ARDELYX®

BREAKTHROUGH SCIENCE FOR **BETTER HEALTH**

Passionately committed to bettering the lives of patients with kidney and cardiovascular diseases

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, including statements regarding the potential for Ardelyx's product candidates in treating the diseases and conditions for which they are being developed, the potential for the use of tenapanor as monotherapy and as part of a dual mechanism approach with tenapanor and binders for the control of serum phosphorus in chronic kidney disease (CKD) patients on dialysis, Ardelyx's expected timing of its submission to the FDA of a NDA for tenapanor for the control of serum phosphorus in CKD patients on dialysis, and Ardelyx's expectation regarding the potential approval of such NDA and the expected timing thereof, the commercial potential for Ardelyx's product candidates, Ardelyx's expectations regarding the size of the patient populations for its product candidates, Ardelyx's ability to establish collaborations in the future and Ardelyx's expectations regarding the exhaustion of its current capital resources. Such forward-looking statements involve substantial risks and uncertainties that could cause the development of Ardelyx's product candidates 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 research and the clinical development process; the uncertainties associated with the regulatory approval process; and the uncertainties in the drug commercialization 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 May 7, 2020, and its future current and periodic reports to be filed with the Securities and Exchange Commission

OUR VISION

To dramatically enhance the lives of patients with kidney and cardiovascular diseases by delivering innovative medicines that matter

Ardelyx Overview

- Lead product candidate, tenapanor, represents first-in-class medicine for the control of serum phosphorus in patients with chronic kidney disease (CKD) on dialysis
- Three successful Phase 3 studies demonstrating tenapanor's ability to reduce phosphate levels, as monotherapy and as part of a dual mechanism approach with phosphate binders
- NDA Submitted June 2020
- Expect FDA approval in mid-2021
- >2.5M U.S. phosphate binder prescriptions[1]
- Opportunity for specialty U.S.-focused renal commercial organization; Ex-US commercialization through collaborations
- IBSRELA® (tenapanor) for IBS-C approved Sept 2019
  - Seeking commercialization partner
- Pipeline program for novel asset in hyperkalemia
- Cash of $223.2M[2] supports operations through early 2022

1. IQVIA 2019 (Retail); Adding estimate for Rxs through dialysis organization specialty pharmacies
2. Cash, cash equivalents and short-term investments as of March 31, 2020

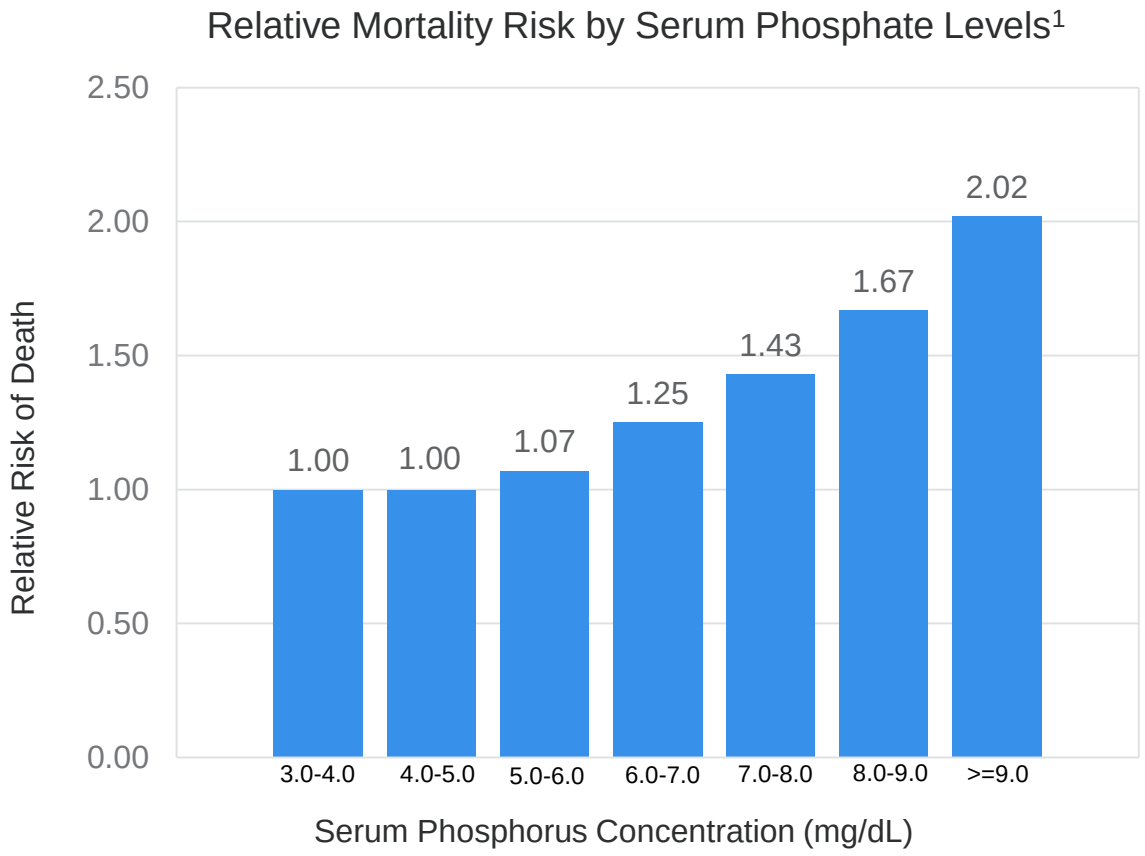
Tenapanor for Hyperphosphatemia

INVESTIGATIONAL, FIRST IN CLASS PHOSPHATE ABSORPTION INHIBITOR THAT PROVIDES AN INNOVATIVE AND DIFFERENTIATED NON-BINDER APPROACH TO PHOSPHORUS CONTROL

ARDELYX®

Phosphate Level is an Independent Predictor of Morbidity and Mortality in Patients on Dialysis[1]

Serious Potential Consequences With Elevated Phosphorus Levels



Increased risk was not diminished by statistical adjustment for coexisting medical conditions, delivered dose of dialysis, nutritional parameters, or markers of noncompliance

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

There is a High Unmet Need for Novel Hyperphosphatemia Treatments

Approximately 95% of CKD patients on dialysis need phosphate control[1]

72%

of patients treated with binders had at least one phosphorus level >5.5 mg/dL in the past six months[2]

