 13.5 days) in patients treated with tenapanor (n=293) compared to sevelamer (n=137), respectively.

About OPTIMIZE
OPTIMIZE is a randomized, open label study, which will include approximately 330 patients with chronic kidney disease (CKD) on dialysis with hyperphosphatemia. The study is designed to evaluate different methods of initiating tenapanor therapy across the hyperphosphatemia treatment paradigm to optimize phosphorus management in both binder-naïve and binder-treated patients. The objective is to evaluate the ability of tenapanor, with its novel blocking mechanism, administered as core therapy for the treatment of hyperphosphatemia in adult patients with CKD on dialysis, alone or in combination with phosphate binders, to achieve target serum phosphorus (s-P) levels ≤5.5 mg/dL. Patients with s-P >5.5 and ≤10.0 mg/dL during stable phosphate binder treatment are being randomized into in a 1:1 ratio to two different treatment cohorts: Cohort 1, a straight switch approach is used where current phosphate binder treatment is discontinued and patients are switched to tenapanor 30 mg twice daily (BID) or Cohort 2 (50% binder reduction), where current phosphate binder dose is reduced by at least 50% and tenapanor therapy is initiated at 30 mg BID. After week 2, investigators can adjust phosphate binder dose to achieve a s-P level of ≤5.5 mg/dL with tenapanor as the core therapy and binders as adjunctive. A third cohort comprised of phosphate binder naïve patients with s-P >4.5 and ≤10.0 mg/dL (Cohort 3) were enrolled and initiated tenapanor 30 mg BID.

About PHREEDOM
PHREEDOM is a one-year Phase 3 study with a 26-week open-label treatment period, a 12-week double-blind, placebo-controlled randomized withdrawal period, and a 14-week open-label safety extension period. The study randomized a total of 564 patients with CKD on dialysis who had a serum phosphorus level between 6.0 mg/dL and 10.0 mg/dL and had an increase in serum phosphorus of at least 1.5 mg/dL after an up to 3-week phosphate binder wash-out period. Patients were randomized 3:1 to either the tenapanor arm (n=423, n=408 intent to treat) or the active safety control arm (sevelamer n=141). Patients randomized to the active safety control arm were treated with sevelamer for 52 weeks. Patients in the tenapanor arm received tenapanor twice daily at a starting dose of 30 mg with dose adjustments allowed based on serum phosphorus level and gastrointestinal tolerability. At the end of the 26-week treatment period, patients in the tenapanor arm were randomized 1:1 to enter the randomized withdrawal period and either remain on the tenapanor dose they were taking or receive placebo. After the randomized withdrawal period, patients continued on the study for an additional three months as part of the long-term safety extension. Patients in the active safety control arm received sevelamer at an initial dose based on its package insert with dose changes allowed at the discretion of the principal investigator for up to one year.

The primary efficacy endpoint of the study was the difference in change in serum phosphorus between the pooled tenapanor-treated patients and placebo-treated patients in the efficacy analysis set from the end of the 26-week treatment period to the endpoint visit of the 12-week randomized withdrawal period. The efficacy analysis set (n=131) included patients who completed the 26-week treatment period and achieved a 1.2 mg/dL decrease in serum phosphorus in the same period.

About Hyperphosphatemia
Hyperphosphatemia is a serious condition resulting in an abnormally elevated level of phosphorus in the blood that is estimated to affect the vast majority of the 550,000 patients in the United States with CKD on dialysis. The kidney is the organ responsible for regulating phosphorus levels, but when kidney function is significantly impaired, phosphorus is not adequately eliminated from the body. As a result, hyperphosphatemia is a nearly universal condition among people with CKD on dialysis with internationally recognized KDIGO treatment guidelines that recommend lowering elevated phosphate levels toward the normal range (2.5-4.5mg/dL).

About Ardelyx, Inc.
Ardelyx is focused on discovering, developing, and commercializing innovative first-in-class medicines to enhance the lives of patients with kidney and cardiorenal diseases. Ardelyx is advancing tenapanor, a novel product candidate to control serum phosphorus in adult patients with CKD on dialysis, for which the company's NDA is currently under review by the FDA, with a PDUFA date of July 29, 2021. Ardelyx is also advancing RDX013, a potassium secretagogue, for the potential treatment of elevated serum potassium, or hyperkalemia, a problem among certain patients with kidney and/or heart disease and has an early-stage program in metabolic acidosis, a serious electrolyte disorder in patients with CKD. In addition, Ardelyx received FDA approval of IBSRELA® (tenapanor) on September 12, 2019. Ardelyx has established agreements with Kyowa Kirin in Japan, Fosun Pharma in China and Knight Therapeutics in Canada for the development and commercialization of tenapanor in their respective territories.

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 CKD patients on dialysis to achieve target phosphorus levels with the use of tenapanor alone or in combination with phosphate binders. Such forward-looking statements involve substantial risks and uncertainties that could cause 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 associated with the clinical development and regulatory approval 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 May 6, 2021, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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