ardelyx®

Founded with a mission to improve the lives of patients by discovering, developing and commercializing innovative, first-in-class medicines that meet significant unmet medical needs

April 2022

Forward-Looking Statements

To the extent that statements contained in this presentation 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, Ardelyx's expectations regarding peak annual net revenue for IBSRELA; Ardelyx's expectations regarding the percentage of the market that Ardelyx expects to capture with IBSRELA; Ardelyx's expectations regarding its ability to generate revenue sufficient to achieve positive cash flow for IBSRELA; Ardelyx's expectations regarding the commercial potential for XPHOZAH, if approved for treating hyperphosphatemia in CKD patients on dialysis, including Ardelyx's expectation regarding the rate of adoption and use of XPHOZAH, if approved; Ardelyx's expectations regarding the size of the patient population and the size of the market for XPHOZAH, if approved for treating hyperphosphatemia in CKD patients on dialysis, and the potential growth thereof; and statements regarding the potential for Ardelyx's product candidates in treating the diseases and conditions for which they are being developed. Such forward-looking statements involve substantial risks and uncertainties that could cause the development and regulatory approval of Ardelyx's product candidates, the commercialization of IBSRELA, or any other products for which Ardelyx may obtain regulatory approval 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, uncertainties associated with the commercialization of drugs, and the regulatory approval process and the uncertainties inherent in research and the clinical development 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 Annual Report on Form 10-K filed with the Securities and Exchange Commission on February 28, 2022, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

Founded with a Mission to Discover, Develop, and Commercialize Innovative, First-in-Class Medicines that Meet Significant Unmet Medical Needs

Specialty Therapeutic Areas

Gastroenterology

Nephrology

Cardiology

Significant Unmet Medical Need

Despite active treatment with currently available therapies, significant proportion of patients are not adequately managed

Portfolio Strategy Centered on First-in-Class, Novel Mechanism Therapies

IBSRELA® (tenapanor) tablets
50mg tablet
Available in the U.S. and Canada

XPHOZAH® (tenapanor) tablets
30mg, 20mg, 10mg tablet
Investigational Late-Stage Asset

RDX013
Investigational Asset

RDX020
Pre-clinical Program

Accessible with Targeted Approach

Concentrated prescriber base accounts for large proportion of opportunity

XPHOZAH (tenapanor) and RDX013 are investigational product candidates. RDX020 is a preclinical program

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IBSRELA® (tenapanor)

First-in-class, NHE3 Inhibitor,
Available in the U.S. and Canada,
for the Treatment of Irritable
Bowel Syndrome with
Constipation (IBS-C) in Adults

IBSRELA: Right Time, Right Product for IBS-C Market

- IBS-C market has grown to become an established prescription market that is poised for new market entrant
  - >1.6M IBS-C patients treated with prescription therapies
  - Limited number of players with 2 actively marketed branded drugs, both GC-C agonists; built market over last decade
  - ~9,000 high writing physicians contributing ~50% of Rx therapy (5M scripts)
- There remains a significant unmet need
  - HCPs report that 35% of patients on IBS-C prescription therapy do not adequately respond to treatment
  - High interest in novel mechanism to address multifactorial pathophysiology of IBS-C
- IBSRELA: First-in-class, NHE3 Inhibitor, available in the U.S. and Canada, indicated for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in Adults
  - IBSRELA meaningfully differentiated MOA and robust clinical data to address unmet need
- Concentrated market, addressable with small, specialized sales force

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IBSRELA Important Safety Information

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS

IBSRELA is contraindicated in patients less than 6 years of age; in nonclinical studies in young juvenile rats administration of tenapanor caused deaths presumed to be due to dehydration. Avoid use of IBSRELA in patients 6 years to less than 12 years of age. The safety and effectiveness of IBSRELA have not been established in patients less than 18 years of age.

CONTRAINDICATIONS

- IBSRELA is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.
- IBSRELA is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

WARNINGS AND PRECAUTIONS

Risk of Serious Dehydration in Pediatric Patients

- IBSRELA is contraindicated in patients below 6 years of age. The safety and effectiveness of IBSRELA in patients less than 18 years of age have not been established. In young juvenile rats (less than 1 week old; approximate human age equivalent of less than 2 years of age), decreased body weight and deaths occurred, presumed to be due to dehydration, following oral administration of tenapanor. There are no data available in older juvenile rats (human age equivalent 2 years to less than 12 years).
- Avoid the use of IBSRELA in patients 6 years to less than 12 years of age. Although there are no data in older juvenile rats, given the deaths in younger rats and the lack of clinical safety and efficacy data in pediatric patients, avoid the use of IBSRELA in patients 6 years to less than 12 years of age.

Diarrhea

Diarrhea was the most common adverse reaction in two randomized, double-blind, placebo-controlled trials of IBS-C. Severe diarrhea was reported in 2.5% of IBSRELA-treated patients. If severe diarrhea occurs, suspend dosing and rehydrate patient.

MOST COMMON ADVERSE REACTIONS

The most common adverse reactions in IBSRELA-treated patients (incidence ≥2% and greater than placebo) were: diarrhea (16% vs 4% placebo), abdominal distension (3% vs <1%), flatulence (3% vs 1%) and dizziness (2% vs <1%).

INDICATION

IBSRELA (tenapanor) is indicated for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in adults.

Please see full Prescribing Information, including Boxed Warning, for additional risk information.

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Both Healthcare Practitioners and Patients Report Inadequate Response with Current Rx Therapy Options

According to Physicians

35%

of patients on IBS-C prescription therapy do not adequately respond

According to Patients

62%

of patients on IBS-C prescription therapy need additional IBS-C symptom relief

Unmet need centered on efficacy parameters of abdominal pain and bloating

Dr. William Chey, Nostrant Professor of Medicine, University of Michigan School of Medicine

*"It is now widely recognized that while people with IBS-C present with similar symptoms, it is a disorder of **heterogeneous pathogenesis**. Therefore, while there has been **much improvement** in our treatment of patients with IBS-C over the last two decades with the introduction and **broad adoption of GC-C agonists**, it should be **no surprise that many patients continue to suffer**. There is a **need for innovation**. The launch of IBSRELA, as a first-in-class NHE3 inhibitor, is exciting, as it offers a unique mechanism of action with compelling clinical data, providing physicians with an important new tool to advance the care of patients with IBS-C."*

Source: Reason Research IBS-C Physician Quant Q3 2021. Base: Gastroenterologists managing patients on each IBS-C therapy. Q13. In your clinical experience, what percent of your patients with IBS-C on each of the therapies below do not adequately respond to treatment? Reason Research IBS-C Patient Study Q3 2021 Base: Patients currently taking prescription therapy for IBS-C ● Q36. Despite use of your current prescription medication for IBS-C, do you need additional symptom relief from your IBS-C?

