Ardelyx Reports Positive Results from Its Phase 2b Clinical Trial Evaluating Tenapanor in IBS-C Patients

October 1, 2014

FREMONT, Calif., Oct. 1, 2014 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage biopharmaceutical company focused on cardio-renal, gastrointestinal and metabolic diseases, today announced positive results from its 371 patient Phase 2b clinical trial evaluating tenapanor in patients with constipation-predominant irritable bowel syndrome (IBS-C). Results from this study demonstrated statistically significant and clinically meaningful improvement in IBS-C symptoms for tenapanor-treated patients compared to patients receiving placebo. At the 50 mg dose, the study met its primary efficacy endpoint of an increase in the complete spontaneous bowel movement (CSBM) responder rate. Most secondary endpoints, including abdominal pain and other abdominal and IBS-C symptoms, demonstrated clinically meaningful improvements. Tenapanor was well-tolerated, and the safety results were consistent with those observed in previous tenapanor trials.

"We are pleased to see that tenapanor continues to demonstrate the degree of activity that was shown in the Phase 2a clinical trial for IBS-C," said Mike Raab, President and CEO of Ardelyx. "We are excited about the potential for tenapanor in IBS-C. We will work with our partner, AstraZeneca, to determine the best approach for the development of tenapanor in IBS-C and the renal indications that we are evaluating."

"The magnitude of the response to tenapanor in this trial, combined with the fact that the drug was well-tolerated, with only a modest incidence of diarrhea is remarkable. In addition, of those subjects who were administered 50 milligrams of tenapanor twice a day, over 65 percent responded that they were 'quite satisfied' or 'very satisfied' with tenapanor versus about 38 percent with placebo, a result that was also statistically significant," said David Rosenbaum, Ph.D., Ardelyx's Vice President of Drug Development.

Tenapanor, a minimally-absorbed inhibitor of the intestinal sodium transporter NHE3, has demonstrated the ability to reduce the absorption of dietary sodium and phosphate. Ardelyx licensed tenapanor to AstraZeneca in October 2012. In addition to IBS-C, Ardelyx and AstraZeneca are evaluating tenapanor for the treatment of hyperphosphatemia in patients with end-stage renal disease (ESRD) in an ongoing Phase 2b study, and in an ongoing Phase 2a study, tenapanor is being evaluated for its effect on markers of kidney disease and fluid status in patients with chronic kidney disease (CKD).

The Phase 2b Clinical Trial

The clinical trial was a Phase 2b, randomized, double blind, placebo-controlled, multi-center study to evaluate the safety and efficacy of three dose levels of tenapanor in 371 subjects with IBS-C as defined by the Rome III criteria and who had active disease as determined during a two-week screening period. Subjects who qualified and who were randomized into the study received 5, 20, or 50 mg of tenapanor or placebo twice daily for 12 consecutive weeks. At the end of this treatment period, subjects were followed for an additional 4 weeks. The primary endpoint, overall CSBM responder rate, was achieved in 60.7 percent of patients receiving tenapanor 50 mg twice daily versus 33.7 percent receiving placebo (p &< 0.001). A responder was defined as a patient who had an increase of greater than or equal to one CSBM from baseline during 6 out of 12 weeks. The results are reported on an intent-to-treat basis.

The overall responder rate, or dual composite endpoint percent, was achieved in 50 percent of patients receiving tenapanor 50 mg twice daily versus 23.6 percent receiving placebo (p &< 0.001). An overall responder was defined as a patient who was an overall CSBM responder and who experienced at least a 30 percent decrease in abdominal pain from baseline in the same week for 6 of 12 weeks.

Most secondary endpoints measured also demonstrated significant improvements for patients receiving 50 mg tenapanor twice daily compared to placebo-treated patients.

A dose response relationship among all doses was observed in the primary endpoint, as well as in most secondary endpoints, although statistical significance was not achieved at the 5 mg or 20 mg doses. Additionally, the activity of tenapanor was maintained throughout the entire 12-week treatment period.

Tenapanor was well-tolerated in these patients, and the safety results were consistent with those observed in previous tenapanor trials. The most common adverse events at 50 mg twice daily (greater than or equal to 5 percent) that occurred more frequently in tenapanor-treated patients compared to placebo-treated patients were diarrhea at 11.2 percent vs. 0 percent, and urinary tract infections at 5.6 percent vs. 4.4 percent. Overall rates of discontinuation due to adverse events were 4.5 percent for the tenapanor-treated patients (50 mg twice daily) and 3.3 percent for the placebo-treated patients. Based on the analysis of plasma samples tested as part of the study, the minimally systemic nature of tenapanor was confirmed. The findings of the clinical study are expected to be presented in an appropriate peer-reviewed forum.

