Ardelyx Presents Positive Data Further Supporting Efficacy and Safety of XPHOZAH® (tenapanor) at National Kidney Foundation 2023 Spring Clinical Meetings

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Three posters support the important role that XPHOZAH, a novel phosphate absorption inhibitor, could potentially play in the treatment of hyperphosphatemia

XPHOZAH consistently lowered serum phosphate in patients, independent of race

Patients with chronic kidney disease (CKD) on maintenance dialysis who responded to treatment for hyperphosphatemia had comparable serum phosphate reductions with XPHOZAH or sevelamer

XPHOZAH was effective at reducing iFGF23 in patients with CKD on maintenance dialysis

WALTHAM, Mass., April 12, 2023 (GLOBE NEWSWIRE) -- Ardelyx, Inc. (Nasdaq: ARDX), a biopharmaceutical company founded with a mission to discover, develop and commercialize innovative, first-in-class medicines that meet significant unmet medical needs, today announced multiple presentations covering additional positive clinical observations of XPHOZAH at the National Kidney Foundation (NKF) 2023 Spring Clinical Meetings, which is taking place in Austin, TX from April 11-15, 2023. Ardelyx has completed three successful Phase 3 pivotal clinical trials, and two additional Phase 4 open-label clinical trials (OPTIMIZE and NORMALIZE) for XPHOZAH, an investigational, novel phosphate absorption inhibitor studied in adult patients with chronic kidney disease (CKD) on maintenance dialysis seeking to control their serum phosphate. XPHOZAH was discovered and developed by Ardelyx.

"The results of these three post hoc analyses reinforce our understanding of the potential value that XPHOZAH offers by expanding the treatment armamentarium for health care providers and their patients with chronic kidney disease on maintenance dialysis who suffer from hyperphosphatemia," said Laura Williams, M.D., M.P.H., chief medical officer of Ardelyx. "These studies demonstrated that patients are seeing measurable benefit from XPHOZAH across different endpoints, and that the novel mechanism of action provides a much-needed additional treatment option for patients."

Posters presented at NKF Spring Clinical Meeting

- Poster # 252 titled ***"Post Hoc Analyses of Serum Phosphate Changes with Tenapanor in Black/African American and White Patients on Maintenance Dialysis"*** reported data on serum phosphate (sP) changes in Black/African American and White patients who were treated with XPHOZAH. This analysis included data from all three Phase 3 registration studies: a 12-week monotherapy study (BLOCK), a 52-week monotherapy study (PHREEDOM) and a four-week combination study (AMPLIFY). For all trials, the first available sP measurement was after one week of treatment, per protocol. Across all three Phase 3 studies, which included a total of 457 patients (53% Black/African American and 47% White), XPHOZAH consistently lowered sP in patients with CKD on maintenance dialysis, regardless of race, and the safety profile was consistent and acceptable across all three studies, with diarrhea being the most common adverse event.
- Poster # 251 titled ***"An In-Depth Analysis of Serum Phosphate Changes in Patients with CKD on Dialysis: Results from the PHREEDOM Study"*** reported results from post hoc analyses of sP concentrations in patients with CKD on maintenance dialysis who were treated with XPHOZAH or sevelamer from the 52-week, Phase 3 monotherapy study (PHREEDOM). In the current analysis, sP concentrations were analyzed in tenapanor-treated and sevelamer-treated patients who had at least a 1.2 mg/dL reduction from baseline at week 26 (defined as sP responders) and for all patients who completed treatment for 52 weeks. This analysis demonstrated these patients had comparable sP reductions when treated with XPHOZAH or sevelamer for hyperphosphatemia. Tenapanor treatment had the added benefit of twice daily dosing and a lower pill burden. Diarrhea was the most common adverse event reported by patients treated with XPHOZAH, with a higher incidence rate in these patients. Prior sevelamer use by over 60% of the sevelamer-treated patients may, in part, explain the lower overall rate of adverse events for these patients compared to the rates reported in the sevelamer prescribing information. Overall, this post hoc analysis of the PHREEDOM study demonstrates the potential value of XPHOZAH as an additional treatment option for hyperphosphatemia in patients with CKD receiving maintenance dialysis.
- Poster # 193 titled **"Evaluation of Changes in Serum FGF23 With Tenapanor Treatment in Patients with Chronic Kidney Disease on Dialysis"** reported data on the effect of XPHOZAH on elevated intact fibroblast growth factor 23 (iFGF23) in patients with CKD on maintenance dialysis from the NORMALIZE and OPTIMIZE studies, an open-label 18-month extension study and a 26-week open label study, respectively. For this analysis, changes in iFGF23 from baseline to the end of NORMALIZE (up to 18 months) and baseline to the end of OPTIMIZE part A (initial 10 weeks of treatment) were evaluated for the full analysis set (FAS) of each study. Among all patients in NORMALIZE from the FAS, median iFGF23 reduction (percent reduction) was 384.0 pg/mL (42.2%) from baseline to the end of the study. In OPTIMIZE, at the end of part A, the median iFGF23 reduction (percent reduction) was 739.2 pg/mL (20%) from baseline in the FAS. While there was variability in the degree of reduction, many patients who responded to XPHOZAH as core therapy, with a reduction in sP levels, also experienced reduction in iFGF23 levels. Results from the NORMALIZE and OPTIMIZE trials demonstrated that XPHOZAH is effective at reducing iFGF23 in patients with CKD on maintenance dialysis, which is consistent with findings from the PHREEDOM study. Results from both NORMALIZE and OPTIMIZE trials support the long-term safety of XPHOZAH. Adverse events were similar to those of previous studies, with diarrhea being the most common adverse event.

