# Ardelyx Presents Positive Data Further Supporting Efficacy and Safety of XPHOZAH® (tenapanor) at National Kidney Foundation 2022 Spring Clinical Meetings

April 7, 2022

- *Four posters support the important role that XPHOZAH, with its novel phosphate blocking mechanism, could potentially play in the treatment of hyperphosphatemia*
- *XPHOZAH alone or in combination with binders, increased the proportion of patients able to achieve target phosphorus levels*
- *Patients reported improved experience with phosphate management routine during OPTIMIZE study, compared to previous phosphate lowering therapies*
- *Responder analysis from PHREEDOM demonstrates 77% of patients experienced phosphate lowering with XPHOZAH, with 41% of responders achieving a > 2 mg/dL decrease*

WALTHAM, Mass., April 7, 2022 /PRNewswire/ -- 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 2022 Spring Clinical Meetings (NKF SCM2022), which is taking place in Boston, MA from April 6-10, 2022. Ardelyx has completed three successful Phase 3 pivotal trials, and two additional Phase 4 clinical trials (OPTIMIZE and NORMALIZE) for XPHOZAH, an investigational, first-in-class, phosphate absorption inhibitor for the control of serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis. XPHOZAH was discovered and developed by Ardelyx.

"The responder analysis from the PHREEDOM trial, the onset of action analysis from the Phase 3 program, and new data generated from our Phase 4 studies further build on the body of evidence that support the potential role that XPHOZAH, as a first-in-class phosphate absorption inhibitor, could play in the management of hyperphosphatemia," said Laura Williams, M.D., M.P.H., chief medical officer for Ardelyx. We continue to pursue approval of XPHOZAH and believe this novel treatment option represents an important innovation for patients and providers in the nephrology community."

Arnold Silva, M.D., Ph.D., director of Clinical Research at Boise Kidney and Hypertension Institute, added, "Achieving target phosphorus levels in our patients with CKD on dialysis is an extraordinary challenge. We need novel mechanism therapies like XPHOZAH that have demonstrated the ability to increase the proportion of patients who achieve target phosphorus levels. Additionally, the patient reported outcomes captured in the OPTIMIZE trial further illustrate the potential value this additional treatment option could bring to patients."

**Posters presented at NKF:**

- Poster # 219 titled ***"Analysis From the OPTIMIZE Trial: Evaluating Options for Initiating Tenapanor in CKD Patients on Dialysis with Hyperphosphatemia"*** reported additional analyses conducted on data from the first part of the Phase 4 OPTIMIZE study. In this first part of the study, the safety and efficacy of XPHOZAH was evaluated for 10 weeks across all three study cohorts. Cohorts 1 and 2 (n=151 and 152, respectively) included patients who were already being treated with phosphate binders (PBs). After the first two weeks of treatment, investigators could adjust XPHOZAH and phosphate binder doses to achieve a target sP level of ≤5.5 mg/dL (primary endpoint). The proportion of patients who achieved a normal sP level of ≤4.5 mg/dL was a secondary endpoint. Cohort 3 (n=30) was in patients who were PB-naïve. For patients with uncontrolled hyperphosphatemia despite being on treatment with phosphate binders upon study entry (cohorts 1 and 2), either switching from phosphate binders to XPHOZAH or adding XPHOZAH to a reduced binder dose enabled 34-38% of these patients to achieve target sP levels ≤5.5 mg/dL. For patients with uncontrolled hyperphosphatemia upon study entry that were naïve to binder therapy (cohort 3), initiating treatment with XPHOZAH monotherapy enabled 63.3% of patients to achieve target sP levels ≤5.5 mg/dL. Mild to moderate diarrhea was the most commonly reported adverse event (39.9%), but only 5.0% of patients discontinued the study because of diarrhea. No new safety findings were identified in this study.
- Poster # 216 titled ***"A Long-Term, Open-Label Study to Evaluate the Ability of Tenapanor (Alone or in Combination with Sevelamer) to Achieve Normal Serum Phosphorus in Patients with Chronic Kidney Disease on Dialysis (NORMALIZE) in Patients Treated for Up to 2.5 Years"*** reported results from this Phase 4 study aimed at normalizing sP levels (≤4.5mg/dL) in line with the 2017 KDIGO guidelines in CKD patients on dialysis with hyperphosphatemia. Patients who completed the Phase 3 PHREEDOM study were eligible to participate in NORMALIZE, which enrolled 172 patients, of which 124 completed this study (72.1%). Patients had a mean sP reduction of 1.96 mg/dL (from 7.27 mg/dL at baseline in