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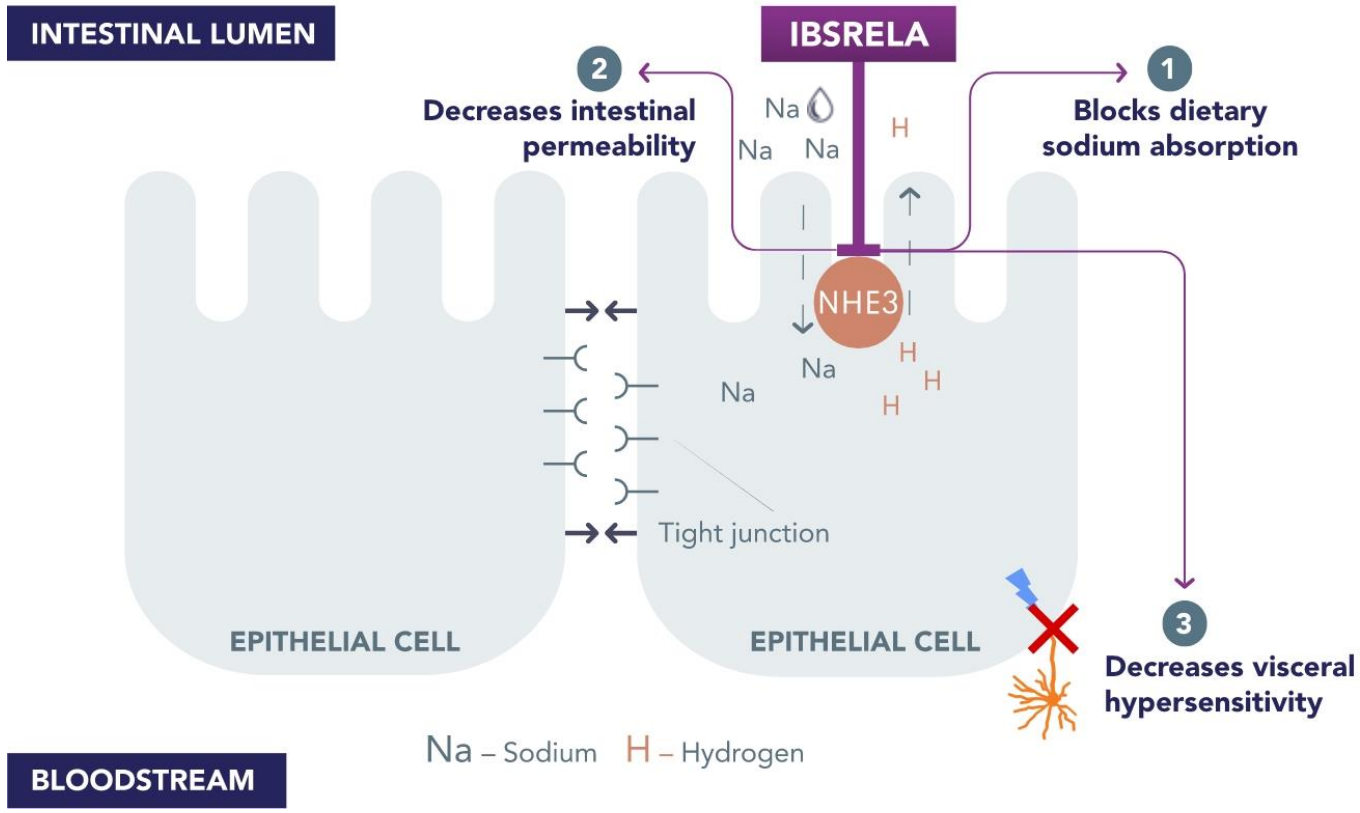
IBSRELA: First-In-Class, Novel Mechanism NHE3 Inhibitor, with a Triple Action to Treat IBS-C



By Inhibiting NHE3, IBSRELA:

1. Blocks dietary sodium absorption, thus retaining luminal water content, which accelerates intestinal transit time and results in a softer stool consistency
2. Decreases intestinal permeability to reduce abdominal pain
3. Decreases visceral hypersensitivity to reduce abdominal pain

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Robust IBSRELA Clinical Data Package: Two Phase 3 Registration Trials, Both Met Primary Endpoint

Key Results from Long-Term Phase 3, T3MPO-2 Trial

- Achieved primary endpoint: Significantly more patients treated with IBSRELA compared to placebo ($p<0.001$) were overall responders*
- Achieved additional secondary endpoints:
  - 54% improvement in abdominal pain from baseline to week 26 (reduced from 6.3 to 2.9)**
  - 47% improvement in abdominal bloating from baseline to week 26 (reduced from 6.7 to 3.4)**
  - Mean increase of 3.3 weekly complete spontaneous bowel movements from baseline to week 26
  - 81% treatment satisfaction (moderately, quite or very satisfied) at week 26
  - 41% improvement in quality-of-life scores at week 26 compared to baseline
- The most common adverse reactions in IBSRELA-treated patients (incidence ≥2% and greater than placebo) were: diarrhea (16% vs 4% placebo), abdominal distention (3% vs <1%), flatulence (3% vs 1%) and dizziness (2% vs <1%) Severe diarrhea was reported in 2.5% of IBSRELA-treated patients.

*Overall responders: at least a 30% reduction in average weekly worst abdominal pain from baseline AND an increase of at least 1 complete spontaneous bowel movement from baseline, both in the same week, for at least 6 of the first 12 weeks of treatment.

**Severity of symptoms (abdominal pain and bloating) assessed on an 11-point scale where 0 represents no symptoms and 10 represents very severe symptoms. The average worst weekly abdominal pain scores. The average weekly abdominal scores were calculated as the average score for all days during a valid week. If a patient did not have data reported for at least 4 days during a given week (either due to a gap in reporting or due to discontinuation), the patient was considered to be a non-responder for the week. Scores reported in the intent-to-treat analysis set.

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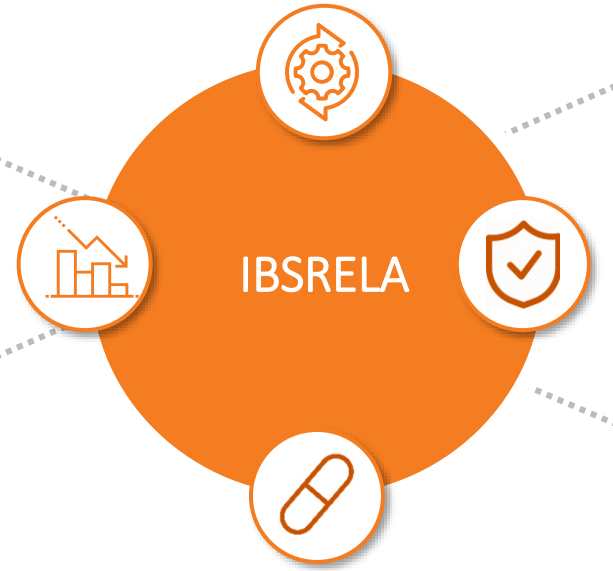
IBSRELA Product Profile is Compelling

MOA

- First-in-Class, NHE3 inhibitor
- Novel mechanism with triple action
  1. Blocks dietary sodium
  2. Decreases intestinal permeability
  3. Decreases visceral hypersensitivity



Efficacy

- Both trials met primary efficacy endpoint
- Improvements from baseline in average weekly CSBMs* and abdominal pain were observed by week 1 with improvement maintained through the end of treatment

Tolerability

- Generally well-tolerated with most common side effect diarrhea (16%); tended to be mild-to-moderate and transient (≤ 1 week in duration)
- Additional adverse reactions reported in at least 2% of patients treated with IBSRELA and incidence above placebo: abdominal distention (3%), flatulence (3%), and dizziness (2%)