IBS-C

IBS-C is a gastrointestinal disorder in which abdominal pain or discomfort is associated with constipation, significantly affecting health and quality of life. It is unknown what causes IBS-C. There is no specific test or biomarker for IBS-C and therefore, its presence is diagnosed by symptoms and by eliminating other disorders. IBS-C is very similar to chronic constipation but is clinically distinguished by its significant pain component.

Based on reports in the literature regarding the prevalence of IBS in the U.S. population and the percentage of individuals who have IBS-C as opposed to other forms of IBS, Ardelyx estimates that approximately 1.4 percent of the U.S. population has IBS-C, or about 4.4 million individuals. Of those, approximately 1.0 million patients have been diagnosed with IBS-C. Additionally, there are about 6.6 million IBS-C patients in Europe and about 3.4 million in Japan.

Tenapanor

Tenapanor (also known as RDX5791 and AZD1722) is a minimally-absorbed small molecule inhibitor of NHE3, a transporter of sodium in the gastrointestinal tract. Orally administered tenapanor has been shown in clinical trials to reduce the intestinal absorption of both dietary sodium and phosphorus. A total of 12 clinical trials of tenapanor have been completed or are ongoing, including over 830 subjects who have been administered tenapanor to date. In addition to the IBS-C Phase 2b clinical trial, Ardelyx and AstraZeneca are evaluating tenapanor in two other indications:

- ESRD patients on hemodialysis to treat hyperphosphatemia: Phase 2b randomized, double-blind, placebo-controlled clinical trial in 150 ESRD patients to evaluate the effects of tenapanor on serum phosphorus. Enrollment is ongoing and the results of this clinical trial are expected in the first half of 2015.
- Stage 3 CKD patients with type 2 diabetes mellitus, the presence of the protein albumin in the urine, or albuminuria, and high blood pressure: Phase 2a randomized, double-blind, placebo-controlled clinical trial in 140 patients to evaluate the effects of tenapanor on kidney function and fluid overload. Enrollment is ongoing and the results of this clinical trial are expected in the second half of 2015.

Conference Call / Web Cast Information

Ardelyx management will host a live conference call and webcast today at 8:00 a.m. Eastern Time to discuss the Phase 2b IBS-C results.

The live webcast and a replay may be accessed by visiting Ardelyx's website at http://ir.ardelyx.com/

Please connect to the Company's website at least 15 minutes prior to the live webcast to ensure adequate time for any software download that may be needed to access the webcast. Alternatively, please call (855) 296-9612 (U.S.) or (920) 663-6277 (international) to listen to the live conference call. The conference ID number for the live call is 13895374. Please dial in approximately 10 minutes prior to the call. Telephone replay will be available approximately two hours after the call. To access the replay, please call (855) 859-2056 (U.S.) or (404) 537-3406 (international). The conference ID number for the replay is 13895374. The telephone replay will be available until October 8, 2014.

About Ardelyx, Inc.

Ardelyx is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, non-systemic, small molecule therapeutics that work exclusively in the gastrointestinal tract to treat cardio-renal, gastrointestinal and metabolic diseases. The Company has developed a proprietary drug discovery and design platform enabling it, in a rapid and cost-efficient manner, to discover and design novel drug candidates. Utilizing this platform, Ardelyx has discovered and designed tenapanor.

Ardelyx formed a collaborative partnership with AstraZeneca in October 2012 to develop and commercialize tenapanor. In addition to tenapanor, the Company has discovered small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in ESRD, a program licensed to Sanofi, and independently is advancing several additional research programs focused in cardio-renal, gastrointestinal and metabolic diseases. Ardelyx is located in Fremont, California. For more information, please visit Ardelyx's website at www.ardelyx.com.

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 tenapanor in treating IBS-C patients, the potential of tenapanor in treating the renal indications for which it is currently being evaluated, the availability and timing of data from ongoing tenapanor clinical trials, and the potential of our drug discovery and design platform. Such forward-looking statements involve substantial risks and uncertainties that could cause the development of tenapanor, 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 inherent in the clinical development process, Ardelyx's reliance upon AstraZeneca for the development of tenapanor, and AstraZeneca's right under the license agreement to choose which indication or indications for which tenapanor will be developed, 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 second quarter report filed on Form 10-Q filed with the Securities and Exchange Commission on August 8, 2014.

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