Ardelyx and Kyowa Kirin Highlight New Data Supporting the Clinical Safety and Efficacy of First-In-Class, Phosphate Absorption Inhibitor Tenapanor at ASN's Kidney Week 2020

October 22, 2020

--Data presented across five posters continue to support the foundational role tenapanorcould play in the treatment of hyperphosphatemia--

--Exhibitor Spotlight presentation highlights advances in the science of phosphate absorption--

FREMONT, Calif. and TOKYO, Oct. 22, 2020 /PRNewswire/ -- **Ardelyx, Inc.** (Nasdaq: ARDX), a biopharmaceutical company developing targeted, first-in-class medicines to improve the lives of patients with kidney and cardiovascular diseases, and **Kyowa Kirin Co., Ltd.** (Kyowa Kirin, TSE: 4151) today highlighted new clinical data presented within five posters at Kidney Week 2020, this year's virtual Annual Meeting of the American Society of Nephrology (ASN) that is now underway.

Of the posters presented today, three highlight tenapanor clinical data from Ardelyx's Phase 3 trials in the U.S., including the BLOCK, AMPLIFY, and PHREEDOM studies, while two present results from the Phase 2 studies evaluating the efficacy and safety of tenapanor in Japanese patients on hemodialysis conducted by Kyowa Kirin, to whom Ardelyx has licensed exclusive rights to develop and commercialize tenapanor in Japan for the treatment of cardiorenal diseases. In Japan, Kyowa Kirin has conducted three Phase 2 trials of tenapanor as KHK7791. Tenapanor, which was discovered and developed by Ardelyx, is a first-in-class therapy currently under review for potential marketing approval by the U.S. Food and Drug Administration (FDA) for the control of serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis.

Kevin Martin, MD, Professor of Internal Medicine and Director, Division of Nephrology, Saint Louis University commented: "Despite the serious cardiovascular consequences of elevated phosphorus levels, and the development of a variety of phosphate binders, we have made little progress in achieving sustained control of hyperphosphatemia over the past 30 years. Recent advances in our mechanistic understanding of phosphate absorption have led to a whole new way of thinking about how to manage hyperphosphatemia. With its novel mechanism of action targeting paracellular phosphate transport and comprehensive clinical data continuing to support its efficacy and safety, I believe tenapanor, if approved, has the potential to truly transform the management of hyperphosphatemia."

Ardelyx Poster Presentations:

- **ePoster #PO0384, entitled "*Long-term Safety and Efficacy of Tenapanor for the Control of Serum Phosphorus in Patients with CKD on Dialysis,*"** further summarizes data from PHREEDOM, a long-term Phase 3 U.S. study evaluating the safety and efficacy of tenapanor for the control of serum phosphorus in patients with CKD on dialysis. New details presented demonstrate that, within the efficacy analysis set, treatment with tenapanor resulted in sustained reductions in serum phosphorus concentrations, decreasing mean serum phosphorus from 7.7 mg/dL at baseline to 5.1 mg/dL at the end of the randomized treatment period.
- **ePoster #PO0374, entitled "*Efficacy of Tenapanor for the Control of Serum Phosphorus in Patients with CKD on Dialysis: Novel Mechanism of Action Allows for Both Monotherapy and Dual Mechanism Approach,*"** presents clinical data from two Phase 3 clinical trials, demonstrating that tenapanor reduces serum phosphorus when used as monotherapy in hyperphosphatemia patients with CKD on dialysis (BLOCK trial) and reduces serum phosphorus levels in patients with difficult-to-control hyperphosphatemia when used with phosphate binders as part of a dual-mechanism approach (AMPLIFY trial). The poster highlights the need for new strategies to manage hyperphosphatemia and suggests that tenapanor, with its novel mechanism of action, could offer a new treatment approach for patients with CKD on dialysis.
- **ePoster #PO0376, entitled "*Tolerability of Tenapanor, an Investigational, First-in-Class, Non-Binder Therapy for the Control of Serum Phosphorus in Patients with CKD on Dialysis,*"** presents an in-depth analysis of the tolerability profile of tenapanor across three pivotal clinical studies, BLOCK, PHREEDOM, and AMPLIFY, concluding that tenapanor was generally well tolerated in all studies and that the overall gastrointestinal tolerability of tenapanor is consistent with its novel mechanism of action.

Kyowa Kirin Poster Presentations:

- **ePoster #PO0382, entitled "*Dose-Response Efficacy and Tolerability of Tenapanor on Hyperphosphatemia in Japanese Hemodialysis Patients: Results of a Randomized Phase 2 Study,*"** concludes that tenapanor significantly decreased serum phosphorus levels in a dose-dependent manner, and was generally well tolerated across doses in Japanese patients. Compared to placebo, the 30mg BID dosing groups produced a statistically significant 2.6 mg/dL mean reduction (p<0.001) in serum phosphorus from baseline to the end of the six-week treatment period.
- **ePoster #PO0375, entitled "*Efficacy and Safety of Add-on Tenapanor to Phosphate Binders for Refractory Hyperphosphatemia in Japanese Patients on Hemodialysis: A Phase 2, Double-Blind Study,*"** concludes that, the efficacy and safety of tenapanor with phosphate binders was consistent with other studies conducted in Japan where tenapanor was administered as a single agent. Compared to placebo and phosphate binders, treatment with tenapanor and phosphate binders achieved a statistically significant 2.1 mg/dL mean reduction (p<0.001) in serum phosphorus, with 87% of patients in the tenapanor group achieving target phosphorus levels.