Dosing

- One pill, BID

*CSBM: complete spontaneous bowel movement

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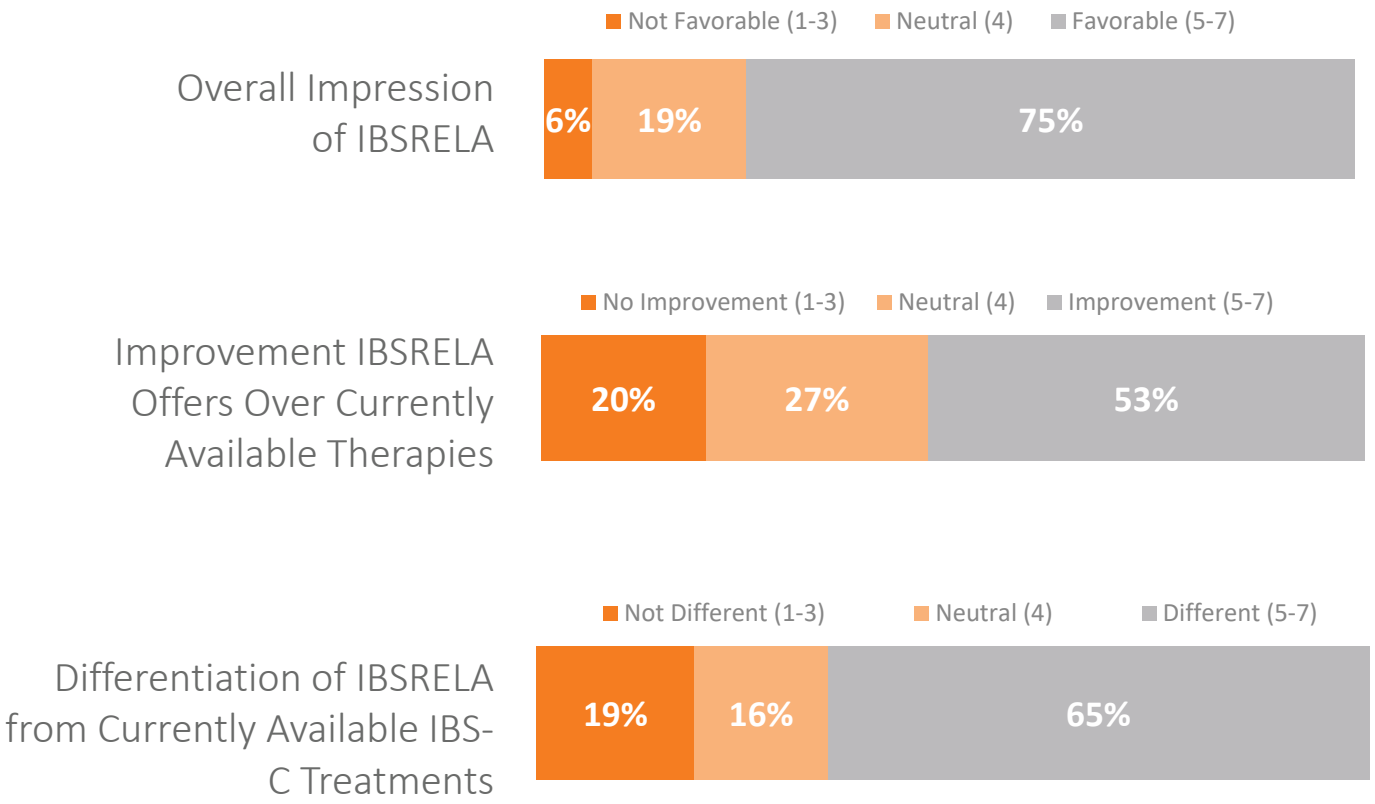
Favorable Response to IBSRELA Product Profile by HCPs



- Differentiated MOA and efficacy rated as most compelling aspects of IBSRELA
- HCPs project use of IBSRELA in a meaningful subset of their patients with IBS-C

Source: Reason Research IBS-C Physician Quant, Q3 2021
Base: All Gastroenterologists ● Q27. What is your overall impression of Product X for the treatment of IBS-C? Please use a scale of 1-7 where 1 is not at all favorable and 7 is extremely favorable ● Q28. How does Product X compare to currently available IBS-C prescription treatment options? Please use a scale of 1-7 where 1 is not at improvement at all and 7 is significant improvement ● Q28b. How different is Product X from currently available IBS-C prescription treatment options? Please use a scale of 1-7 where 1 is very similar to other treatments and 7 is very different than other treatments

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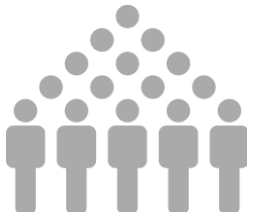
Well-Established IBS-C Rx Market Accessible Via Targeted Approach



11M

U.S. Patients with IBS-C [1]

1.65M

Patients with IBS-C Treated with a Prescription Therapy[2]

9,000

Physicians account for approximately 50% of the Rx volume[3]

1. Meta-analysis: 11.2% of population has IBS. 11.2% of 300 million in US = 33.6 million with IBS. Source: The Epidemiology of Irritable Bowel Syndrome, Clinical Epidemiology 2014:6 71–80; % of IBS that is estimated to be IBS-C is approximately one-third, thus 11 million with IBS-C. Source: Global IBS Impact Report.
2. Irritable Bowel Syndrome Executive Insights, Decision Resources Group, January 2019
3. IQVIA Xponent, May 2020 – April 2021

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IBSRELA Positioning Centered on Novel Mechanism with Triple Action to Treat IBS-C, a Condition with a Multifactorial Pathophysiology

- IBSRELA: A first in class NHE3 inhibitor with triple action to treat IBS-C. The novel mechanism with triple action is differentiated from the MOA of existing therapies and has been shown to provide significant improvement in abdominal pain, bloating, and constipation, with a quick onset of action, sustained efficacy, patient reported treatment satisfaction, and improved quality of life vs placebo
- IBSRELA, with its new mechanistic approach and triple action, provides another meaningful tool in the treatment toolkit for HCPs who treat patients with IBS-C
- IBSRELA Go-To-Market Strategy
  focused on driving IBSRELA use in patients that are already "in the funnel" - those being treated by high writing HCPs. Sales force effort amplified via innovative omnichannel initiatives – peer-to-peer, social, EHR, third-party, email, banner ads, paid search, conferences. Penetration of this market ***does not*** require DTC

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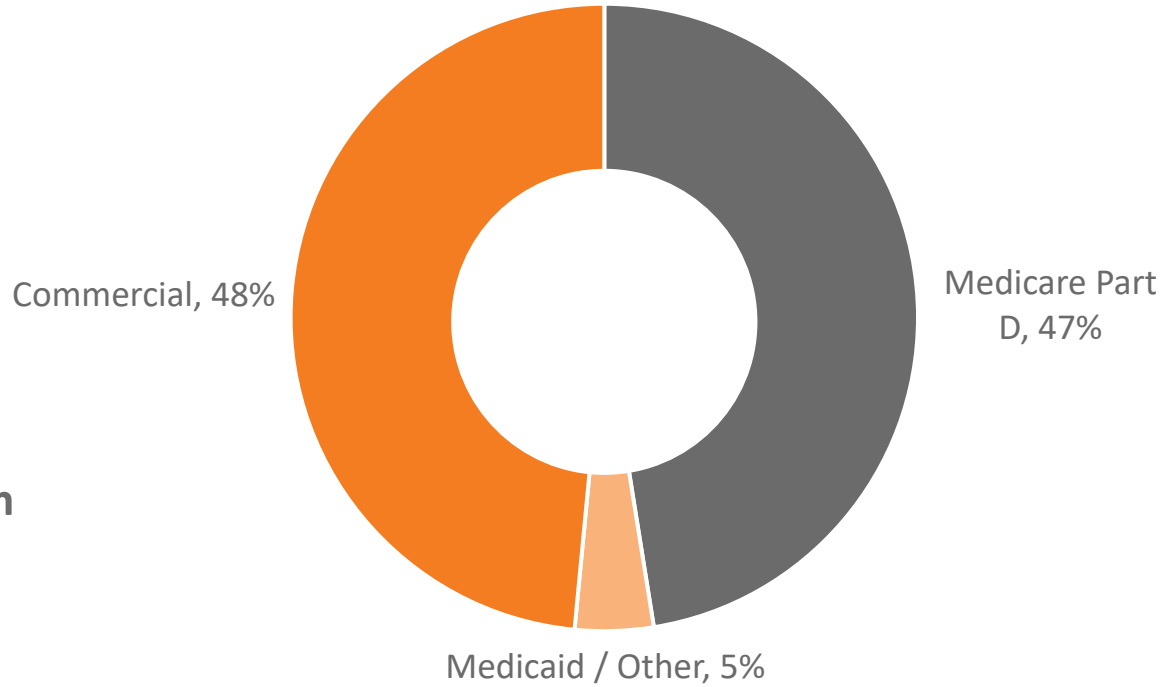
Favorable Payor Landscape for IBS-C Rx Therapies

48% Commercial / 52% Medicare, Medicaid, Other

Approximately 50% of prescriptions flow through commercial payors

Launch with:
- ✓ **commercial co-pay program**
- ✓ **patient assistance program**



NPA Extended Insights Audit, Trx Payor Mix, 2020

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Summary: IBS-C Market is Poised for IBSRELA

