Ardelyx Presents Positive Results from Its Phase 2b Clinical Trial Evaluating Tenapanor in IBS-C Patients at Digestive Disease Week 2015

May 19, 2015

FREMONT, Calif., May 19, 2015 /PRNewswire/ -- Ardelyx, Inc. (NASDAQ: ARDX), a clinical-stage biopharmaceutical company focused on cardio-renal, gastrointestinal, and metabolic diseases, today presented Phase 2b clinical trial results that demonstrated statistically significant and clinically meaningful improvement in IBS-C symptoms for tenapanor-treated patients compared to patients receiving placebo. As previously reported, at the 50 mg dose of tenapanor, 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.

The findings were presented today in an oral presentation entitled, "*Efficacy and Safety of Tenapanor in Patients with Constipation Predominant Irritable Bowel Syndrome: A 12-Week, Double-Blind, Placebo-Controlled, Randomized Phase 2b Trial*" at the Digestive Disease Week (DDW) 2015 conference being held in Washington, D.C. from May 16-19, 2015.

"IBS-C impacts the quality of life of millions of patients yet is still one of the most enigmatic diseases of the gut," said William Chey, MD, Professor of Internal Medicine at University of Michigan. "Tenapanor, if successfully developed, would represent an entirely new mechanism of action for the treatment of IBS-C that could give patients important options for their disease."

"More than 14 million people worldwide are estimated to suffer from IBS-C, many of whom are not effectively treated by current marketed therapies," said Mike Raab, President & Chief Executive Officer of Ardelyx. "Based on tenapanor's clinical results through the Phase 2b program, we believe that it has the potential to offer a best-in-class treatment for this underserved population."

Phase 2b Clinical Trials for Tenapanor in IBS-C

The Phase 2b clinical trial was a randomized, double blind, placebo-controlled, multi-center study to evaluate the safety and efficacy of three dose levels of tenapanor in 356 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 abdominal pain responder rate was achieved in 65.5 percent of patients receiving tenapanor 50 mg twice daily versus 48.3 percent receiving placebo (p = 0.026). An overall abdominal pain responder was defined as a patient who experienced at least a 30 percent decrease in abdominal pain from baseline for 6 of 12 weeks.

The overall responder rate, or dual composite endpoint percent, was achieved in 50.0 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 both an overall CSBM responder and an overall abdominal pain responder in the same week for 6 of 12 weeks.

As shown in the table, other key secondary endpoints that exhibited significant improvements for patients receiving 50 mg tenapanor twice daily compared to placebo-treated patients included abdominal discomfort, abdominal bloating, straining, stool consistency, CSBM per week and SBM per week.

Phase 2b Primary and Key Secondary Endpoints

Endpoint	Placebo	Tenapanor 50mg twice daily	p-value
Primary Endpoint: responder analysis ≥6 of 12 weeks*			
≥1 CSBM increase	33.7%	60.7%	p &< 0.001
Secondary Endpoints: responder analysis ≥6 of 12 weeks*			
≥30% abdominal pain reduction	48.3%	65.5%	p=0.026
≥30% abdominal pain reduction and ≥1 CSBM increase in same week	23.6%	50.0%	P &< 0.001
Secondary Endpoints: LS mean change from baseline to week 12**			
Abdominal pain (0-10)	-2.3	-3.1	P=0.014
Abdominal discomfort (0-10)	-2.0	-3.0	P=0.004
Abdominal bloating (0-10)	-1.6	-2.6	P=0.023
Straining (0-5)	-0.7	-1.2	P=0.006
Stool consistency BSFS***	1.0	2.2	P &< 0.001
CSBM/week	0.9	2.7	P &< 0.001
SBM/week	1.6	3.4	P=0.006

* P-value uses Cochran-Mantel-Haenszel analysis
** P-Value Uses Analysis of covariance analysis
*** BSFS is the Bristol Stool Form Scale with 1 = hard and 7 = watery

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 (3.3 percent due to diarrhea) 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 abstract for oral presentation is available in Gastroenterology, Vol. 148, Issue 4, S-191-S-192, 2015. Please refer to Ardelyx's website for a copy of the DDW slide presentation at http://ir.ardelyx.com.

Ardelyx formed a partnership with AstraZeneca in October 2012 to develop and commercialize tenapanor. Under the terms of the agreement, AstraZeneca is obligated to communicate to Ardelyx, on or before June 29, 2015, whether it will continue the development of tenapanor. Should AstraZeneca decide to pursue the development of only the IBS-C indication, Ardelyx will be entitled to a milestone payment of $10 million. Should AstraZeneca decide to pursue the development of any other indication or multiple indications, Ardelyx will be entitled to receive a $20 million milestone payment. Ardelyx is scheduled for an end of phase 2 meeting with the FDA scheduled in June. If AstraZeneca decides to return the program to Ardelyx, the Company seeks to be in a position to initiate a Phase 3 clinical program for tenapanor in IBS-C in the fourth quarter of 2015.

About Irritable Bowel Syndrome with Constipation (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.

About Ardelyx, Inc.

Ardelyx is a clinical-stage biopharmaceutical company focused on the discovery, development and commercialization of innovative, minimally-systemic, small molecule therapeutics that work exclusively in the gastrointestinal tract to treat cardio-renal, gastrointestinal and metabolic diseases. Ardelyx 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, the Company has discovered and designed tenapanor. Ardelyx formed a partnership with AstraZeneca in October 2012 to develop and commercialize tenapanor. In addition to tenapanor, Ardelyx has discovered small molecule NaP2b inhibitors for the treatment of hyperphosphatemia in patients on dialysis, 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 timing of AstraZeneca's decisions regarding its future plans for tenapanor, the potential receipt and timing of milestone payments from AstraZeneca in connection with any decision by it to continue the development of tenapanor and our future development plans and the timing thereof, if the rights to tenapanor are returned to us. 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, AstraZeneca's right under the license agreement to choose which indication or indications for which tenapanor will be developed, and AstraZeneca's right under the license agreement to terminate the agreement upon written notice to Ardelyx. 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 filed on Form 10-Q with the Securities and Exchange Commission on May 12, 2015.

Logo - http://photos.prnewswire.com/prnh/20140619/119451