FDA Grants Appeal for Ardelyx's XPHOZAH® (tenapanor)

December 29, 2022

Office of New Drugs directs the Division of Cardiology and Nephrology to work with Ardelyx to develop a label to support the commercialization of XPHOZAH; Ardelyx to resubmit NDA in the first half of 2023

Upon approval, XPHOZAH would be the first and only phosphate absorption inhibitor, offering patients a novel mechanism

Conference call to be held Dec. 29, 2022, at 8:00 AM ET

WALTHAM, Mass., Dec. 29, 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 that the Office of New Drugs (OND), Center for Drug Evaluation and Research of the U.S. Food and Drug Administration (FDA) granted the appeal to the Complete Response Letter (CRL) for the New Drug Application (NDA) for XPHOZAH.

In the response letter, OND directed the FDA's Division of Cardiology and Nephrology (DCN) to work with Ardelyx to develop an appropriate label. Ardelyx believes that a label could reflect an indication for patients whose hyperphosphatemia is insufficiently managed on binder therapy. In addition, the letter guided Ardelyx to request a meeting with the DCN to determine specific information that will form the basis for resubmission of the NDA for XPHOZAH. Ardelyx will request this meeting as soon as possible to enable the company to resubmit the NDA in the first half of 2023.

"By granting the appeal, we believe that OND has sent a powerful message regarding the importance of bringing innovation to the more than 400,000 patients on dialysis who struggle every day, at every meal, to control their phosphorus levels and yet are unable to do so. For more than 60 years, the only choice physicians had for patients has been phosphate binders, and the patients have desperately needed novel mechanism therapies. This is a momentous day for Ardelyx and for all the members of the broader kidney disease community who have supported the development of XPHOZAH over the past ten years," said Mike Raab, president and chief executive officer of Ardelyx. "We appreciate the FDA's responsiveness to the clear guidance from the Cardiovascular and Renal Drugs Advisory Committee, recognizing the importance of providing a novel therapy for physicians. This could not have been accomplished without the support from members of the kidney community who spoke at the Advisory Committee meeting about the significant unmet patient need and the important role XPHOZAH could play in the hyperphosphatemia treatment paradigm. We look forward to working with the FDA to bring this important medicine to patients and their treating physicians."

Kevin Martin, M.D., Professor of Internal Medicine in the Division of Nephrology at St. Louis University, added, "This FDA decision is extremely positive for the kidney community and brings us one step closer to having a much-needed novel therapy for the treatment of hyperphosphatemia. The majority of patients are in need of a different approach, as today, despite best efforts with phosphate binders, close to 80% of patients are unable to consistently achieve guideline-established target serum phosphate levels. In clinical trials, XPHOZAH, with its unique mechanism of action that blocks intestinal phosphate transport, provided clinically meaningful reductions in serum phosphate with one small pill twice a day. As was clear during last month's Advisory Committee meeting, patients and physicians are anxious to have access to XPHOZAH."

The OND's decision follows a favorable outcome of the November 16, 2022 CRDAC meeting, where the Advisory Committee voted nine to four that the benefits of treatment with XPHOZAH outweigh its risks for the control of serum phosphorus in adults with chronic kidney disease (CKD) on dialysis when administered as a monotherapy, and voted ten to two, with one abstention, that the benefits of treatment with XPHOZAH in combination with phosphate binder treatment outweigh its risks. The NDA for XPHOZAH for the control of serum phosphorus is supported by a comprehensive development program involving more than 1,200 patients and included three Phase 3 clinical trials, all of which met their primary and key secondary endpoints. Upon approval, XPHOZAH would be the first and only phosphate absorption inhibitor for adult patients with CKD on dialysis with hyperphosphatemia.

Conference Call Information
The company will host a conference call on December 29, 2022, at 8:00 AM ET. To participate in the conference call, please call (866) 374-5140 (toll-free) or (404) 400-0571 (toll) and reference call ID number 65128972#. A webcast of the call can also be accessed by visiting the Investor page of the company's website at www.ardelyx.com and will be available on the website for 30 days following the call.

About XPHOZAH (tenapanor) for Hyperphosphatemia
XPHOZAH (tenapanor), discovered and developed by Ardelyx, is an investigational first-in-class phosphate absorption inhibitor (PAI). XPHOZAH, with its unique blocking mechanism of action, 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 30 mg tablet BID (twice daily) dosing regimen. The most common side effect with XPHOZAH in clinical trials was diarrhea.

About Hyperphosphatemia
Elevated levels of serum phosphorus in the blood, or hyperphosphatemia (HP), 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 with internationally recognized KDIGO treatment guidelines that recommend lowering elevated phosphate levels toward the normal range (2.5-4.5mg/dL).

The only adverse reaction reported in more than 5% of patients treated with XPHOZAH in the Phase 3 trials was diarrhea, with an incidence of 47%. The majority of these events occurred during the 26-week randomized treatment period and were mild-to-moderate in severity and transient in nature, occurring soon after initiation of treatment, and generally resolving with continued treatment. Severe diarrhea was reported in 5% of XPHOZAH-treated patients in these trials.

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 management of hyperphosphatemia in adult patients with 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 @Ardelyx, 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, Ardelyx's expectation regarding the timing of the resubmission of the NDA for XPHOZAH; Ardelyx's expectation regarding the development of a label for the commercialization of XPHOZAH; Ardelyx's belief regarding what indication may be included in such label; and Ardelyx's expectations regarding the opportunity to bring XPHOZAH to patients and treating physicians. 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 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 November 3, 2022, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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