- IBS-C market has grown to become an established market and is favorable for new market entrant
  - >1.6M IBS-C patients treated with prescription therapies
- Significant unmet need with a large proportion of patients not adequately managed with available Rx therapies
  - Limited to 2 actively marketed branded drugs that are same mechanism of action (both GC-C agonists)
- First-in-class, FDA-approved, NHE3 Inhibitor indicated for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in Adults
- IBSRELA, with a meaningfully differentiated MOA and robust clinical data to address unmet need
- Concentrated market addressable with small, specialized sales force
  - ~9,000 high writing physicians contributing ~50% of Rx therapy 5M scripts
- Mid to high single-digit penetration can result in peak annual net revenue of >$500M
  - Clear path to breakeven and ultimately, profitability for IBSRELA

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XPHOZAH® (tenapanor)

First-in-class product candidate for the control of serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis

XPHOZAH: An Investigational First-in-Class Phosphate Absorption Inhibitor for Treatment of Hyperphosphatemia

- Control of serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis is important
  - Elevated phosphorus is associated with cardiovascular morbidity and mortality
  - Control of serum phosphorus has been unachievable for the majority of patients with currently available therapies
- XPHOZAH provides a unique MOA as a first-in-class phosphate absorption inhibitor (PAI) that blocks the primary pathway of phosphate absorption (the paracellular pathway)
- Positive data in three successful Phase 3 pivotal trials with >1,000 patients
  - Met all primary and key secondary endpoints
  - Supporting data from two additional clinical trials, NORMALIZE and OPTIMIZE
- Pursuing Formal Dispute Resolution Request (FDRR) to appeal the issuance of a CRL by the FDA
  - According to the CRL, while the FDA agrees that "the submitted data provide substantial evidence that tenapanor is effective in reducing serum phosphorus in CKD patients on dialysis," they characterize the magnitude of the treatment effect as "small and of unclear clinical significance." *There were no safety, clinical pharmacology/biopharmaceutics, CMC or non-clinical issues identified in the CRL*
- Established commercial capabilities position us favorably to support the potential launch of XPHOZAH

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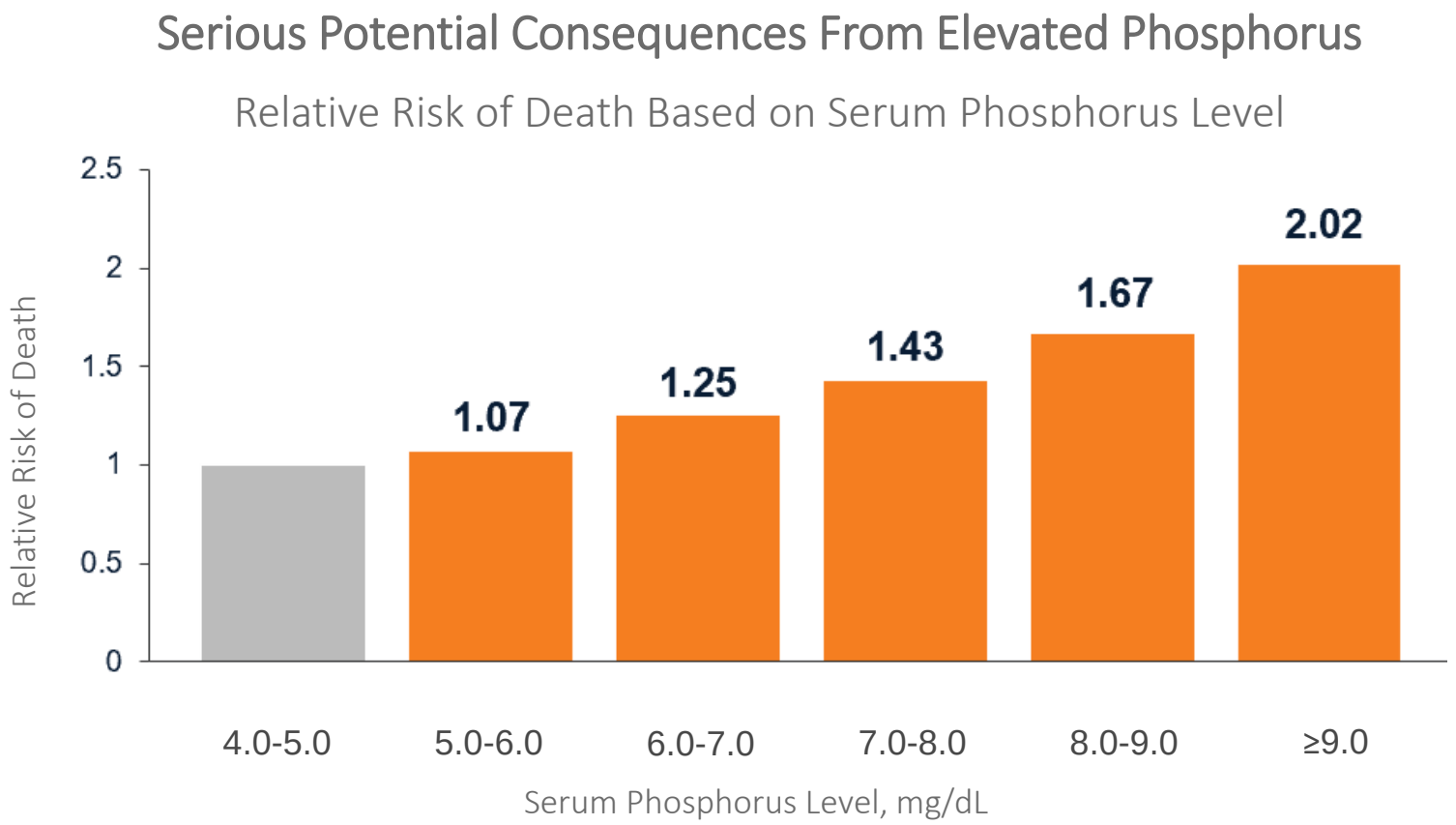
Serum Phosphorus Levels are an Independent Predictor of Morbidity and Mortality in Patients on Dialysis[1]



Increased serum phosphorus levels of 0.5 to 1 mg/dL over the reference range resulted in a **significant increase in relative risk of death**

Elevated serum phosphorus also increases the relative **risk of hospitalization by up to 38%**

1. Block, GA, et al. Mortality, and Morbidity in Maintenance Hemodialysis. J Am Soc Nephrol 15: 2208–2218, 2004

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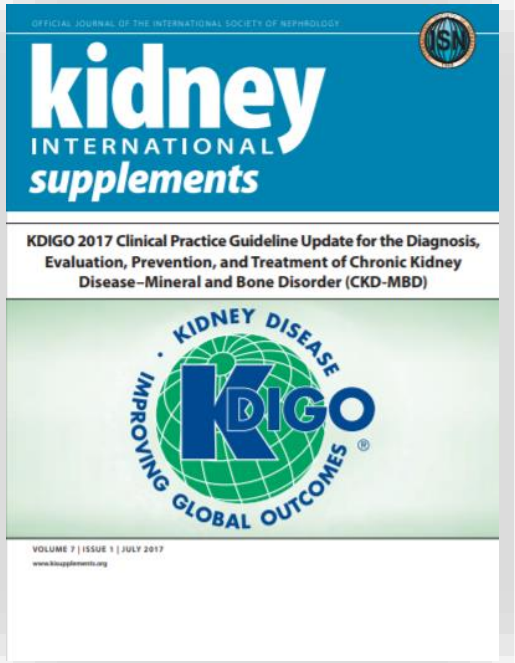
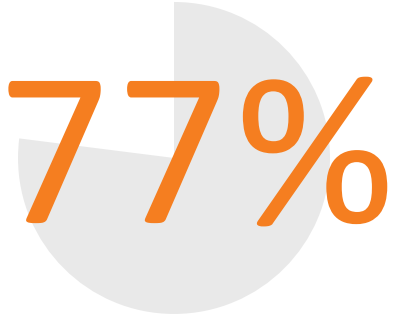
Majority of Patients are Unable to Consistently Maintain Target Phosphorus Levels



2017

4.1.2. In patients with CKD G3a–G5D, we suggest lowering elevated phosphate levels toward the normal range[1]
(Adults: 2.5 to 4.5 mg/dL)



of patients treated with binders were unable to consistently maintain phosphorus levels <=5.5 mg/dL over a six-month period[2]

