# UNITED STATES
# SECURITIES AND EXCHANGE COMMISSION
**Washington, D.C. 20549**

# FORM 8-K

**CURRENT REPORT**
**Pursuant to Section 13 or 15(d)**
**of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): May 19, 2015**

# ARDELYX, INC.
**(Exact name of registrant as specified in its charter)**

| **Delaware** | **001-36485** | **26-1303944** |
|---|---|---|
| **(State or other jurisdiction of incorporation)** | **(Commission File Number)** | **(IRS Employer Identification Number)** |

**34175 Ardenwood Blvd.**
**Fremont, CA 94555**
**(Address of principal executive offices, including Zip Code)**

**Registrant's telephone number, including area code: (510) 745-1700**

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

**Item 7.01 Regulation FD Disclosure.**

On May 19, 2015, Ardelyx, Inc. (the "Company") announced that it will present clinical results from a Phase 2b trial evaluating tenapanor in patients with irritable bowel syndrome at the Digestive Disease Week (DDW) 2015 conference being held in Washington, D.C., from May 16-19, 2015. A copy of the press release is attached hereto as Exhibit 99.1, and a copy of the presentation of the data is attached hereto as Exhibit 99.2.

The information furnished under this Item 7.01 shall not be considered "filed" under the Securities Act of 1934, as amended, nor shall it be incorporated by reference into any future filing under the Securities Act of 1933, as amended, or under the Securities Exchange Act of 1934, as amended, unless the Company expressly sets forth in such future filing that such information shall be considered "filed" or incorporated by reference therein.

**Item 9.01 Financial Statements and Exhibits.**

**(d) Exhibits.**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release dated May 19, 2015 |
| 99.2 | Corporate Presentation of Ardelyx, Inc. |

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

Date: May 19, 2015

ARDELYX, INC.

By: /s/ Mark Kaufmann
Mark Kaufmann
Chief Financial Officer

**EXHIBIT INDEX**

| Exhibit No. | Description |
|---|---|
| 99.1 | Press Release dated May 19, 2015 |
| 99.2 | Corporate Presentation of Ardelyx, Inc. |

**Exhibit 99.1**

34175 Ardenwood Blvd
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www.ardelyx.com

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

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SOURCE Ardelyx, Inc.

# Efficacy and safety of tenapanor in patients with constipation-predominant irritable bowel syndrome: a 12-week, double-blind, placebo-controlled, randomized phase 2b trial

William D Chey,[1] Anthony J Lembo,[2] James A Phillips,[3] David P Rosenbaum[4]

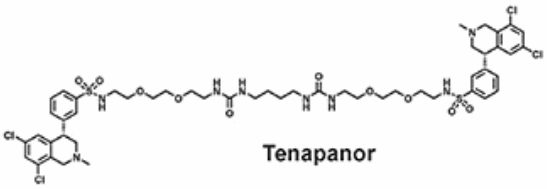
[1]Division of Gastroenterology, Department of Medicine, University of Michigan Health System, Ann Arbor, MI, USA; [2]Division of Gastroenterology, Department of Medicine, Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, USA; [3]Sage Statistical Solutions, Inc., Efland, NC, USA; [4]Ardelyx, Inc., Fremont, CA, USA

# Disclosures

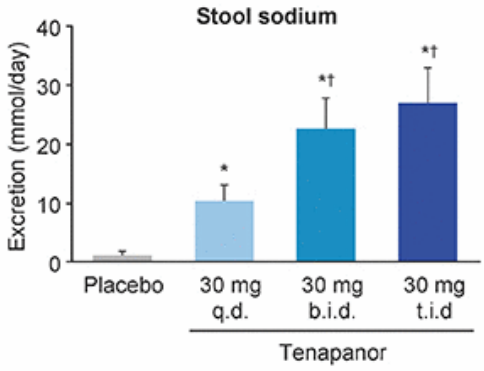
- William D Chey
  - Consultancy: Ardelyx, Asubio Pharmaceuticals, AstraZeneca, Forest Laboratories (Actavis), Ironwood Pharmaceuticals, Nestlé Health Science, Prometheus Laboratories, QOL Medical, Salix Pharmaceuticals, SK Biopharmaceuticals, Sucampo and Takeda
  - Research funding: Ironwood Pharmaceuticals, Nestlé Health Science, Perrigo Company, Prometheus Laboratories, Synthetic Biologics and Vibrant Pharma
- Anthony J Lembo
  - Consultancy: Ardelyx, Salix Pharmaceuticals, Ironwood Pharmaceuticals, Forest Laboratories (Actavis) and Prometheus Laboratories
- James A Phillips
  - Consultancy: Ardelyx
- David P Rosenbaum
  - Employment and ownership interests: Ardelyx
- This study was funded by AstraZeneca and Ardelyx