SUB-OPTIMAL AND INCONSISTENT PHOSPHORUS CONTROL WITH PHOSPHATE BINDERS

1. Savica, V Nephrol Dial Transplant 2006 21: 2065-2068
2. Spherix RealWorld Dynamix, Dialysis 2018

Inherent Limitations with Phosphate Binder Mechanism of Action

BIND DIETARY PHOSPHATE IN THE GUT

- MOA requires dosing with every meal
- Dosing frequency

LIMITED BINDING CAPACITY

- Number of pills
- Size of pills
- Formulation

POOR TOLERABILITY

- Constipation
- Bloating
- Nausea
- Diarrhea

Challenges with Efficacy and Patient Adherence

Novel Mechanism of Action with Tenapanor Provides a Solution

TENAPANOR FIRST-IN-CLASS APPROACH

Unlike phosphate binders,
tenapanor is a phosphate absorption inhibitor that…

1

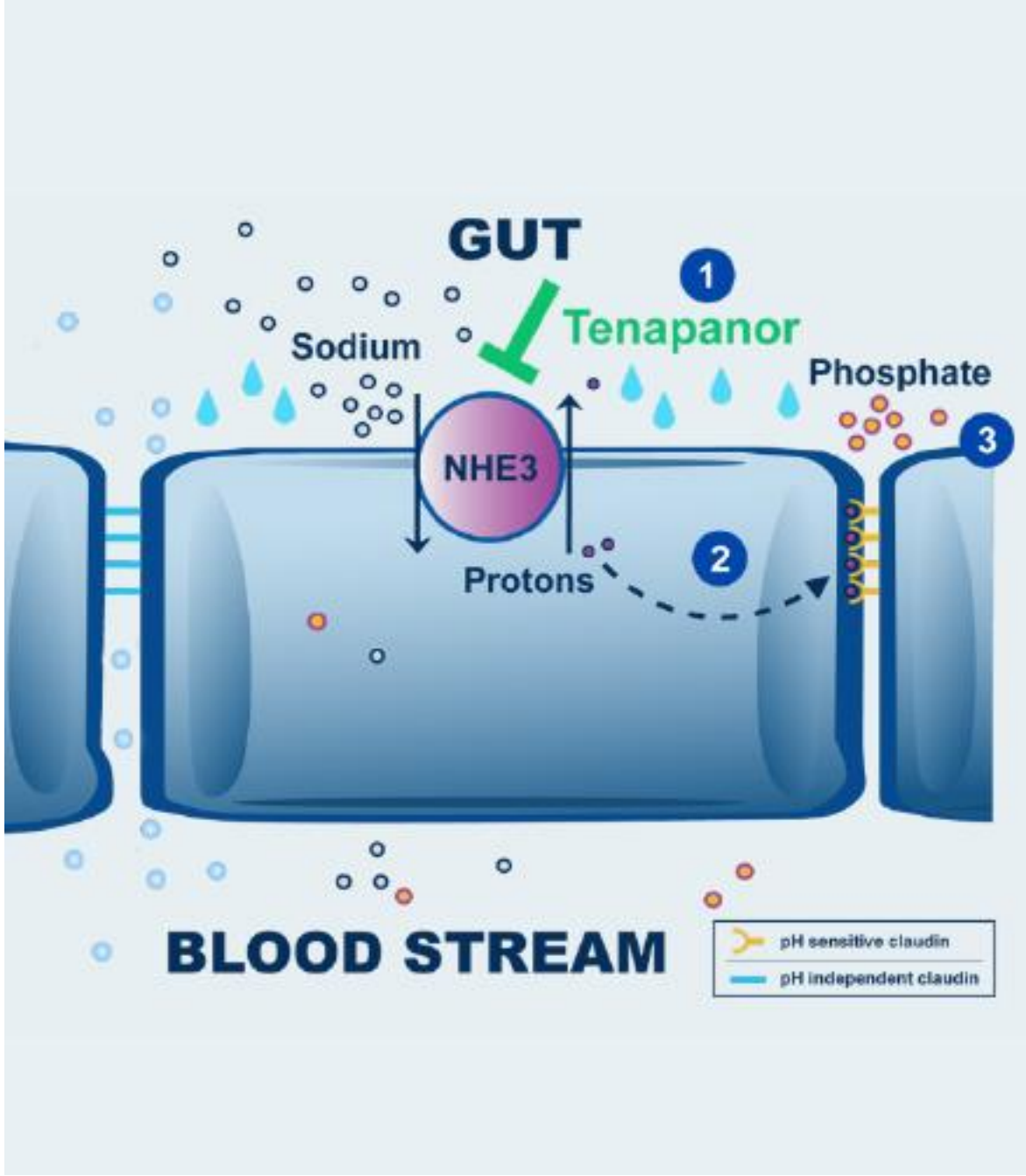
TARGETS
primary pathway of phosphate absorption

2

BLOCKS
paracellular uptake of phosphorus

3

WORKS
without inherent limitations of binders



Tenapanor Controls Phosphorus with One Small Pill Taken Twice Daily

One week dose of
Tenapanor[1]
1 pill BID

FEWER PILLS

SMALLER PILLS

LESS FREQUENT DOSING

DIFFERENTIATED TOLERABILITY

One week dose of most prescribed phosphate binder
~3+ pills TID with meals and snacks

1. As observed in clinical studies of 10-30 mg tenapanor, an investigational medicine, taken twice per day per study protocols. 10 mg shown here for illustrative purposes

Tenapanor Clinical Development Program

Comprehensive Development Program Supports Tenapanor Opportunity

MONOTHERAPY	DUAL MECHANISM BENEFIT	MONOTHERAPY long-term use	NORMALIZE targeting normal serum phosphorus
✓ **First Phase 3**	✓ **Phase 3 AMPLIFY**	✓ **Phase 3 PHREEDOM**	**Phase 4 NORMALIZE**
Primary and Secondary Endpoints met	Primary and Key Secondary Endpoints met	Primary Endpoint and Key Secondary Analyses met	Initial Analysis Demonstrates Increased % of Patients Achieving Goal

Expect FDA approval in mid-2021

First Phase 3: Blinded, Placebo-Controlled Pivotal Trial

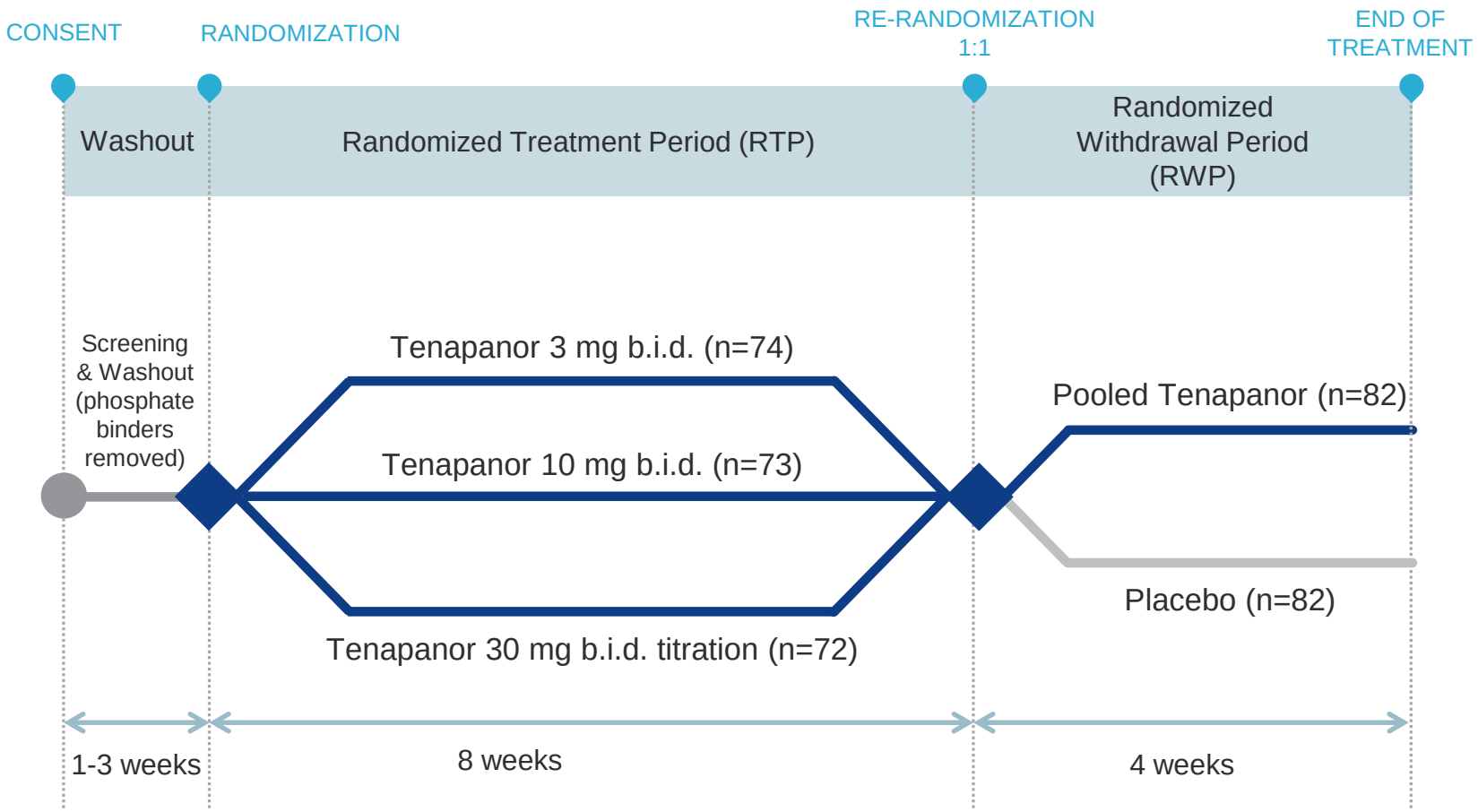
Evaluated the short-term efficacy and safety of tenapanor monotherapy