1. KDIGO 2017 Clinical Practice Guideline Update for the Diagnosis, Evaluation, Prevention, and Treatment of Chronic Kidney Disease–Mineral and Bone Disorder (CKD-MBD). Kidney International Supplements. 2017:7;1-59.
2. Spherix RealWorld Dynamix, Dialysis 2019

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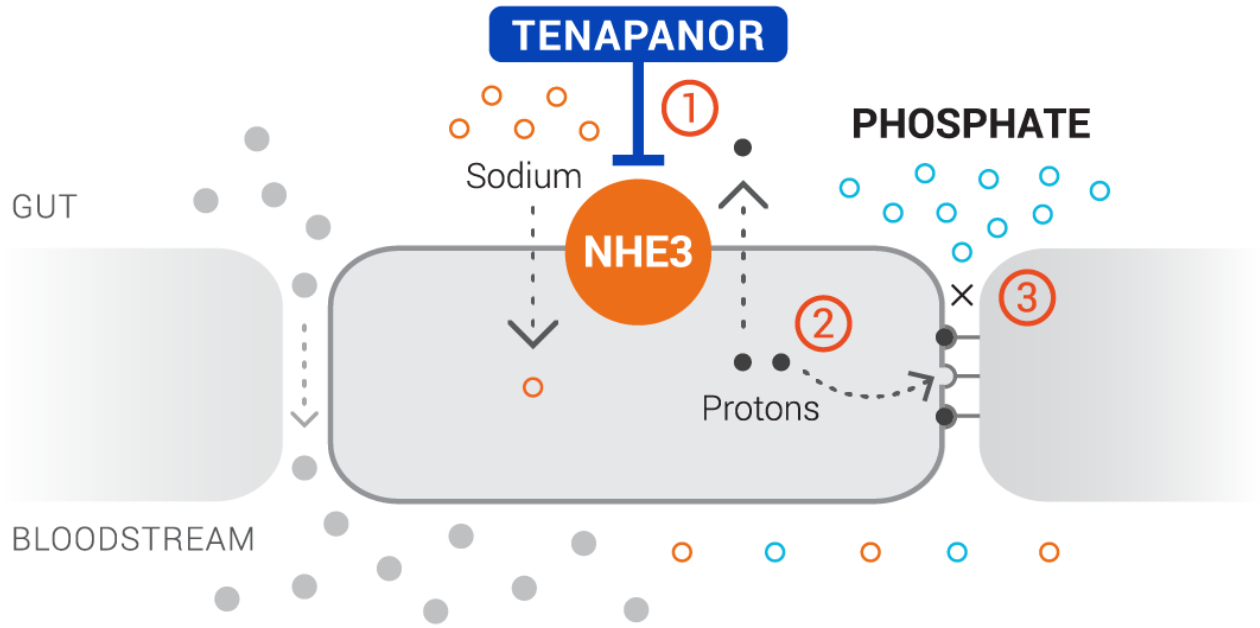
XPHOZAH: An Investigational First-In-Class Phosphate Absorption Inhibitor

TARGETS
primary pathway of phosphate absorption

BLOCKS
paracellular absorption of phosphorus[1]

DOSED
as one pill twice per day[2]



1. Inhibits NHE3, reducing sodium absorption resulting in modest intracellular proton retention

2. Proposed induction of conformational change in claudin proteins

3. Specifically blocks absorption of phosphate through the paracellular pathway

1. King et al. Inhibition of sodium/hydrogen exchanger 3 in the gastrointestinal tract by tenapanor reduces paracellular phosphate permeability. Sci Transl Med 10, eaam6474. DOI: 10.1126/scitranslmed.aam6467. Accessed on August 29, 2018.
2. In clinical trials, dosing is 1 pill BID

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XPHOZAH Clinical Data Package is Robust with Three Phase 3 Trials

BLOCK

Short Term Monotherapy Study (n=219)

Primary endpoint: statistically significant (p<0.01) difference in least squared mean serum phosphorus change (0.82 mg/dL) between XPHOZAH and placebo

Secondary analysis: At the end of the 8-week randomized treatment period, XPHOZAH-treated patients in the intent-to-treat population experienced a mean decrease in serum phosphorus from baseline of 1.1 mg/dL

PHREEDOM

Long Term Monotherapy Study (n=564)

Primary endpoint: statistically significant (p<0.0001) difference in least squared mean serum phosphorus change (1.4 mg/dL) between XPHOZAH and placebo

Secondary analysis: At the end of the 26-week randomized treatment period, XPHOZAH-treated patients in the intent-to-treat population experienced a mean decrease in serum phosphorus from baseline of 1.4 mg/dL

AMPLIFY

Short Term Combination Therapy Study (n=236)

Primary endpoint: statistically significant difference in reduction of serum phosphorus levels (p=0.0004) compared to binders alone at week four

Secondary analysis: ~2 times more patients achieved the serum phosphorus treatment goal of <5.5 mg/dL with XPHOZAH and phosphate binders vs. phosphate binders alone (p≤0.0097)

In the three Phase 3 trials combined, diarrhea (47%) was the only adverse reaction reported in at least 5% of XPHOZAH-treated patients. The majority of diarrhea was reported to be mild-to-moderate and transient, occurring early in treatment with a median resolution of two weeks with continued treatment. 5% of patients in clinical trials experienced severe diarrhea

BLOCK: Block, GA, et al.. Efficacy and Safety of Tenapanor in Patients with Hyperphosphatemia Receiving Maintenance Hemodialysis: A Randomized Phase 3 Trial. J Am Soc Nephrol 30: 641-652, 2019
PHREEDOM: Block, GA, et al. Safety and Efficacy of Tenapanor for Long-Term Serum Phosphate Control in Maintenance Dialysis: A 52-Week Randomized Phase 3 Trial (PHREEDOM). Kidney360 2(10): 1600-1610, 2021
AMPLIFY: Pergola, PE, et al. A Randomized Trial of Tenapanor and Phosphate Binders as a Dual-Mechanism Treatment for Hyperphosphatemia in Patients on Maintenance Dialysis (AMPLIFY). J Am Soc Nephrol 32 (6): 1465-1473, 2021

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Additional Positive Trials Supporting the Central Role of Blocking Mechanism in the Management of Hyperphosphatemia

NORMALIZE

Open Label Extension Study (n=172)

Primary objective: Evaluate the ability of XPHOZAH, alone or in combination with sevelamer, to achieve normal serum phosphorus levels in patients with CKD on dialysis

- Long-term safety data: 2.5 year exposure to drug (extension study of PHREEDOM)
- >47% of patients able to achieve normal phosphorus levels with XPHOZAH alone or XPHOZAH and binders

OPTIMIZE

Randomized Open Label Study (n=330)

Primary objective: Evaluate various strategies for integrating XPHOZAH into clinical practice in binder-treated and binder-naïve patients, to optimize phosphorus management (achieve serum phosphorus levels ≤5.5 mg/dL)

- Demonstrated that integration of XPHOZAH enables greater proportion of patients to achieve target phosphorus levels
- Improved overall patient experience and benefit of one pill twice daily dosing regimen with XPHOZAH compared to binder therapies, based on patient reported outcomes

Similar to the Phase 3 trials, diarrhea was the most common adverse reaction in the additional studies.

KI Reports 2021:6, S123. Optimize reference: ERA-EDTA, 2021: MO1062.

XPHOZAH Product Profile is Compelling

MOA

- First-in-Class, non-binder, phosphate absorption inhibitor
- Blocks paracellular (primary pathway) phosphate absorption

Dosing and Administration

- One pill
- BID dosing

Efficacy

- All trials met primary and secondary efficacy endpoints
- Reduced serum phosphorus levels in patients with CKD on dialysis

Tolerability

- Generally well-tolerated
- Diarrhea (47%) tended to be mild-to-moderate and transient

XPHOZAH (tenapanor) is an investigational product candidate and has not been approved by the U.S. Food and Drug Administration (FDA) or any other regulatory authority.