# Tenapanor (AZD1722) acts locally in the gut to reduce sodium absorption

- Sodium/hydrogen exchanger isoform 3 (NHE3) plays an important role in intestinal sodium/fluid homeostasis
- Tenapanor is a small-molecule inhibitor of NHE3
- Preclinical and phase 1 studies show that tenapanor reduces sodium absorption and has minimal systemic availability
- In a preclinical model, tenapanor showed antinociceptive effects on stress-induced mechanical colorectal hypersensitivity



Tenapanor



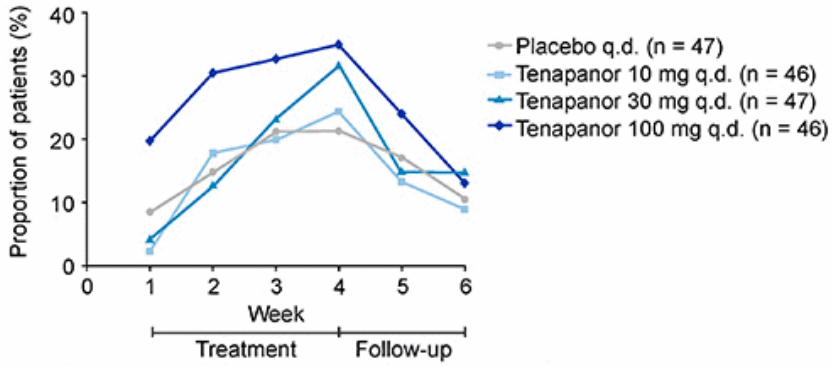

*$p$ < 0.05 versus placebo; †$p$ < 0.05 versus tenapanor 30 mg q.d. b.i.d., twice daily; q.d., once daily; t.i.d., three times daily

Eutamene H *et al. Gastroenterology* 2011;140:S-57–8; Schultheis PJ *et al. Nat Genet* 1998;19:282–5; Spencer AG *et al. Sci Transl Med* 2014;6:27ra36; Tse CM *et al. J Biol Chem* 1992;267:9340–6

# Tenapanor is a potential treatment for constipation-predominant irritable bowel syndrome (IBS-C)

- IBS is a common, symptom-based condition defined by the presence of abdominal pain and altered bowel habits
  - In IBS-C, stools are hard/lumpy in ≥ 25% of bowel movements and loose/watery in < 25% of bowel movements
- Phase 2a data suggest that tenapanor improves IBS-C symptoms

**Patients with a ≥ 30% decrease in abdominal pain and an increase of ≥ 1 in complete spontaneous bowel movements (CSBM) per week**




IBS-C, constipation-predominant irritable bowel syndrome; CSBM, complete spontaneous bowel movement; q.d., once daily

ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT01340053 (accessed 20 April 2015); Longstreth GF *et al. Gastroenterology* 2006;130:1480–91