OBJECTIVE

12-week trial to evaluate different doses of tenapanor, as well as the efficacy, safety and tolerability of tenapanor monotherapy in CKD patients on dialysis

PRIMARY END POINT

Mean change in serum phosphate over the 4-week RWP for the tenapanor group (using pooled data) versus the placebo group



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

Tenapanor First Phase 3 Pivotal Monotherapy Trial Met Primary Endpoint

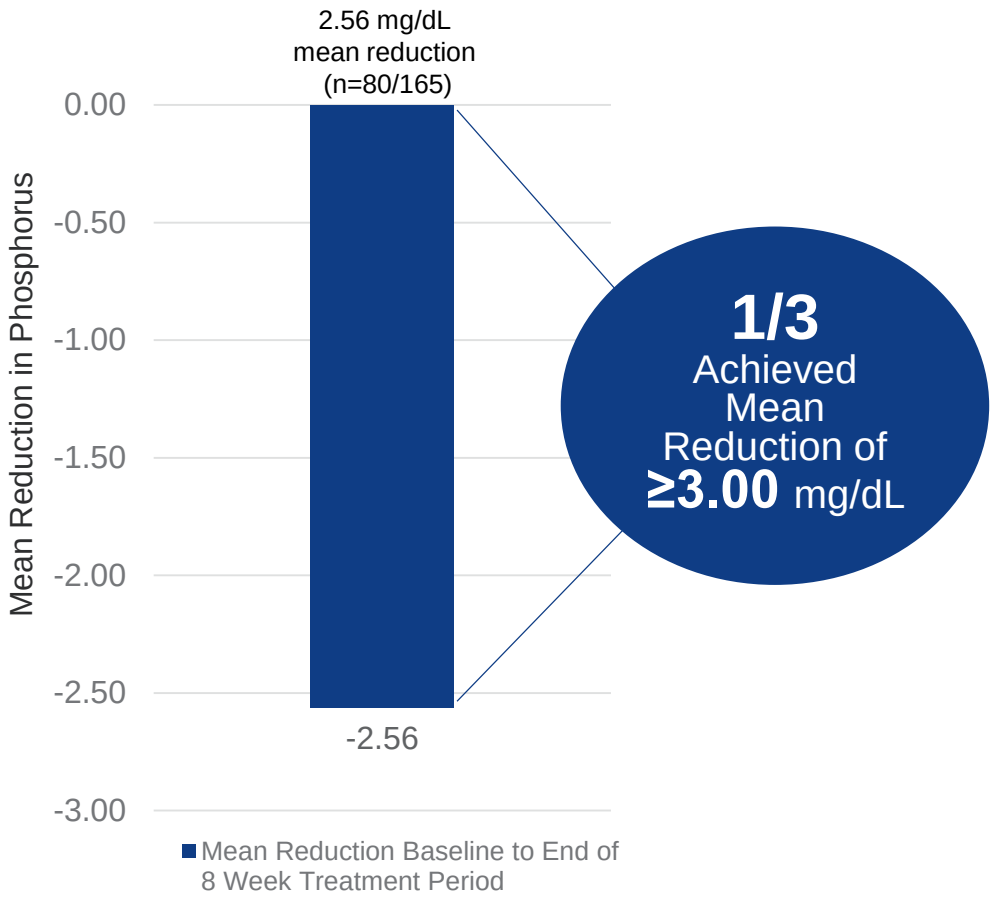
STATISTICALLY SIGNIFICANT DIFFERENCE IN SERUM PHOSPHOROUS LEVELS

- Primary endpoint achieved
  - Statistically significant difference for tenapanor vs. placebo (-0.82 mg/dL; p=0.01)
- ~50% of tenapanor-treated patients achieved a mean phosphorus reduction of 2.56 mg/dL over 8-week period

FAVORABLE TOLERABILITY

- Diarrhea most common AE – mostly mild to moderate
- Only 8% discontinuation due to diarrhea