All poster presentations are now publicly available and can be accessed on demand HERE.

In addition to the poster presentations during the ASN Annual Meeting, an Exhibitor Spotlight presentation, sponsored by Ardelyx, provides information on advances in the science of phosphate absorption and clinical data on tenapanor:

"ADVANCING THE SCIENCE OF PHOSPHATE ABSORPTION: Paracellular Pathway and Implications for Phosphorus Management." Guest speakers focus on the following topics:

- **New Understanding of Phosphate Absorption May Explain Challenges in Phosphorus Management**
  PRESENTED BY: KAMYAR KALANTAR-ZADEH, MD, MPH, PhD, Professor of Medicine, Pediatrics, Public Health, Epidemiology, and Nursing Sciences, Chief, Division of Nephrology and Hypertension and Kidney Transplantation, University of California, Irvine, School of Medicine
- **Tenapanor: An Investigational Therapy for the Treatment of Hyperphosphatemia**
  PRESENTED BY: GLENN M. CHERTOW, MD, MPH, Chief, Division of Nephrology Stanford University School of Medicine

To view the full presentation, click on the Ardelyx Exhibitor Spotlight program **HERE**.

About Tenapanor for Hyperphosphatemia
Tenapanor, discovered and developed by Ardelyx, is a first-in-class, phosphate absorption inhibitor currently under review by the FDA (PDUFA date: April 29, 2021) for the control of serum phosphorus in adult patients with CKD on dialysis. Tenapanor has a unique mechanism of action that acts locally in the gut to inhibit the sodium hydrogen exchanger 3 (NHE3). This results in a conformational change of the epithelial cell junctions, thereby significantly reducing paracellular uptake of phosphate at the primary pathway of phosphate absorption. Tenapanor has been studied in three Phase 3 clinical trials in the U.S., all of which have met their primary endpoint and support the potential role of tenapanor as a foundational treatment in the management of hyperphosphatemia. In 2017, Ardelyx and Kyowa Kirin entered into a license agreement that provides Kyowa Kirin exclusive rights to develop and commercialize tenapanor in Japan for the treatment of cardiorenal diseases. In Japan, Kyowa Kirin has conducted three Phase 2 trials of tenapanor as KHK7791.

About Hyperphosphatemia
Hyperphosphatemia is a serious condition resulting in an abnormally elevated level of phosphorus in the blood that is estimated to affect more than 745,000 dialysis patients in major developed countries. 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. Despite treatment with phosphate binders (the only approved therapy for hyperphosphatemia), 77% of CKD patients on dialysis are unable to consistently maintain phosphorus levels ≤5.5 mg/dL over a six-month period (Spherix Global Insights: RealWorld Dynamix, Dialysis 2019). Phosphorus levels greater than 5.5 mg/dL have been shown to be an independent risk factor for cardiovascular morbidity and mortality in patients requiring dialysis (Block 2004), and internationally recognized treatment guidelines recommend lowering elevated phosphate levels toward the normal range (<4.6mg/dL).

About Ardelyx, Inc.
Ardelyx is a biopharmaceutical company translating scientific breakthroughs into promise for patients, driven to advance targeted therapies where significant medical needs persist. We have developed a unique and innovative platform that has enabled the discovery of new biological mechanisms and pathways to create targeted, first-in-class, oral, small molecule therapies to meet these needs. Our lead candidate, tenapanor, is currently under FDA review for the control of serum phosphorus in adult patients with chronic kidney disease on dialysis. Our discovery platform has also led us to the discovery of a lead candidate in our RDX013 program for the potential treatment of high potassium, or hyperkalemia, a common condition in patients with kidney and/or heart disease. For more information, please visit https://ardelyx.com/.

About Kyowa Kirin Co., Ltd.
Kyowa Kirin commits to innovative drug discovery driven by state-of-the-art technologies. The company focuses on creating new values in the four therapeutic areas: nephrology, oncology, immunology/allergy and neurology. Under the Kyowa Kirin brand, the employees from 40 group companies across North America, EMEA, and Asia/Oceania unite to champion the interests of patients and their caregivers in discovering solutions wherever there are unmet medical needs. You can learn more about the business of Kyowa Kirin at: https://www.kyowakirin.com.

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 for tenapanor to be approved for marketing by the FDA for the control of serum phosphorus in chronic kidney disease patients on dialysis. Such forward-looking statements involve substantial risks and uncertainties that could cause the development of Ardelyx's product candidates 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 associated with the regulatory approval process, and uncertainties in the drug commercialization 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 August 6, 2020, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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