ARDELYX®

BREAKTHROUGH SCIENCE FOR **BETTER HEALTH**

Passionately committed to bettering the lives
of patients with cardiorenal 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 treatment of hyperphosphatemia, the potential for tenapanor with binders to achieve serum phosphorus levels of less than 5.5 mg/dL and less than 4.6 mg/dL, Ardelyx's expected timing of its NDA submission for tenapanor for hyperphosphatemia, the commercial potential for Ardelyx's product candidates, and Ardelyx's expectations regarding the size of the patient populations for its product candidates, 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, including the continuation of trends in initial analysis through the full clinical trial; 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 the section titled "Risk Factors" and the other disclosures included in Ardelyx's Annual Report on Form 10-Q filed with the Securities and Exchange Commission on November 6, 2019, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

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Implications of Positive Phase 3 PHREEDOM Results:

Tenapanor for the Treatment of Hyperphosphatemia

- PHREEDOM data support tenapanor as monotherapy
  - Successfully achieved primary endpoint with statistically significant results ($p<0.0001$)
  - 77% of tenapanor-treated patients in the intent-to-treat population had a mean reduction in serum phosphorus of 2.0 mg/dL from baseline
  - Generally well tolerated with the majority of AE's mild to moderate and were transient in nature
- Comprehensive data package supporting NDA submission expected mid-2020
- Commercial differentiation of tenapanor's ability to get most patients to goal
  - PHREEDOM confirms the potential for monotherapy
  - AMPLIFY demonstrates the benefits of a dual mechanism in the hardest to treat patients
  - NORMALIZE demonstrating tenapanor's ability to significantly increase the number of patients who can get to goal
  - If approved, tenapanor will be a first-in-class, non-binder phosphate absorption inhibitor
  - Potential to disrupt the binder market with new option of just one small pill BID

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Comprehensive Development Program Supports Tenapanor Opportunity

MONOTHERAPY

✓ **First Phase 3**

Primary and Secondary Endpoints met

DUAL MECHANISM BENEFIT

✓ **Phase 3 AMPLIFY**

Primary and Key Secondary Endpoints met

MONOTHERAPY long-term use

✓ **Phase 3 PHREEDOM**

Primary Endpoint and Key Secondary Analyses met

NORMALIZE real-world study

Phase 4 NORMALIZE

Initial Analysis Demonstrates Increased % of Patients Achieving Goal

Expect Potential: NDA submission in mid-2020
FDA approval in mid-2021

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PHREEDOM and NORMALIZE Results
David Rosenbaum, Ph.D., Chief Development Officer

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

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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

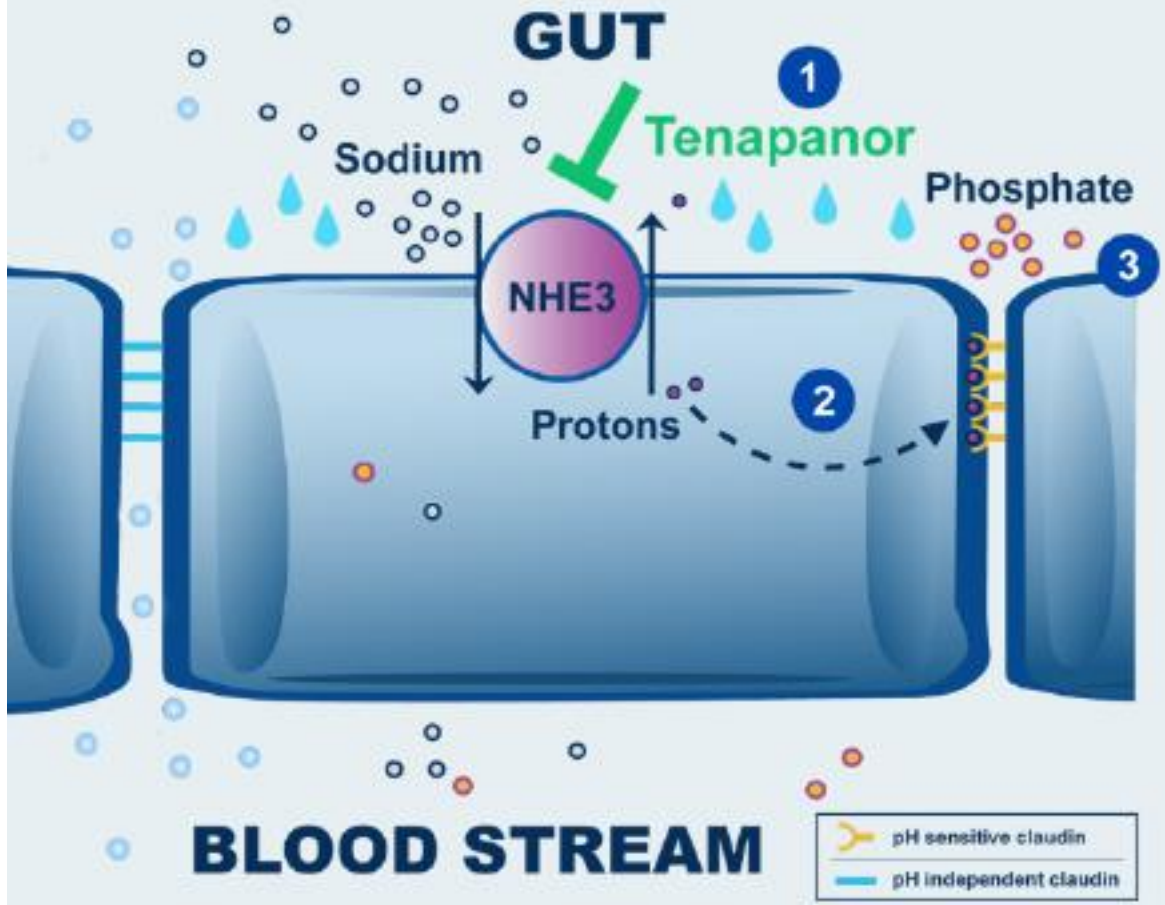
TARGETS
primary pathway of phosphate absorption