EIGHT-WEEK TREATMENT PERIOD



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

AMPLIFY Pivotal Phase 3

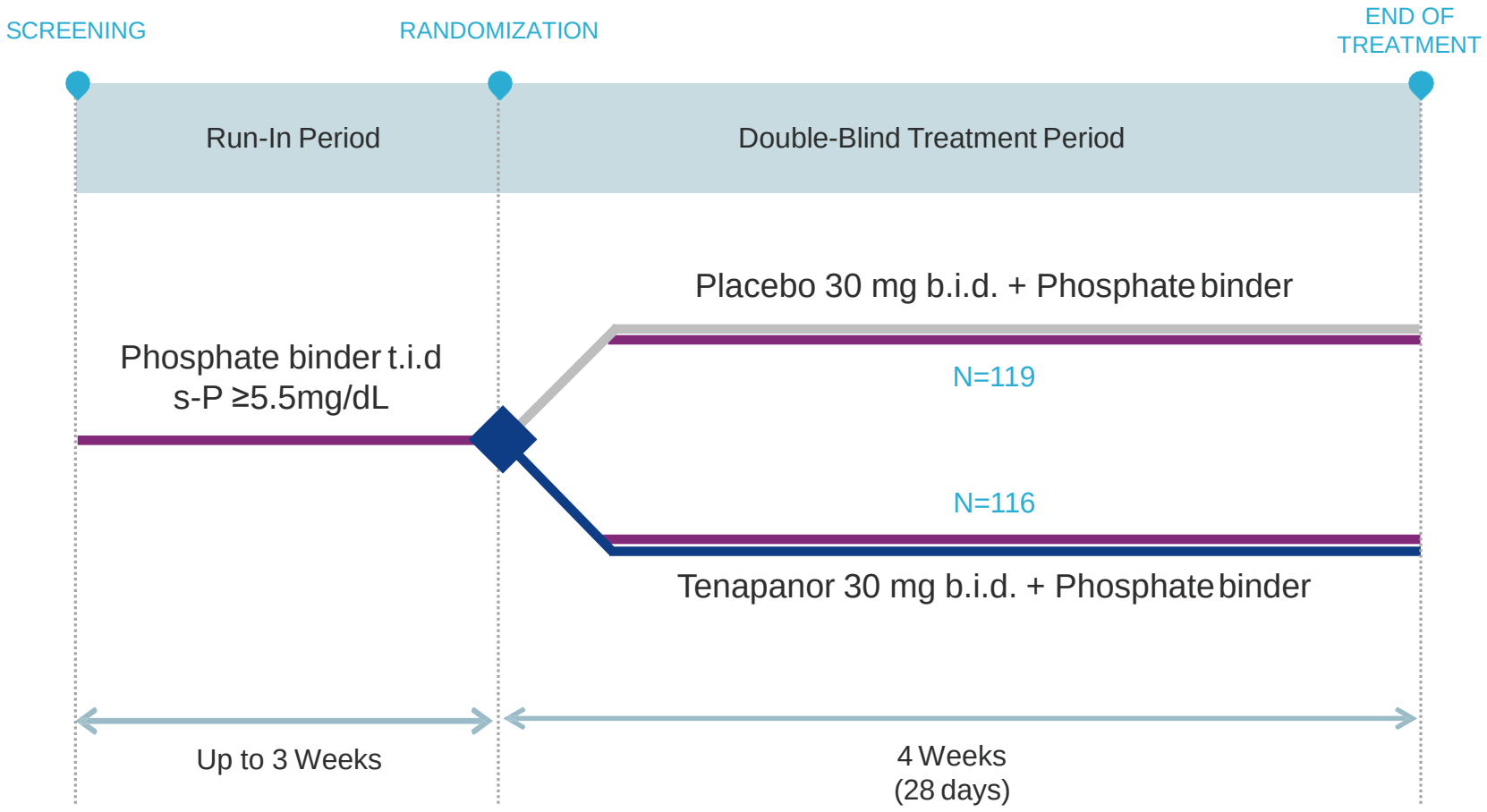
Evaluated tenapanor in combination with a different MOA

OBJECTIVE

To evaluate tenapanor and phosphate binders (two distinct MOAs) when used in combination

PRIMARY END POINT

Comparison of change from baseline in serum phosphorus at week 4 between tenapanor + phosphate binder (tenapanor arm) and placebo + phosphate binder (binder arm)



AMPLIFY: Statistically Significant Pivotal Phase 3 Results

Primary and all key secondary endpoints were met

STATISTICALLY SIGNIFICANT DIFFERENCE IN REDUCTION OF SERUM PHOSPHOROUS LEVELS

- Statistically significant (p=0.0004) reduction of serum phosphorus compared to binders alone at week 4
- ~2x more patients achieved established serum phosphorus treatment goal of <5.5 mg/dL (p-values≤0.0097) for each week of treatment
- Statistically significant reduction (p-values≤0.0027) in FGF23 levels

FAVORABLE TOLERABILITY

- Tenapanor was well tolerated
  - 4.3% of patients in tenapanor arm discontinued vs. 2.5% in the binder arm
  - Mean dose of tenapanor was 24.2 mg
- The single adverse event with a placebo-adjusted rate >3% was loose stools/diarrhea
  - Quick onset: vast majority reported in first 5 days
  - Transient and resolved quickly: median resolution of 4 days after onset
  - Only 3 (out of 116) patients discontinued treatment due to loose stools/diarrhea

PHREEDOM Pivotal Phase 3

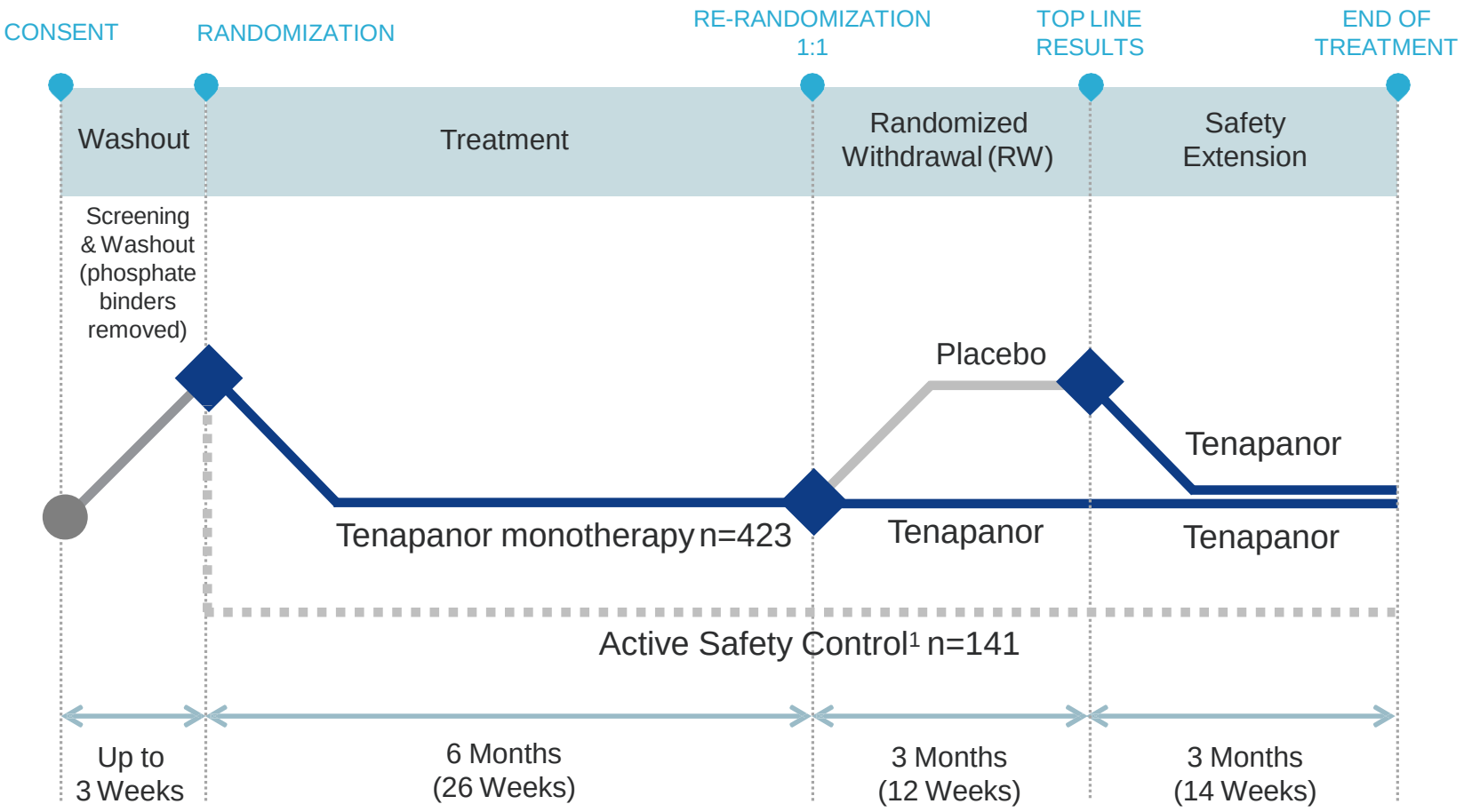
Evaluating the Long-Term use of Tenapanor Monotherapy

OBJECTIVE

52-week trial to evaluate the long-term efficacy, safety and tolerability of monotherapy tenapanor in CKD patients on dialysis

PRIMARY END POINT

The difference in change in serum phosphorus between the pooled tenapanor-treated patients and placebo-treated patients in the efficacy analysis set from the end of the 26-week treatment period to the end of the 12-week randomized withdrawal period.