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 maintenance dialysis who had a serum phosphate between 6.0 mg/dL and 10.0 mg/dL and had an increase in serum phosphate of at least 1.5 mg/dL after an up to 3-week phosphate binder wash-out period. The primary efficacy endpoint of the study was the difference in change in serum phosphate between the XPHOZAH-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 phosphate in the same period. This study also included an active safety comparator (sevelamer), which had no prespecified efficacy comparisons.

About NORMALIZE
Patients completing the Phase 3 PHREEDOM trial from both the XPHOZAH arm and the sevelamer safety control arm had the option to participate in NORMALIZE, an open-label 18-month extension study. Patients entering the study from the XPHOZAH arm with serum phosphate levels in the normal range were followed with no medication changes. Patients entering the study from the XPHOZAH arm with serum phosphate greater than 4.5 mg/dL had sevelamer tablets added incrementally to achieve normal serum phosphate levels. Patients entering the study from the sevelamer safety control arm had XPHOZAH tablets added to their treatment regimen while reducing sevelamer tablets based on their serum phosphate value to achieve normal serum phosphate levels. The primary objective of the study was to evaluate the ability of XPHOZAH alone or in combination with sevelamer to achieve serum phosphate levels within the normal range (2.5 to 4.5 mg/dL) in patients with CKD on maintenance dialysis whose serum phosphate levels were greater than 6.0 mg/dL at baseline.

About AMPLIFY
AMPLIFY, a double-blind, placebo-controlled, randomized study, enrolled a total of 236 patients with CKD on maintenance dialysis, who, despite phosphate binder therapy, had a serum phosphate level greater than or equal to 5.5 mg/dL and less than or equal to 10.0 mg/dL at screening. After a run-in of two to four weeks, patients were randomized 1:1 to receive tenapanor or placebo twice daily while continuing their established phosphate binder regimen. Baseline serum phosphate at randomization was at a mean level of 6.8 mg/dL. Tenapanor was initiated at a starting dose of 30 mg twice daily with tenapanor dose adjustments allowed based on serum phosphate level and gastrointestinal tolerability. The primary endpoint of the study was the comparison of the change from baseline in serum phosphate levels at week four between the tenapanor and binder arms. The key secondary endpoints included a comparison of the proportion of patients achieving a serum phosphate level below 5.5 mg/dL at week four and relative change from baseline in fibroblast growth factor 23 (FGF23) levels between the tenapanor and binder arms at week four.

About OPTIMIZE
OPTIMIZE is a randomized, open label study, which included 330 patients with CKD on maintenance dialysis with hyperphosphatemia. The study was designed to evaluate different methods of initiating XPHOZAH to optimize phosphate management in both binder-naïve and binder-treated patients. The objective was to evaluate the ability of XPHOZAH, with its novel blocking mechanism, administered as core therapy for the treatment of hyperphosphatemia in adult patients with CKD on maintenance dialysis, alone or in combination with phosphate binders, to achieve target serum phosphate (sP) levels less than or equal to 5.5 mg/dL. The study randomized patients on a stable dose of phosphate binder treatment with sP greater 5.5 and less than or equal to 10.0 mg/dL in a 1:1 ratio to two different treatment cohorts, as well as patients who were phosphate binder naïve with sP greater than 4.5 and less than or equal to 10.0 mg/dL in a third cohort.

About XPHOZAH® (tenapanor)
XPHOZAH, discovered and developed by Ardelyx, is a first-in-class, phosphate absorption inhibitor that has a novel mechanism of action and acts locally in the gut to inhibit the sodium hydrogen exchanger 3 (NHE3), reducing phosphate absorption through the paracellular pathway, the primary pathway of phosphate absorption. This novel blocking mechanism enables a one 30mg tablet twice daily dosing regimen. The most common side effect with XPHOZAH in clinical trials was diarrhea.

About Hyperphosphatemia
Hyperphosphatemia is a serious condition resulting in an abnormally elevated level of phosphate in the blood that is estimated to affect the vast majority of the 550,000 patients in the United States with chronic kidney disease (CKD) on maintenance dialysis. The kidney is the organ responsible for regulating phosphate, but when kidney function is significantly impaired, phosphate is not adequately eliminated from the body. As a result, hyperphosphatemia is a nearly universal condition among people with CKD on maintenance 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 was founded with a mission to discover, develop and commercialize innovative, first-in-class medicines that meet significant unmet medical needs. Ardelyx's first approved product, IBSRELA® (tenapanor) is available in the United States and Canada. Ardelyx is developing XPHOZAH® (tenapanor), a novel product candidate for the control of serum phosphate in adult patients with chronic kidney disease (CKD) on dialysis, which has completed three successful Phase 3 trials. Ardelyx has a Phase 2 potassium lowering compound, RDX013, for the potential treatment of elevated serum potassium, or hyperkalemia, a problem among certain patients with kidney and/or heart disease and an early-stage program in metabolic acidosis, a serious electrolyte disorder in patients with CKD. 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. For more information, please visit https://ardelyx.com/ and connect with us on Twitter, LinkedIn and Facebook.

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 role that tenapanor can play in offering new treatment options for patients with hyperphosphatemia. 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, uncertainties associated with the process for drug development, regulatory approval and commercialization. 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 on Form 10-K filed with the Securities and Exchange Commission on March 2, 2023, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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