# 12-week dose-ranging study evaluating tenapanor 5 mg, 20 mg or 50 mg b.i.d. vs placebo (1/2)

**Study aim**

- To evaluate the efficacy and safety of tenapanor for the treatment of IBS-C

**Key inclusion criteria** ✓

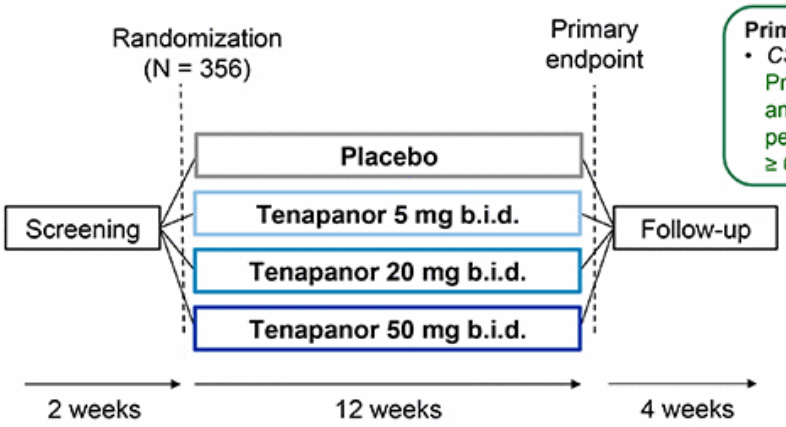
- Age 18–75 years
- IBS-C as defined by Rome III criteria
- Active disease during the screening period
  - < 3 CSBMs/week
  - < 5 SBMs/week
  - abdominal pain ≥ 3 (0–10 rating scale)

**Key exclusion criteria** ✗

- IBS with diarrhea (IBS-D), mixed IBS (IBS-M) or unsubtyped IBS as defined by Rome III criteria
- Diagnosis or treatment of any clinically symptomatic biochemical or structural abnormality of the gastrointestinal tract in the 6 months before screening
- Use of medication known to affect stool consistency

SBM, spontaneous bowel movement
ClinicalTrials.gov, https://clinicaltrials.gov/ct2/show/NCT01923428 (accessed 29 April 2015)

# 12-week dose-ranging study evaluating tenapanor 5 mg, 20 mg or 50 mg b.i.d. vs placebo (2/2)




**Primary endpoint**
- *CSBM responder rate*
  Proportion of patients with an increase of ≥ 1 CSBM per week from baseline for ≥ 6/12 treatment weeks

**Key secondary endpoints**
- *Overall responder rate*[a]
- *Abdominal pain responder rate*[b]

**Exploratory endpoints**
- *Abdominal bloating, straining, IBS severity, constipation severity*

**Safety assessments**
- *Adverse event reporting throughout the trial*
- *Clinical laboratory tests (serum chemistry, hematology and urinalysis)*
- *Vital signs*
- *12-lead ECG*
- *Physical examinations*

[a]Proportion of patients with a ≥ 30% decrease in abdominal pain and an increase of ≥ 1 CSBM per week versus baseline for ≥ 6/12 treatment weeks
[b]Proportion of patients with a ≥ 30% decrease in abdominal pain from baseline for ≥ 6/12 treatment weeks

## Statistical analysis methods (1/2)

- CSBM responder rate (primary endpoint), overall responder rate and abdominal pain responder rate (key secondary endpoints)
  - Treatment comparisons versus placebo are presented as risk differences (slides 8, 10, 11)
  - A screening test was performed based on a 2-degree of freedom Cochran–Mantel–Haenszel test for an association between treatment (placebo, tenapanor 20 mg b.i.d. and tenapanor 50 mg b.i.d.) and responder rate, stratified by pooled investigator sites
  - If this test was significant, a Cochran–Mantel–Haenszel test was used to calculate *p* values based on 1 degree of freedom for the association between treatment (placebo paired with each dose group separately) and responder rate, stratified by pooled investigator sites

## Statistical analysis methods (2/2)

- Stool consistency (secondary endpoint), abdominal bloating, straining, IBS severity and constipation severity (exploratory endpoints)
  - Treatment comparisons versus placebo are presented as differences in LS mean changes from baseline (slide 11, 12)
  - A screening test was performed based on a 2-degree of freedom F-test from a full ANCOVA model to test for differences in mean changes from baseline among the placebo, tenapanor 20 mg b.i.d. and tenapanor 50 mg b.i.d. groups
  - LS means, 95% confidence intervals and *p* values were calculated using an ANCOVA model, with treatment and pooled investigator site as factors and baseline value as a covariate