1. Active safety control arm added to compare major safety events to tenapanor for risk/benefit analysis as suggested by FDA

PHREEDOM: Achieved Statistically Significant Primary Endpoint

- Primary endpoint:
  - Statistically significant ($p<0.0001$) difference in least squared mean serum phosphorus change
  - A delta of 1.4 mg/dL as compared to placebo
- Secondary analyses:
  - In the 26-week open label treatment period, 77% of tenapanor patients in the intent-to-treat population (n=408) achieved a decrease in serum phosphorus, with a mean decrease of 2.0 mg/dL
- Tenapanor generally well tolerated
  - 26-week open-label treatment period:
    - 17.2% of 419 tenapanor-treated patients vs. 22.6% of 137 sevelamer treated-patients (active safety control) experienced a SAE
    - Loose stools/diarrhea (52%) only adverse event >5% - vast majority mild to moderate
    - 5% severe diarrhea

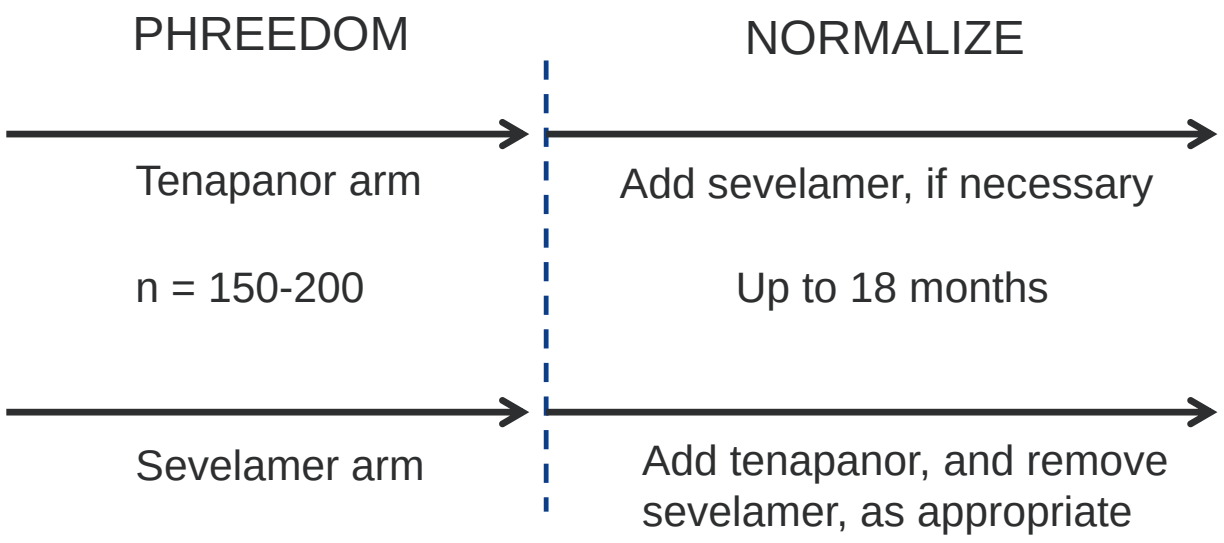
NORMALIZE: Ongoing Phase 4

WHY NORMALIZE?

- To further our understanding of the potential for the dual mechanism of tenapanor and sevelamer to reduce patients' serum phosphorus levels to normal (<4.6 mg/dL) while minimizing medication burden
- To develop a roadmap to demonstrate to physicians how to use tenapanor
  - Monotherapy
  - Binder added to tenapanor
  - Tenapanor added to binder with binder dose reduction

STUDY DESIGN

- 18-month open-label extension study of PHREEDOM
- Dose adjustments are based on serum phosphorus, aimed to favor use of tenapanor and remove or decrease amount of sevelamer used



NORMALIZE: Results (as of March 31, 2020)

- Serum phosphorus (sP)
  - Baseline (PHREEDOM): 7.27 mg/dL
  - Last Assessment (NORMALIZE): 4.94 mg/dL
  - Reduction: 2.33 mg/dL

- Majority of patients on tenapanor alone or tenapanor + low-dose sevelamer

- More patients able to achieve normal phosphorus compared to current clinical practice
  - Up to 47% within normal range (2.5 – 4.5 mg/dL) in NORMALIZE
  - 29% < 4.6 mg/dL in DOPPS

Tenapanor Commercialization

Significant Opportunity for Tenapanor in Hyperphosphatemia Market

>500K
U.S. Dialysis Patients[1]

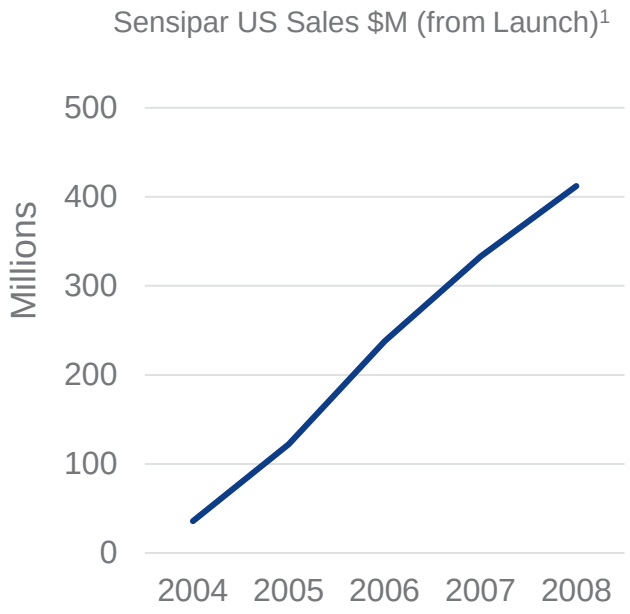
3-4%
Annualized Growth Rate of U.S. Dialysis Population[1]

>2.5M
U.S. Phosphate Binder Prescriptions[2]

1. United States Renal Data System. 2018 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, 2018.
2. IQVIA 2019 (Retail); Adding estimate for Rxs through dialysis organization specialty pharmacies

Ardelyx is Well-Positioned to Commercialize Tenapanor in the U.S.