PHREEDOM to 5.31 mg/dL at the last post-baseline sP assessment in NORMALIZE). Up to 49.4% of patients treated with XPHOZAH monotherapy or XPHOZAH in combination with sevelamer achieved a sP level within the normal range during the 18-month treatment period, which is 66.3% better than standard of care, at 29.7%, as shown in DOPPS February 2021. The most reported adverse event was diarrhea (22.1%), with only 4 (2.3%) patients discontinuing the study due to diarrhea. No new safety signals were identified.

- Poster # 217 titled ***"Tenapanor Rapidly Lowers Serum Phosphorus (sP) in Patients on Dialysis: An Analysis of Three Trials"*** reported data on the time it took for patients being treated with XPHOZAH to achieve sP lowering. This analysis included data from a 12-week monotherapy study (BLOCK), a 52-week monotherapy study (PHREEDOM), and a 4-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 607 patients, XPHOZAH rapidly reduced sP in dialysis patients with hyperphosphatemia by an average >1 mg/dL at the first timepoint measured, among those who completed at least one week of treatment (n=573).
- Poster # 218 titled ***"The Effect of Tenapanor on Lowering Serum Phosphate (sP): A Responder Analysis From PHREEDOM"*** reported an analysis of the response to treatment from the 26-week randomized treatment period (RTP) of PHREEDOM, the Phase 3 trial that evaluated treatment with monotherapy XPHOZAH or an active safety control (sevelamer), followed by a 12-week placebo-controlled randomized withdrawal period and a 14-week safety extension period. In this analysis, the total change in sP from baseline to the end of the 26-week RTP (or last recorded sP) for each patient was calculated. Of the 407 patients treated with XPHOZAH during the RTP, 76.7% (312/407) had a reduction in sP (i.e., responders). Among responders, 41.3% (129/312) had a decrease in sP of >2 mg/dL, 33.3% (104/312) had a decrease in sP between 1 and 2 mg/dL, and 25.3% (79/312) had a decrease in sP of <1 mg/dL. These results demonstrate that the majority of XPHOZAH-treated patients respond to treatment with a clinically meaningful reduction in sP.

**About OPTIMIZE**

OPTIMIZE is a randomized, open label study, which included 330 patients with chronic kidney disease (CKD) on dialysis with hyperphosphatemia. The study was designed to evaluate different methods of initiating XPHOZAH to optimize phosphorus 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 chronic kidney disease (CKD) on dialysis, alone or in combination with phosphate binders, to achieve target serum phosphorus (s-P) levels ≤5.5 mg/dL. The study enrolled patients with s-P >5.5 and ≤10.0 mg/dL during stable phosphate binder treatment which were randomized in a 1:1 ratio to two different treatment cohorts, as well as patients who were phosphate binder naïve with s-P >4.5 and ≤10.0 mg/dL in a third cohort.

**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. The primary efficacy endpoint of the study was the difference in change in serum phosphorus between the pooled 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 phosphorus in the same period.

**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 phosphorus levels in the normal range were followed with no medication changes. Patients entering the study from the XPHOZAH arm with serum phosphorus > 4.5 mg/dL had sevelamer tablets added incrementally to achieve normal serum phosphorus 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 phosphorus value to achieve normal serum phosphorus levels. The primary objective of the study was to evaluate the ability of XPHOZAH alone or in combination with sevelamer to achieve serum phosphorus levels within the normal range (2.5 to 4.5 mg/dL) in patients with chronic kidney disease on dialysis whose serum phosphorus levels were greater than 6.0 mg/dL at baseline.

**About XPHOZAH® (tenapanor)**

XPHOZAH, discovered and developed by Ardelyx, is a first-in-class phosphate absorption inhibitor (PAI) that has a unique 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 BID 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 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 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. Ardelyx is developing XPHOZAH® (tenapanor), a novel product candidate to control serum phosphorus in adult patients with CKD on dialysis, which has completed three successful Phase 3 trials. 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. 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 the potential for XPHOZAH in treating hyperphosphatemia, either 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, uncertainties associated with the commercialization of drugs, the drug development process and the 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 28, 2022, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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