# Patient demographics and baseline disease characteristics

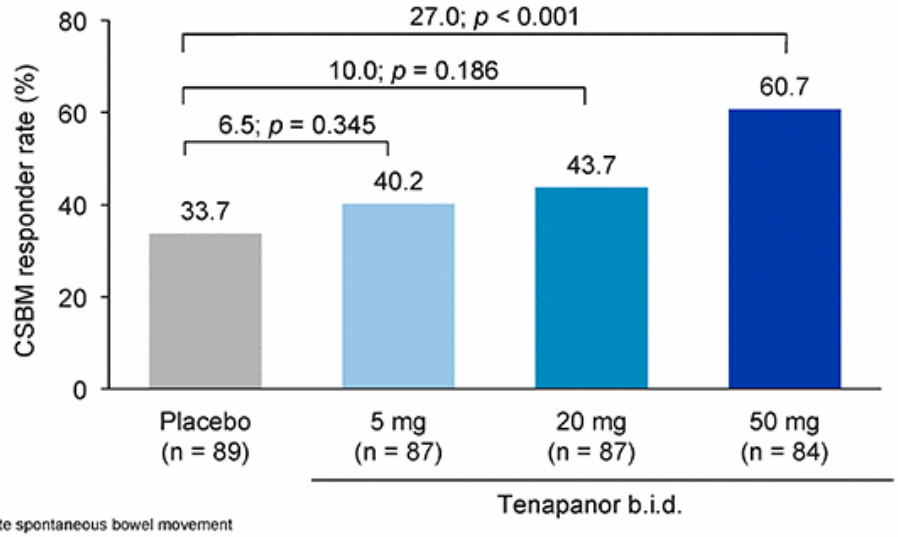
- 356 patients with IBS-C were randomized
  - The majority of patients were women (87%), < 65 years old (93%; mean age 45.7 years) and white (76%)

| Baseline disease parameter | Placebo (n = 89) | Tenapanor 5 mg b.i.d. (n = 87) | Tenapanor 20 mg b.i.d. (n = 87) | Tenapanor 50 mg b.i.d. (n = 84) |
|---|---|---|---|---|
| CSBMs per week | 0.2 (0.4) | 0.2 (0.4) | 0.2 (0.4) | 0.2 (0.4) |
| SBMs per week | 2.0 (1.2) | 1.9 (1.3) | 1.9 (1.1) | 2.0 (1.3) |
| Stool consistency[a] | 1.8 (1.0) | 1.8 (1.0) | 1.6 (0.8) | 1.8 (0.9) |
| Straining[b] | 3.1 (1.2) | 3.1 (1.1) | 3.1 (1.3) | 3.2 (1.3) |
| Constipation severity[c] | 4.1 (0.7) | 4.2 (0.6) | 4.0 (0.7) | 4.0 (0.8) |
| IBS severity[c] | 3.8 (0.7) | 3.9 (0.7) | 3.9 (0.8) | 3.8 (0.7) |
| Abdominal pain[d] | 6.1 (1.5) | 6.1 (1.6) | 6.3 (1.5) | 6.0 (1.5) |

ITT, intention-to-treat; SD, standard deviation. Data are mean (SD) for the ITT population. Baseline was defined as the mean of weeks -1 and -2
[a]Assessed using the 7-point Bristol Stool Form Scale; weekly mean calculated from scores for all SBMs during the week
[b]Assessed for each SBM using a 5-point scale: 1 = not at all, 2 = a little bit, 3 = a moderate amount, 4 = a great deal, 5 = an extreme amount; mean weekly score calculated from scores for all SBMs during the week
[c]Assessed weekly using a 5-point scale: 1 = none, 2 = mild, 3 = moderate, 4 = severe, 5 = very severe
[d]Assessed daily using a 10-point scale: 0 = none to 10 = very severe; mean weekly score was calculated from scores for all days during a valid week