Historically, novel mechanisms in renal outperformed and built significant markets



1. EvaluatePharma 2019
Sensipar was approved by the FDA in March 2004

Commercial Team with Experience in Kidney and Cardiovascular Diseases

Building Specialized U.S. Commercial Organization

- Targeting Nephrologists (~6,000)
- Clear unmet need
- Innovative product with differentiated and novel MOA to meet unmet need

Favorable Reimbursement Landscape for Novel Therapies Like Tenapanor

Tenapanor expected payer mix likely to be similar to existing prescription phosphate binder market

- 65 - 70% Medicare Part D (largely driven by low income subsidy patients with low copays and no coverage gap)
- 20 - 25% Commercial
- 10 - 15% Medicaid / Government Funded (VA/Tricare)

Clinically-driven payer value proposition

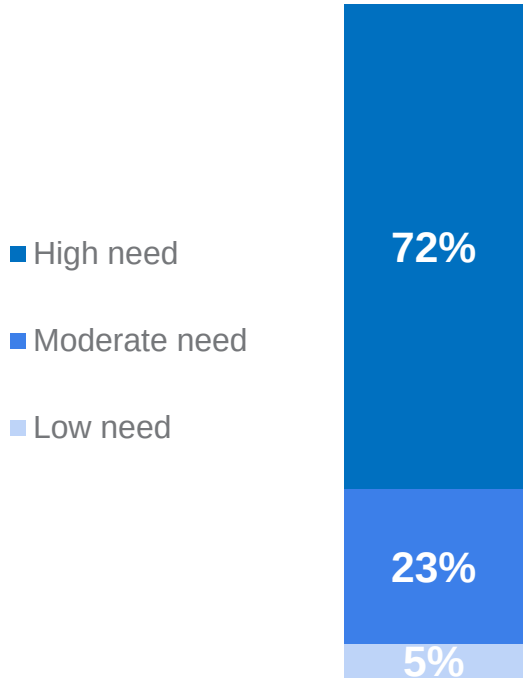
- Phosphorus management guidelines exist (KDOQI, KDIGO)
- Sub-optimal and inconsistent phosphorus control with phosphate binders
- Tenapanor's novel, non-binder MOA targets the primary pathway of phosphate absorption and is easier for patients to take, providing an opportunity to achieve guidelines

Oral-only medications not slated to be in the dialysis bundle until 2025, and potential for further delay

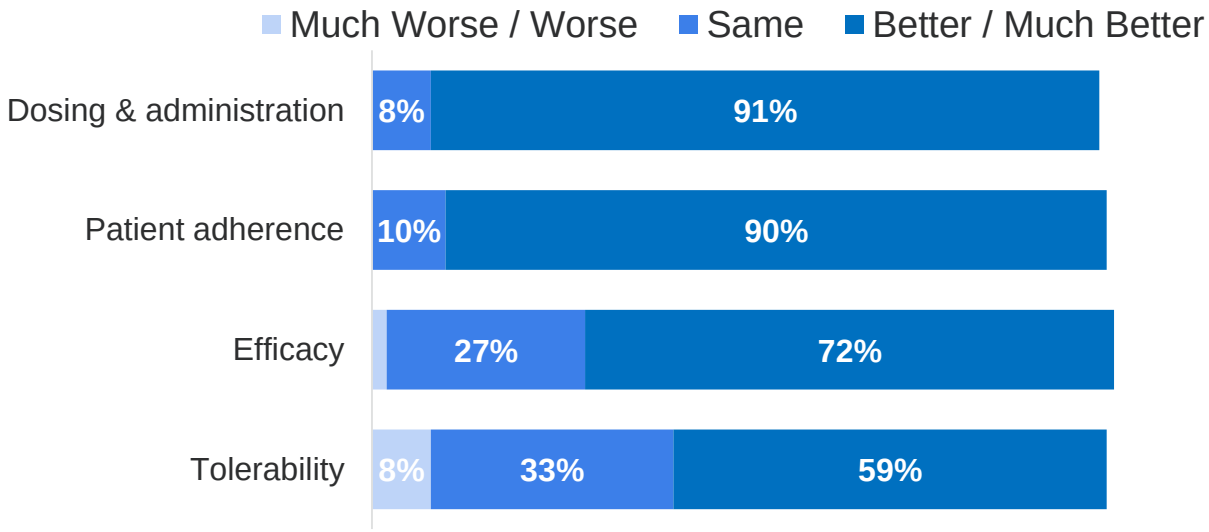
- Originally slated for 2014, then pushed to 2016, then pushed to 2025

Nearly 3 out of 4 Nephrologists See a High Need for New Treatments and View Tenapanor As a Strong Improvement Over Phosphate Binders

How Much of a Need for New Treatments?



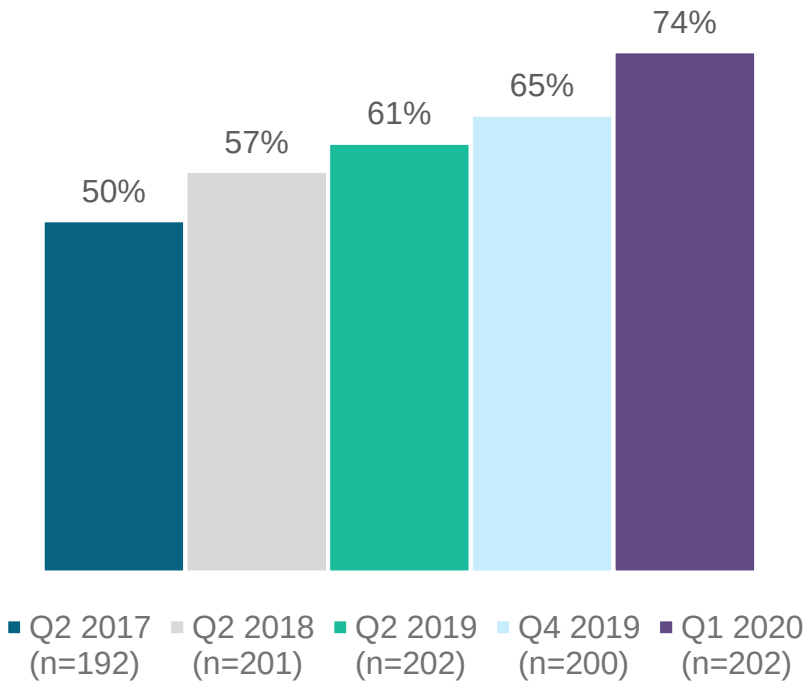
How Does Tenapanor Compare to Phosphate Binders?



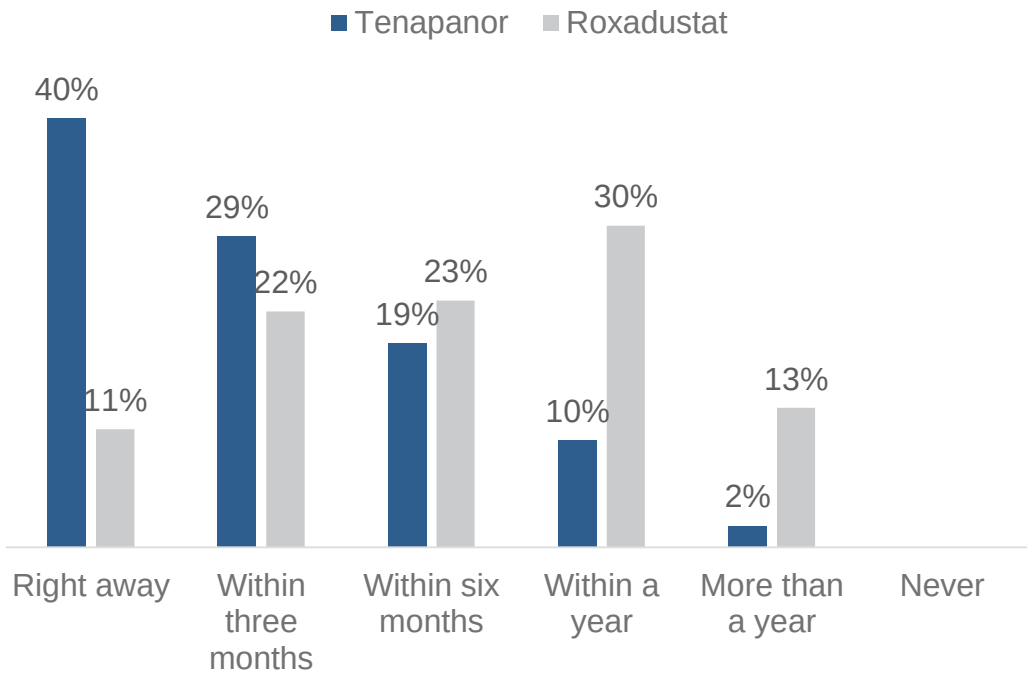
Ardelyx market research study conducted by Hawk Partners, December 2019