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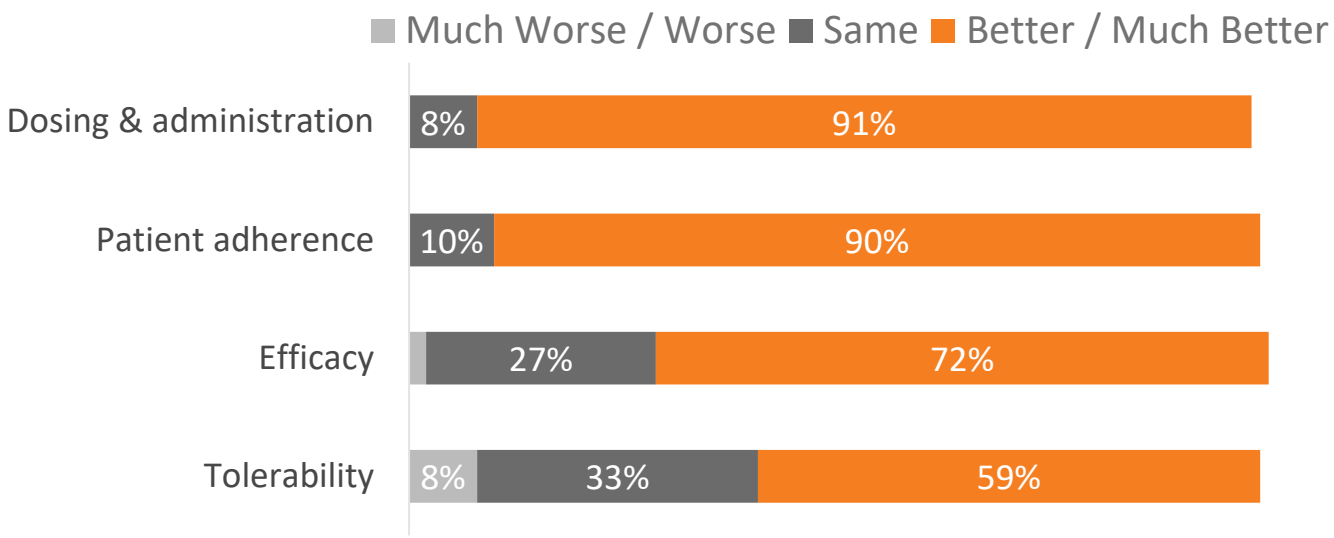
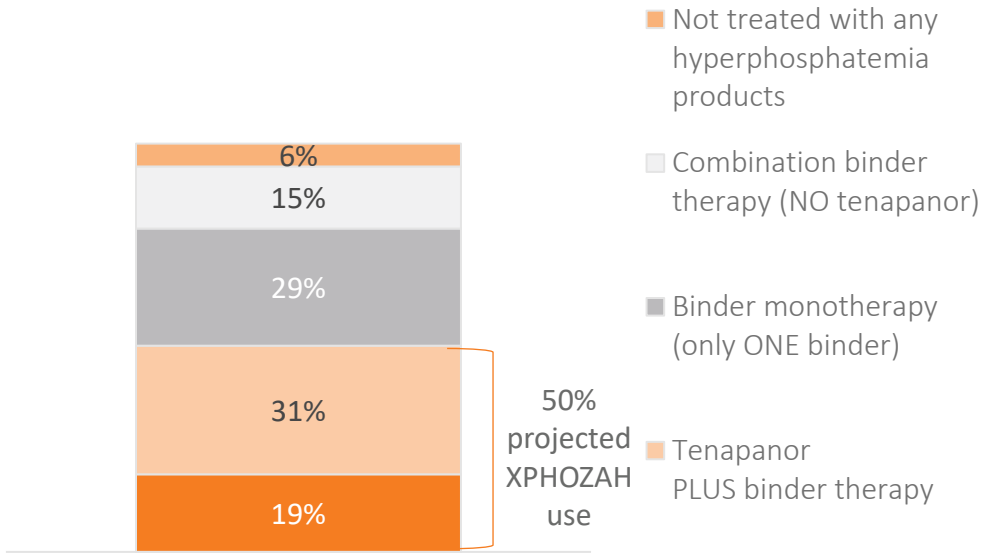
Most HCPs Expect XPHOZAH to Provide an Improvement Compared to Phosphate Binders* and Project Use in 50% of Patients on Hemodialysis

How Does XPHOZAH Compare to Phosphate Binders?*



82% of nephrologists intend to adopt XPHOZAH within the first six months, with 33% intending to adopt right away***

Projected Use of XPHOZAH in HD**



** Spherix RealTime Q4 2021

*Physician perceptions of XPHOZAH relative to phosphate binders based on XPHOZAH product profile. There have been no head-to-head studies comparing XPHOZAH to phosphate binders. Ardelyx market research study conducted by Hawk Partners, December 2019. **Spherix RealTime Dynamix Bone and Mineral Metabolism, Q4 2021: Now, please assume that tenapanor is approved and available in the US for at least six months. Once it has been on the market for six months, what percent of your hemodialysis patients and peritoneal dialysis patients do you anticipate will be treated with: (n=205)***Spherix RealTime Dynamix Bone and Mineral Metabolism, Q4 2021: Assuming tenapanor were FDA approved, how soon would you anticipate prescribing it to a dialysis patient (n=205)

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Well-Established Market Growing at 3-4% Annually

>550K

U.S. Dialysis Patients[1]

~80%

Are treated for hyperphosphatemia[2]

~440,000

Patients in total addressable market

8,000

HCPs account for 90% of Rxs[3]

1. United States Renal Data System. 2019 USRDS annual data report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2019.
2. US-DOPPS: https://www.dopps.org/DPM/Files/PBINDER_use_c_overallTAB.htm. Accessed on 1/31/2020
3. IQVIA Xponent data, rolling 12 months thru Aug 2019

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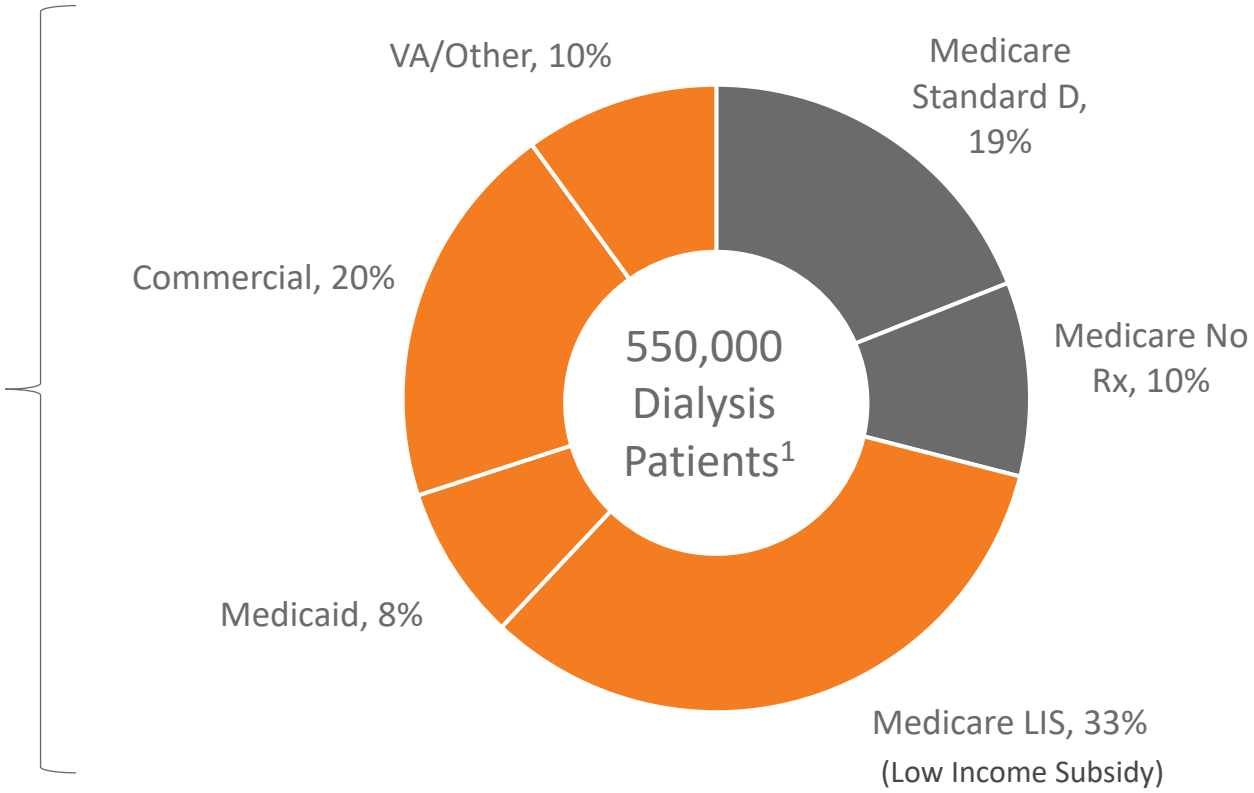
Favorable Payor Landscape for Hyperphosphatemia Rx Therapies