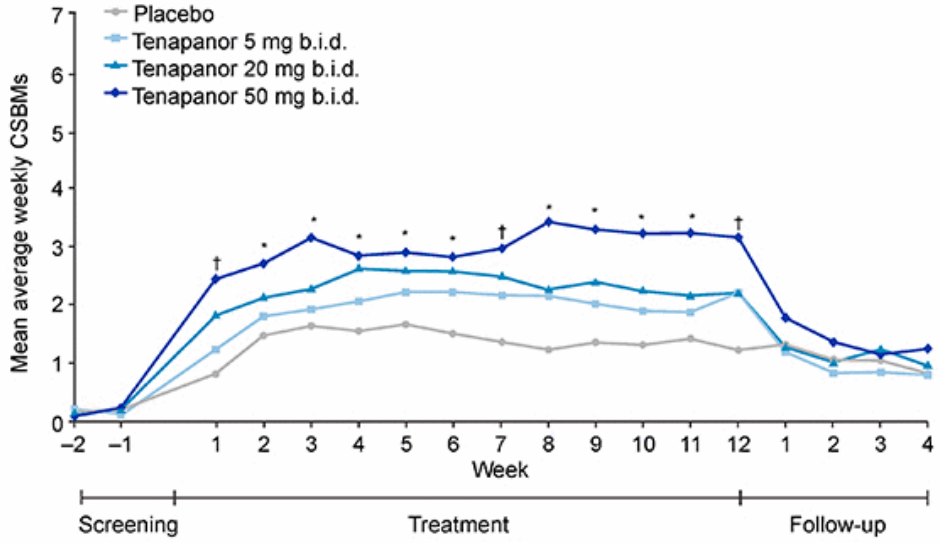
# Tenapanor 50 mg b.i.d. resulted in a significantly higher CSBM responder rate than placebo

- Primary endpoint (CSBM responder rate): proportion of patients with an increase of ≥ 1 CSBM per week from baseline for ≥ 6/12 treatment weeks (ITT analysis)




CSBM, complete spontaneous bowel movement

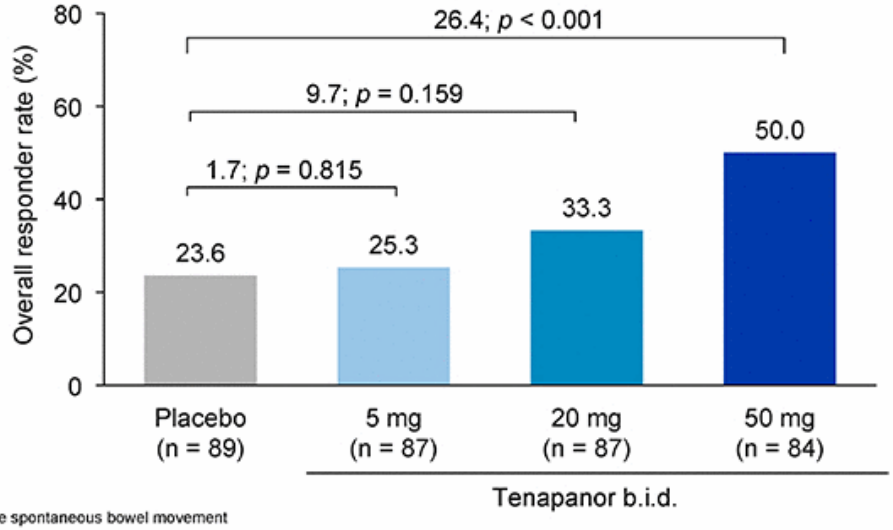
# CSBM improvements were maintained over the 12 weeks in a dose-dependent manner




CSBM, complete spontaneous bowel movement
*$p < 0.05$, tenapanor 50 mg b.i.d. versus placebo
†$p < 0.05$, tenapanor 20 mg b.i.d. and 50 mg b.i.d. versus placebo