2

BLOCKS
paracellular uptake of phosphorus

3

WORKS
without inherent limitations of binders



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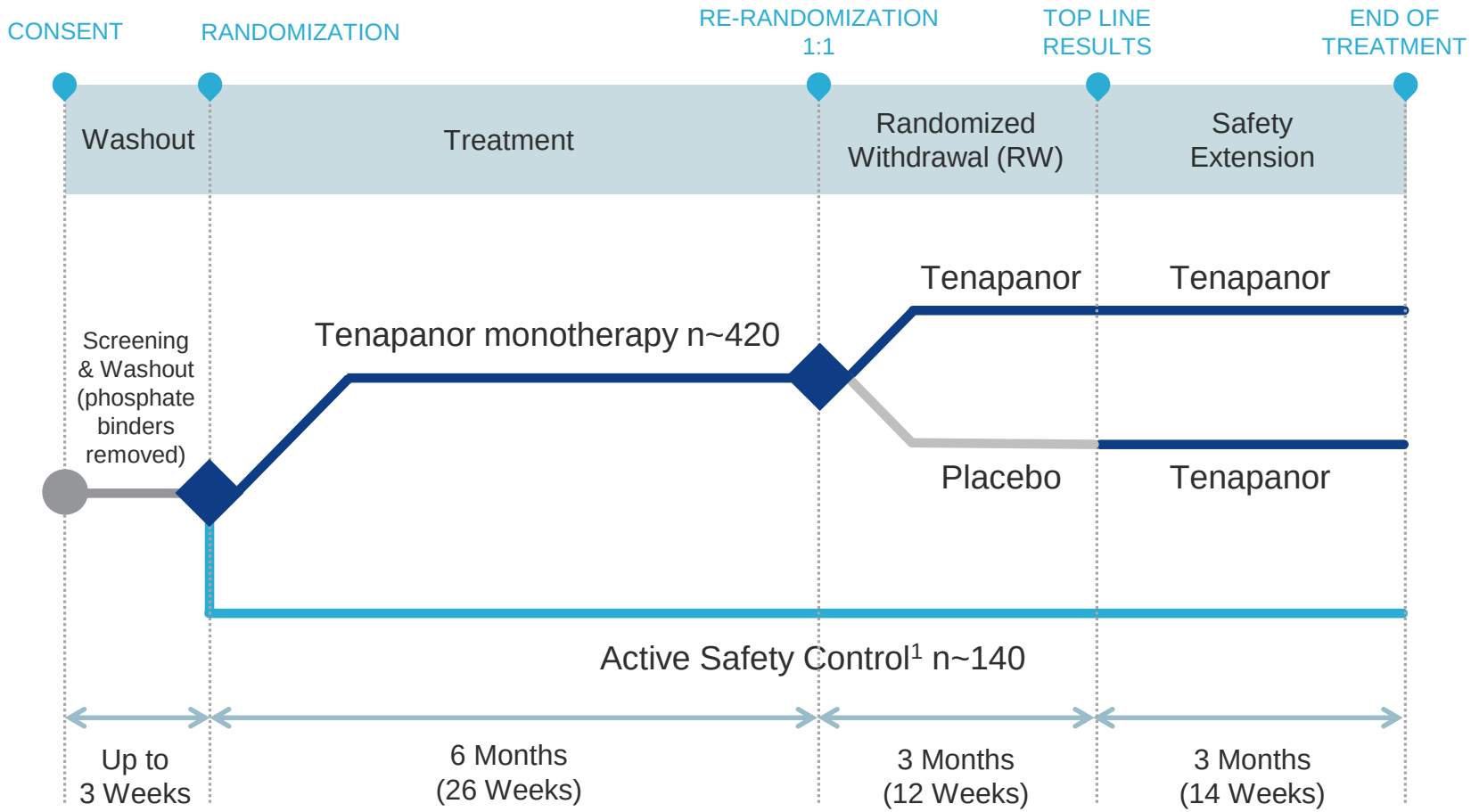
PHREEDOM Pivotal Phase 3:
Evaluating the long-term use of tenapanor monotherapy