62% Medicare / 38% Commercial, Medicaid, Other

XPHOZAH Launch Landscape:
70% Access and Affordability Potential



1. United States Renal Data System. 2019 USRDS Annual Data Report: Epidemiology of kidney disease in the United States. National Institutes of Health, National Institute of Diabetes and Digestive and Kidney Diseases, Bethesda, MD, 2019. Calculated from USRDS 2019 data (2017 actuals) with growth projections.
Payor Mix Estimates: Spherix RealWorld Dynamix Dialysis 2019 and USRDS 2018 Medicare Breakdown

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XPHOZAH Positioning Establishes Central Role of Blocking Across Hyperphosphatemia Treatment Paradigm, to Help More Patients Achieve Target Phosphorus Levels

- XPHOZAH: an investigational, first-in-class, non-binder, Phosphate Absorption Inhibitor (PAI) that aims to make consistently achieving phosphorus targets possible with its novel blocking mechanism, that blocks the primary pathway of phosphate absorption so that more patients may be able to achieve target phosphorus levels
- XPHOZAH Go-To-Market Strategy
  focused on establishing the central role of blocking across the hyperphosphatemia treatment paradigm. Blocking may enable a greater proportion of patients to achieve target phosphorus levels, which has been a significant challenge with the currently available phosphate-lowering therapies that all act via the binding mechanism

XPHOZAH (tenapanor) is an investigational product

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Summary: Investigational Product Candidate, XPHOZAH, Would Address Clinical Unmet Need. HCPs are Highly Aware and Report Strong Intent to Adopt

- Significant unmet need with a large proportion of patients unable to achieve target phosphorus levels with currently available therapies
- XPHOZAH provides a novel mechanism, as first-in-class phosphate absorption inhibitor, that blocks the primary pathway of phosphate absorption
- Blocking mechanism provides meaningful differentiation
- Strong clinical data to address unmet need
- Concentrated market addressable with specialized sales force and omnichannel approach
  - ~8,000 high writing HCPs account for 90% of prescriptions
- HCP projected uptake supports strong revenue potential

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RDX013 for Hyperkalemia

Investigational, first-in-class potassium lowering secretagogue

Leverages the GI's natural ability to secrete potassium into the lumen of the gut to reduce serum potassium levels

RDX013: First-in-Class Potassium Secretagogue for Treatment of Hyperkalemia

- Approximately 2 million people in the U.S. with CKD and/or heart failure with hyperkalemia
  - Potassium lowering therapies limited to binder mechanism of action
  - Current market defined by acute episodic intervention with significant growth potential with more proactive chronic management
- Significant unmet need for a therapy that enables more active management to minimize episodes of hyperkalemia
- RDX013 first-in-class potassium secretagogue under development with a meaningfully differentiated mechanism of action
  - Potent
  - Tablet formulation
- Concentrated market addressable with specialized sales force

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RDX013-101: Phase 1 Data Demonstrates Comparable PD Response to Potassium Binders in Healthy Subjects at a Significantly Lower Dose

Design: Double-blind, placebo-controlled, healthy volunteer study

- N=112 - 8 groups with different doses and regimens over 12 days/ 11 nights

Results:

Binder	K-binding capacity (human stool data)	Maintenance dose	Fecal potassium excretion (Healthy volunteers)
NaPSS/CaPSS*	~0.4-0.8 mEq/g	~10g – 30g QD [1]	~0.4-0.8 mEq/g
Veltassa	~1-1.5 mEq/g	8.4-16.8 g QD	~9-17 mEq/d [2]
Lokelma	1.8 mEq/g	5-10 g QD	~9-18 mEq/d [3]
RDX013	NA	RDX013 (~100 mg) BID	19 mEq/d [4]

- Well Tolerated
  - There were no treatment-related trends in terms of AEs; majority of TEAEs reported were mild in severity and resolved without treatment

* NaPSS- Sodium Polystyrene Sulfonate. CaPSS-Calcium Polystyrene Sulfonate 1. Not approved for chronic use in US, but reported studies showed these doses reduced serum [K] by 0.9-1.0 mEq/L (7d to 9Mo studies) (LePage_2016; Yu_2017) 2. Patiromer K-binding capacity appears to be non-linear, with higher capacity at low doses; at approved doses binding capacity is ~1 mEq/g (Li_2016) 3. Lokelma K-binding capacity appears linear with dose (Lokelma package insert) 4. Data from Ardelyx Phase 1b study

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RDX013-201: Phase 2 Study Design

Objective

Part A

- To evaluate the safety and pharmacodynamics of RDX013 at different doses to identify the best dose for further evaluation in Part B of the study

Part B

- To assess the safety and efficacy of 4-week treatment with RDX013 at the optimal dose in patients with hyperkalemia

Key Inclusion Criteria

- sK value 5.1 to < 6.5 mmol/L at Screening
- Chronic kidney disease with eGFR ≥ 15 to < 60 mL/min/1.73m^2, most recent historical value (MDRD or CKD-EPI formula)

Key Exclusion Criteria

- Treatment with potassium-lowering drugs (e.g. Kayexalate®, Lokelma®, Veltassa®), within 7 days prior to enrollment/randomization
- Treatment with glucocorticoids
- Treatment with aldosterone receptor antagonists