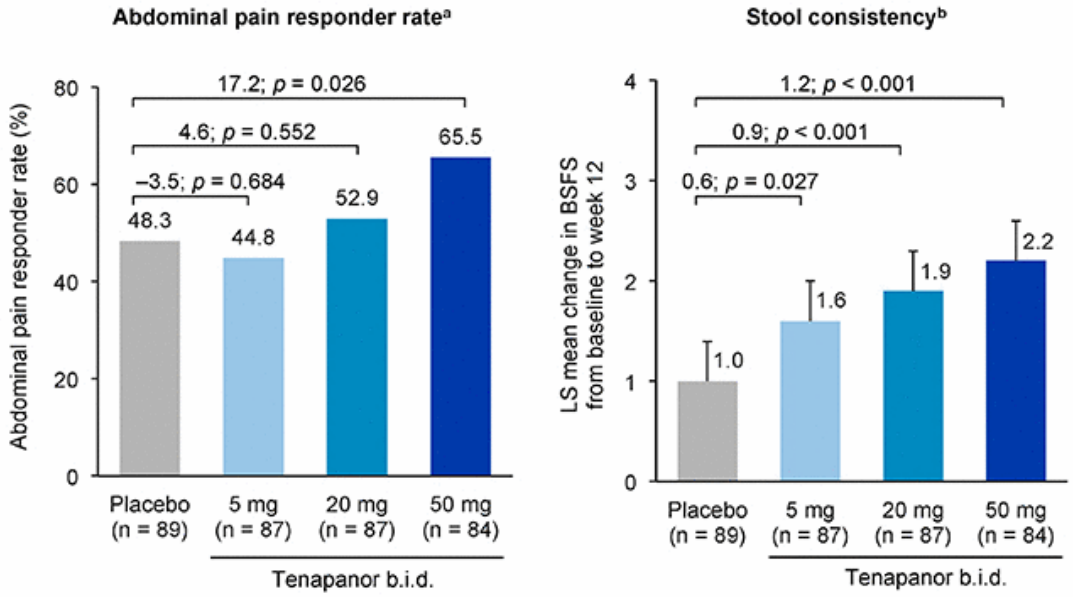
# Tenapanor 50 mg b.i.d. resulted in a significantly higher overall responder rate than placebo

- Overall responder rate: proportion of patients with a ≥ 30% decrease in abdominal pain and an increase of ≥ 1 CSBM per week versus baseline for ≥ 6/12 treatment weeks




CSBM, complete spontaneous bowel movement

# Improvements in other key secondary endpoints with tenapanor

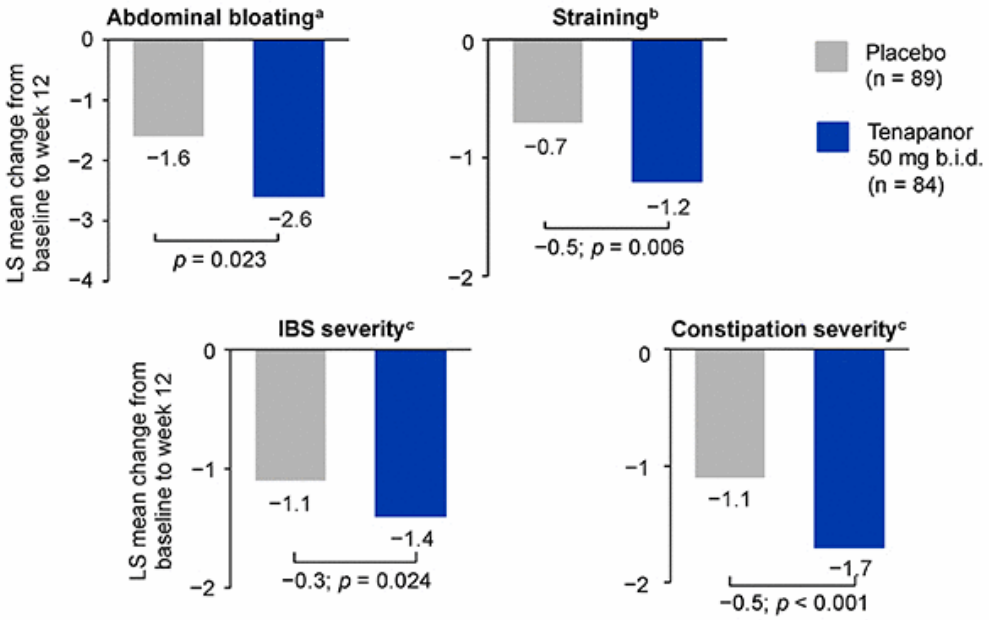



BSFS, Bristol Stool Form Scale; LS, least-squares

[a]Proportion of patients with a ≥ 30% decrease in abdominal pain from baseline for ≥ 6/12 treatment weeks; treatment comparisons versus placebo represent the risk difference