There is a High and Growing Interest in Tenapanor – and Nephrologists Expect Tenapanor Uptake to be Quicker than that of the First Anticipated HIF

Interest in Tenapanor
% indicating high interest



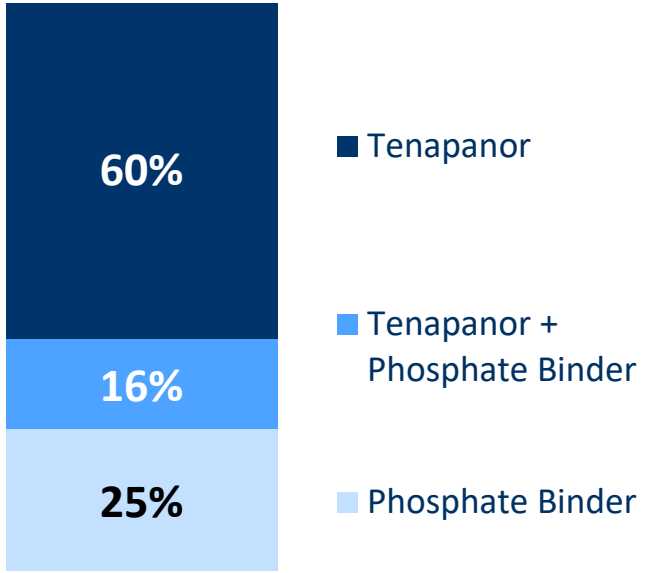
Timeline for Trial
% of respondents



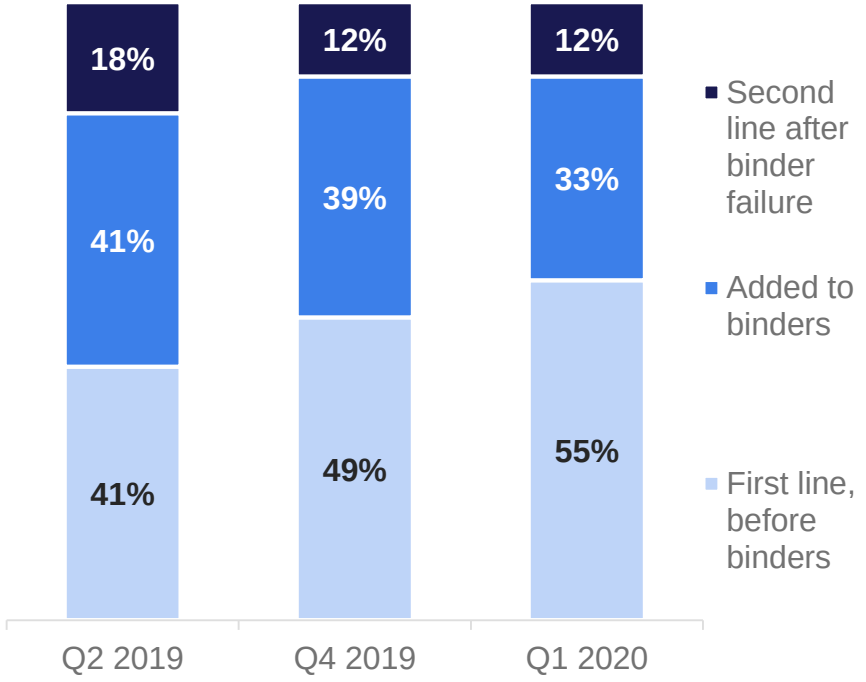
Spherix, RealTime Dynamix Bone and Mineral Metabolism, Q1 2020. Assuming tenapanor were FDA approved, how soon would you anticipate prescribing it to a dialysis patient? (n=202). Spherix, RealTime Dynamix Anemia, Q1 2020. Based on what you currently know, how soon after approval would you estimate trial of roxadustat in the dialysis and non-dialysis settings? *Excerpt from RealTime Dynamix: Bone and Mineral Metabolism, Q1 2020 (n=202)

The Majority of Nephrologists in Two Distinct Studies Expect to Use Tenapanor as Their First Line Hyperphosphatemia Therapy

Most Likely First Line Hyperphosphatemia Treatment % of respondents



Tenapanor Anticipated Line of Therapy % of respondents



Ardelyx market research study conducted by Hawk Partners, December 2019. Assuming Product X [tenapanor] is established in the market, from a clinical perspective (removing cost and access considerations), what would you be most likely to prescribe as first line therapy in a dialysis patient who requires a phosphate lowering treatment and is naïve to any phosphate lowering therapy? (n=205)
Spherix, RealTime Dynamix Bone and Mineral Metabolism, Q1 2020. If tenapanor were approved by the FDA for the management of hyperphosphatemia, how would you be most likely to use it? (n=202)

Ardelyx is Well-Positioned to Commercialize Tenapanor Outside of the U.S. with Established Partners

Ex-U.S. Cardiorenal Partnerships

CANADA

Knight Therapeutics, Inc.

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

CHINA

Fosun Pharma

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

JAPAN

Kyowa Kirin Co., Ltd.

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

RDX013 for Hyperkalemia

INVESTIGATIONAL, FIRST-IN-CLASS SMALL MOLECULE

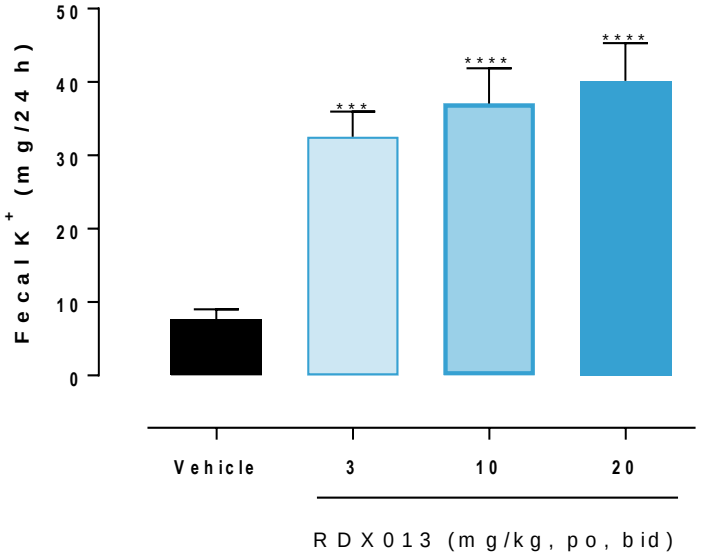
LEVERAGES THE GI TRACT'S NATURAL ABILITY TO SECRETE POTASSIUM INTO THE LUMEN OF THE GUT TO REDUCE SERUM POTASSIUM LEVELS