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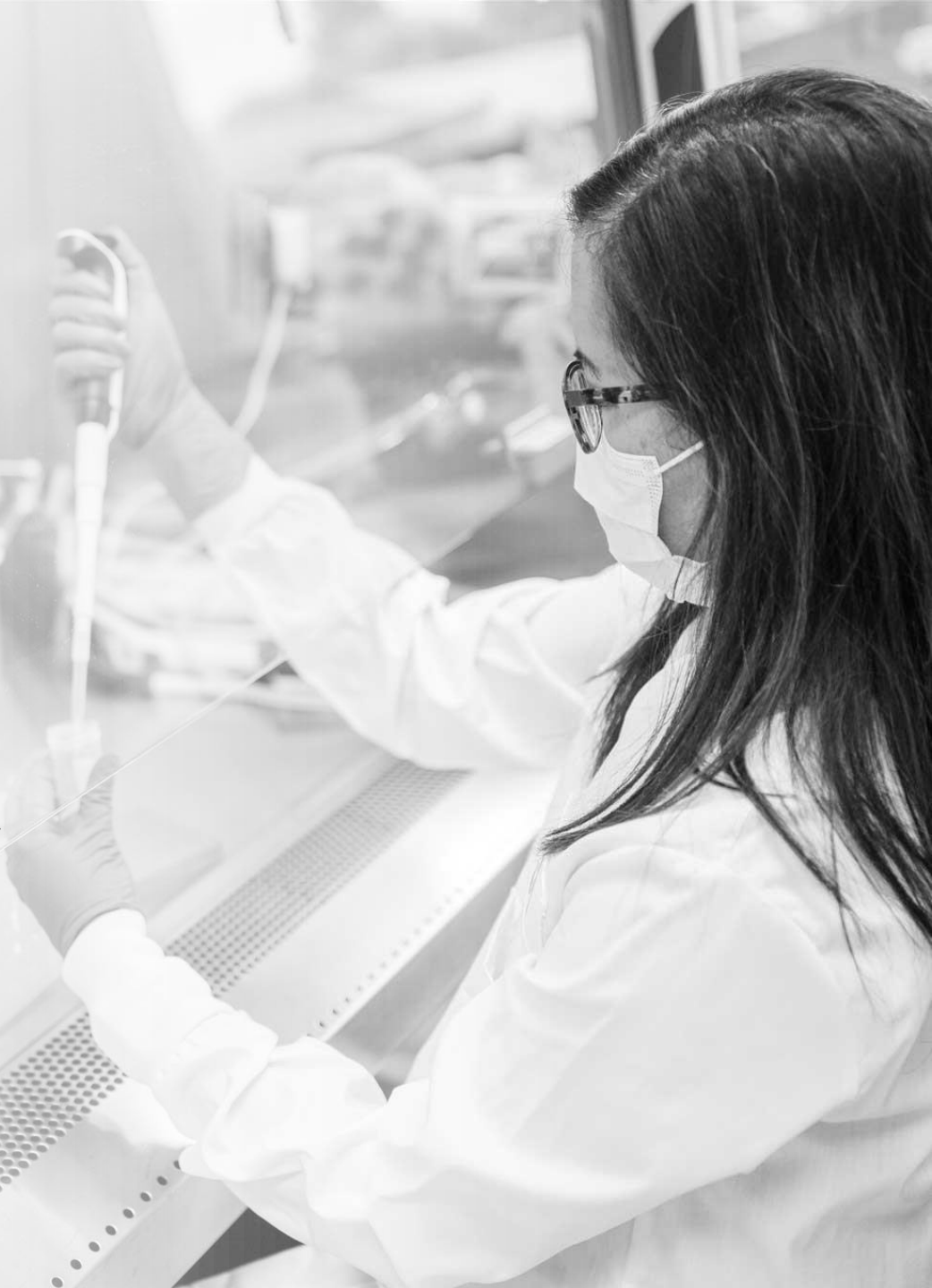
RDX020 for Metabolic Acidosis

First-in-class agent for treating metabolic acidosis by inhibiting intestinal bicarbonate exchange

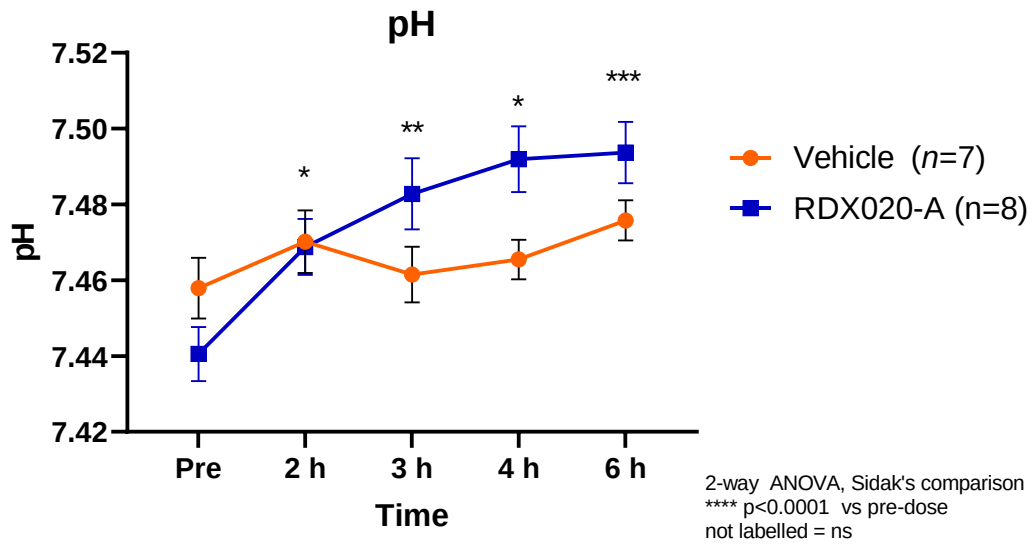


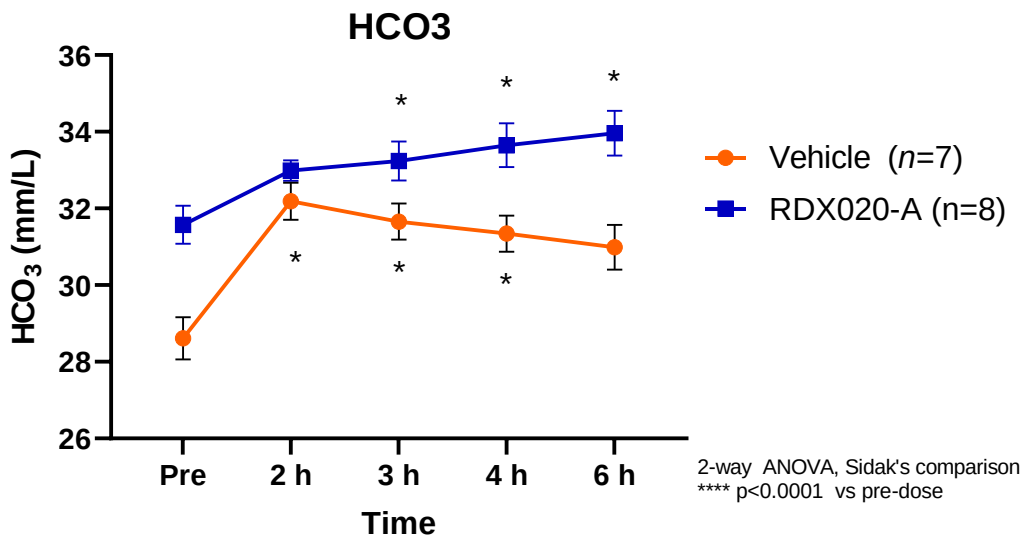
RDX020: Pre-Clinical Lead Compound Demonstrates Promising Pharmacodynamic Activity

Metabolic acidosis is a highly prevalent comorbidity in CKD, strongly correlated with disease progression and adverse outcomes. There are no approved treatments.

Rats dosed with RDX020-A exhibited a progressive increase in blood pH over the 6-hour time period of the experiment

Ardelyx bicarbonate secretion inhibitor modulated blood pH





A slight increase in blood bicarbonate level was noted over time in both groups

Male SD rats (n=8/group); JVC cannulated; Route: PO, single dose; Time-points: pre-dose, 2, 3, 4 and 6 h

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Portfolio Wrap Up & Partnerships

Ardelyx has Developed a Suite of Novel Products to Address Unmet Medical Needs Across GI and Cardio Renal Therapeutic Areas

Approved Product

IBSRELA® (tenapanor) tablets

NHE3 Inhibitor available in the U.S. and Canada for the Treatment of Irritable Bowel Syndrome with Constipation (IBS-C) in Adults

Late-Stage Asset

XPHOZAH® (tenapanor) tablets

First-in-class investigational product for the control of serum phosphorus in adult patients with chronic kidney disease (CKD) on dialysis

Continued Innovation

- RDX013 for Hyperkalemia
- RDX020 for Metabolic Acidosis

Accelerating Top-Line Growth

- IBSRELA® launched in April 2022 and available in U.S. and Canada.
- Peak annual net revenue estimate of >$500M
- Cash of $116.7M[1]

1. Cash, cash equivalents and short-term investments as of December 31, 2021

Reaching Ex-US Geographies Through Partners

Japan:
Kyowa Kirin Co., Ltd.

- $30M upfront payment, up to $55M and 8.5B Yen in milestones, high-teen royalties

China:
Fosun Pharma

- $12M upfront payment, up to $113M in milestones, mid-teen to 20% royalties

Canada:
Knight Therapeutics, Inc.

- Up to CAD $25M in upfront payment and milestones, tiered royalties ranging from mid-single digits to low twenties
- IBSRELA launched

Maintaining flexibility in Europe

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Thank You