[b]Error bars represent upper limit of 95% confidence interval

# Improvements in exploratory endpoints with tenapanor 50 mg b.i.d.




[a]Assessed daily using a 10-point scale: 0 = none to 10 = very severe; average weekly score was calculated from scores for all days during a week
[b]Assessed for each SBM using a 5-point scale: 1 = not at all to 5 = an extreme amount; average weekly straining score calculated from scores for all SBMs during the week
[c]Assessed weekly using a 5-point scale: 1 = none to 5 = very severe

# Tenapanor was generally well tolerated and had minimal systemic availability

| AE summary, n (%) | Placebo (n = 90) | Tenapanor 5 mg b.i.d. (n = 88) | Tenapanor 20 mg b.i.d. (n = 89) | Tenapanor 50 mg b.i.d. (n = 89) |
|---|---|---|---|---|
| Any AE | 38 (42.2) | 43 (48.9) | 32 (36.0) | 45 (50.6) |
| Treatment-related AEs | 13 (14.4) | 22 (25.0) | 15 (16.9) | 17 (19.1) |
| Serious AEs | 1 (1.1) | 2 (2.3) | 1 (1.1) | 0 (0.0) |
| AEs leading to discontinuation[a] | 3 (3.3) | 9 (10.2) | 6 (6.7) | 4 (4.5) |

- Most AEs were mild to moderate in severity and none of the three serious AEs in patients receiving tenapanor were judged to be treatment-related
- No clinically meaningful changes from baseline were reported for clinical laboratory parameters, vital signs, electrocardiographic parameters or physical examination findings
- Tenapanor had minimal to no systemic availability
  - Tenapanor concentrations were below the lower limit of quantification (0.5 ng/mL) in > 97% (283/291) samples (highest concentration measured: 1.03 ng/mL)

AE, adverse event

[a]Most common AEs leading to discontinuation: diarrhea (3 [3.4%] patients each in 5 mg, 20 mg and 50 mg b.i.d. groups), abdominal distension (3 [3.4%] patients in 5 mg b.i.d. group); no other specific AE led to discontinuation in > 2 patients in any treatment group

# AEs occurring in ≥ 3% of patients in any tenapanor group and more frequently than in the placebo group

| Individual event, n (%) | Placebo (n = 90) | Tenapanor 5 mg b.i.d. (n = 88) | Tenapanor 20 mg b.i.d. (n = 89) | Tenapanor 50 mg b.i.d. (n = 89) |
|---|---|---|---|---|
| Diarrhea | 0 (0.0) | 7 (8.0) | 11 (12.4) | 10 (11.2) |
| Nausea | 1 (1.1) | 6 (6.8) | 4 (4.5) | 3 (3.4) |
| Abdominal pain | 2 (2.2) | 7 (8.0) | 0 (0.0) | 4 (4.5) |
| Vomiting | 0 (0.0) | 4 (4.5) | 1 (1.1) | 2 (2.2) |
| GERD | 1 (1.1) | 3 (3.4) | 0 (0.0) | 1 (1.1) |
| Abdominal distension | 0 (0.0) | 3 (3.4) | 1 (1.1) | 0 (0.0) |
| Urinary tract infection | 4 (4.4) | 3 (3.4) | 2 (2.2) | 5 (5.6) |
| Influenza | 0 (0.0) | 2 (2.3) | 1 (1.1) | 3 (3.4) |
| Headache | 5 (5.6) | 6 (6.8) | 1 (1.1) | 3 (3.4) |

GERD, gastroesophageal reflux disease

## Conclusions

- Tenapanor 50 mg b.i.d. significantly improved CSBM responder rate (primary endpoint) compared with placebo in patients with IBS-C
- Tenapanor 50 mg b.i.d. also improved key secondary endpoints compared with placebo, including overall responder rate, abdominal pain responder rate and stool frequency
- In addition, improvements were observed in several exploratory endpoints addressing a range of symptoms in patients with IBS-C
- Tenapanor was generally well tolerated and had minimal systemic availability
- Tenapanor shows promise as a future treatment option for patients with IBS-C

## Acknowledgments


- The investigators acknowledge and thank the study participants, the study centres and the clinical teams
- The clinical operations were managed by Susan Edelstein, Lori Marshall and Jocelyn Tabora from Ardelyx
- Medical writing support was provided by Steven Inglis and Carolyn Brechin of Oxford PharmaGenesis, UK and was funded by Ardelyx