ARDELYX

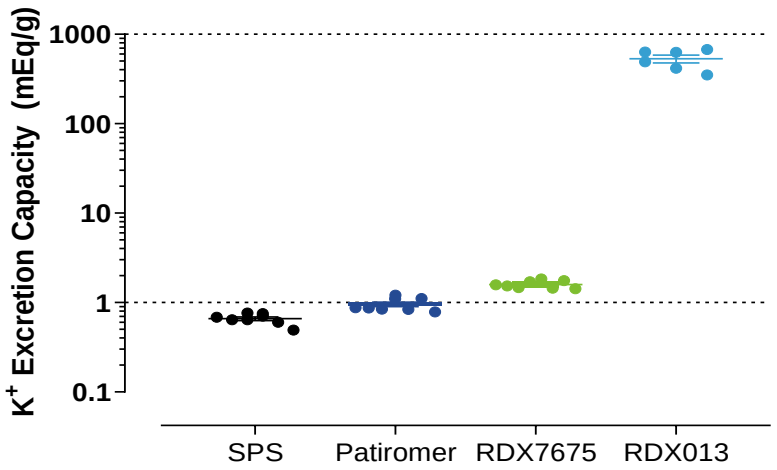
RDX013 Program:
Expanding our renal footprint

- Novel, oral small molecule potassium secretagogue program
- Convenient, small pill dosing
- Increases fecal potassium excretion; reduces serum potassium
- Allows optimal dosing of anti-hypertensives
- ~1000x improved *in vivo* efficiency vs binders

In Vivo Fecal Potassium Excretion



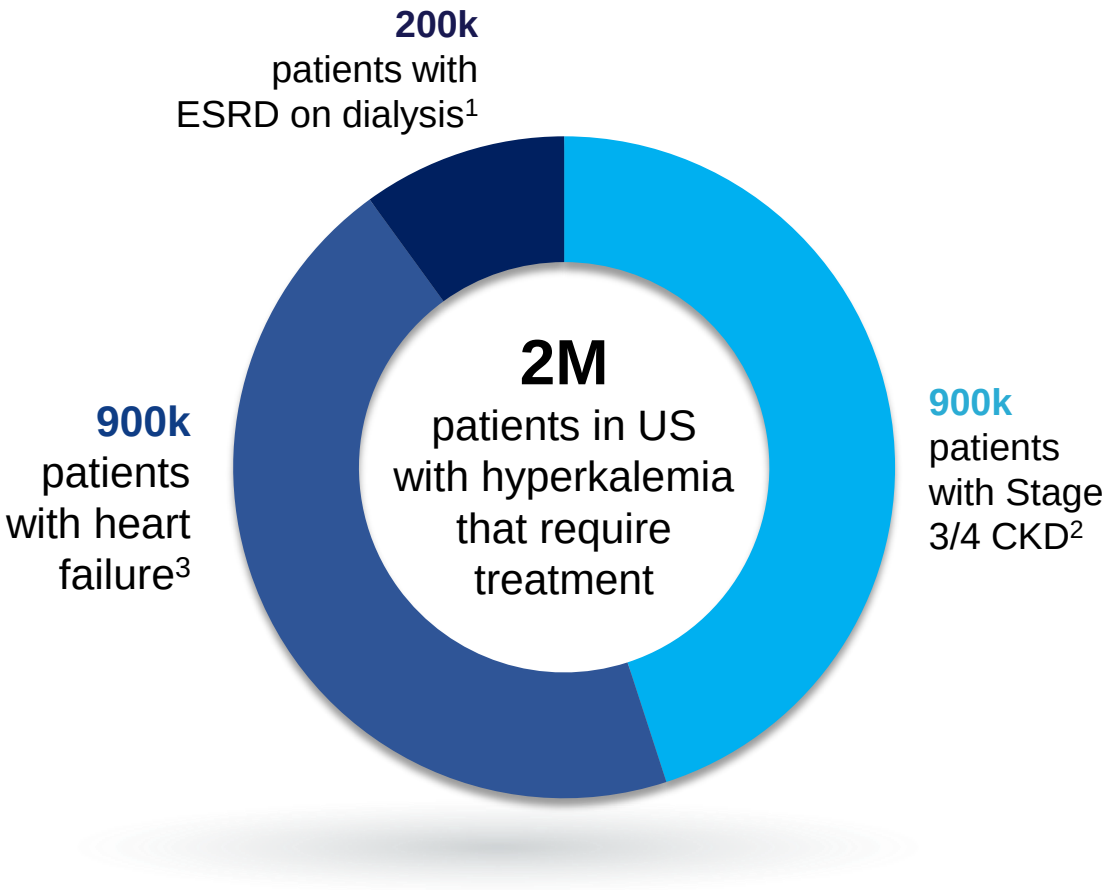
- RDX013 produces dose-dependent increases in fecal potassium excretion in rodents
- Preclinical studies indicate once-daily dosing is effective



*K+ binding capacity determined in mouse

~1,000x
Improved In Vivo Efficiency vs Binders*

RDX013: Significant Hyperkalemia Market Waiting to be Tapped



THE POTENTIAL FOR RDX013

Target Product Profile

- Preferred dose formulation
- Improved onset of action in both acute and chronic settings
- Designed for cardio and renal safety
- Enables administration of lifesaving drugs that can cause hyperkalemia (RAASi's, Entresto, Etc.)

Build upon the market being created by Lokelma and Veltassa

1. Independent Market Research, Spherix Global Insights
2. Einhorn LM, et al. Arch Intern Med. 2009 Jun 22;169(12):1156-62
3. Mozaffarian D, et al. Circulation. 2015 Jan 27;131(4):e29-322

IBSRELA® (tenapanor) in Irritable Bowel Syndrome with Constipation (IBS-C)

FIRST-IN-CLASS SMALL MOLECULE

LEVERAGES TENAPANOR'S ABILITY TO INHIBIT SODIUM UPTAKE IN THE GUT

ARDELYX

IBSRELA® (tenapanor) FDA Approved to Treat IBS-C in Adults

- Approval supported by extensive clinical and safety data package with two Phase 3 trials and a long-term safety extension study
- Achieved statistical significance for primary endpoints across all trials supporting the efficacy and safety profile of tenapanor and durable effect on reducing constipation and abdominal pain associated with the condition.
- Novel MOA offers a new and differentiated option for patients with IBS-C and the physicians who treat them
- Over 11 million people in U.S. with IBS-C
- Seeking commercial collaboration partner with broad-reaching launch and marketing capabilities
- Our collaboration partner in Canada, Knight Therapeutics, received marketing approval from Health Canada in April 2020

COVID-19: Minimal Impact to Business

- NDA: Currently no impact to our FDA interactions to-date
  - Leveraging much of the NDA work from IBSRELA®
- NORMALIZE: Study-related visits are 1x every 3 months at dialysis centers, where patients are still going 3x per week for dialysis
- Operations: Employees successfully working remotely; important pre-commercial activities continue

Committed to the Welfare of our Employees, Patients and Communities
And to Continuing our Work to Bring Medicines to Patients in Need

24-Month View of Potential Milestones and Catalysts

- AMPLIFY Phase 3 results to be presented at scientific meetings throughout 2020+
- PHREEDOM Phase 3 results to be presented at scientific meetings throughout 2020+
- NORMALIZE Phase 4 results to be presented at scientific meetings throughout 2020+
- Ongoing market development and pre-commercial activities
- Expect NDA acceptance for substantive review in late August 2020
- Expect tenapanor approval for hyperphosphatemia in mid-2021
- Potential partnership for IBSRELA
- Advancing our kidney and cardiovascular franchise with RDX013
- Ongoing progress with our partners in Japan, China and Canada

ARDELYX®

BREAKTHROUGH SCIENCE FOR **BETTER HEALTH**

Thank you