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

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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
- Safety analysis:
  - In the safety analysis set of the 26-week open-label treatment period, 17.2% of 419 tenapanor-treated patients compared to 22.6% of 137 sevelamer treated-patients experienced a SAE
  - Median dose for tenapanor was 60 milligrams/day throughout the study vs. 4.8 grams/day median dose for sevelamer after randomization which increased to 7.2 grams/day by the end of the 26-week open-label treatment period.

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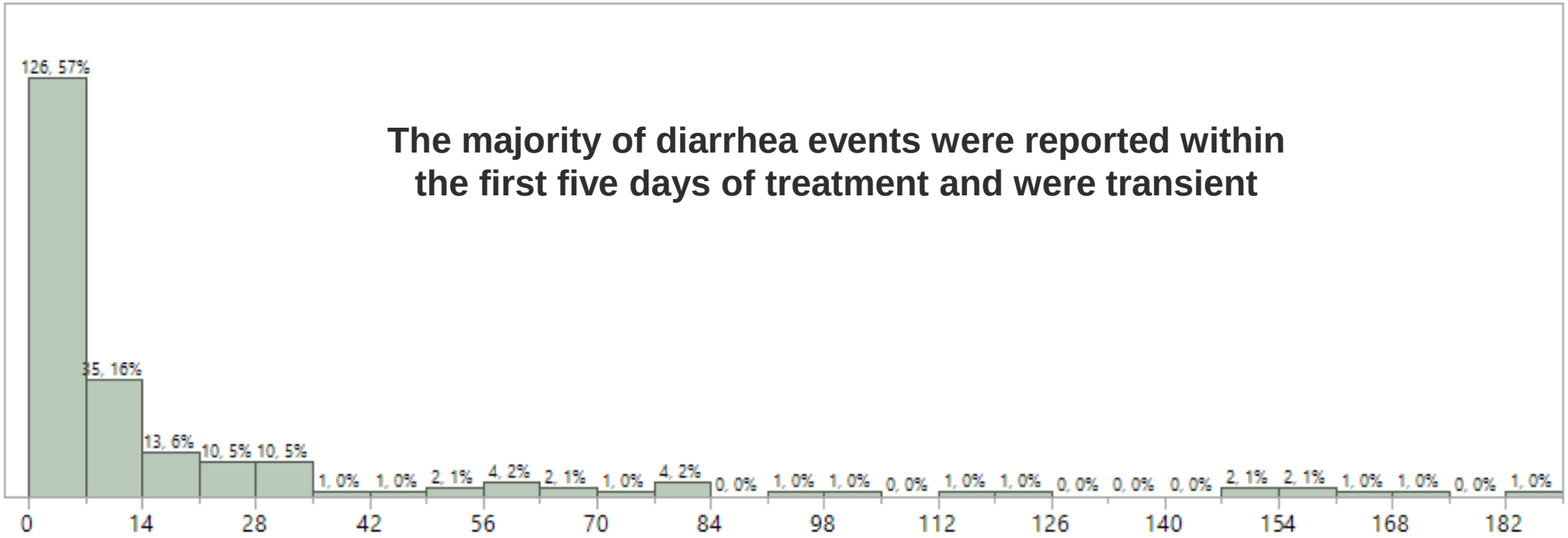
Tenapanor was Generally Well Tolerated



- 52% (220/419) of patients self-reported loose stools/diarrhea during the open label 26-week treatment period
  - Approximately 90% (196/220) events were judged by the investigator to be mild to moderate in nature
    - 16% of tenapanor-treated patients in the 26-week open-label treatment period discontinued due to loose stools/diarrhea
    - 0.8% of tenapanor-treated patients in the randomized withdrawal period discontinued due to loose stools/diarrhea

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NORMALIZE: Ongoing Phase 4

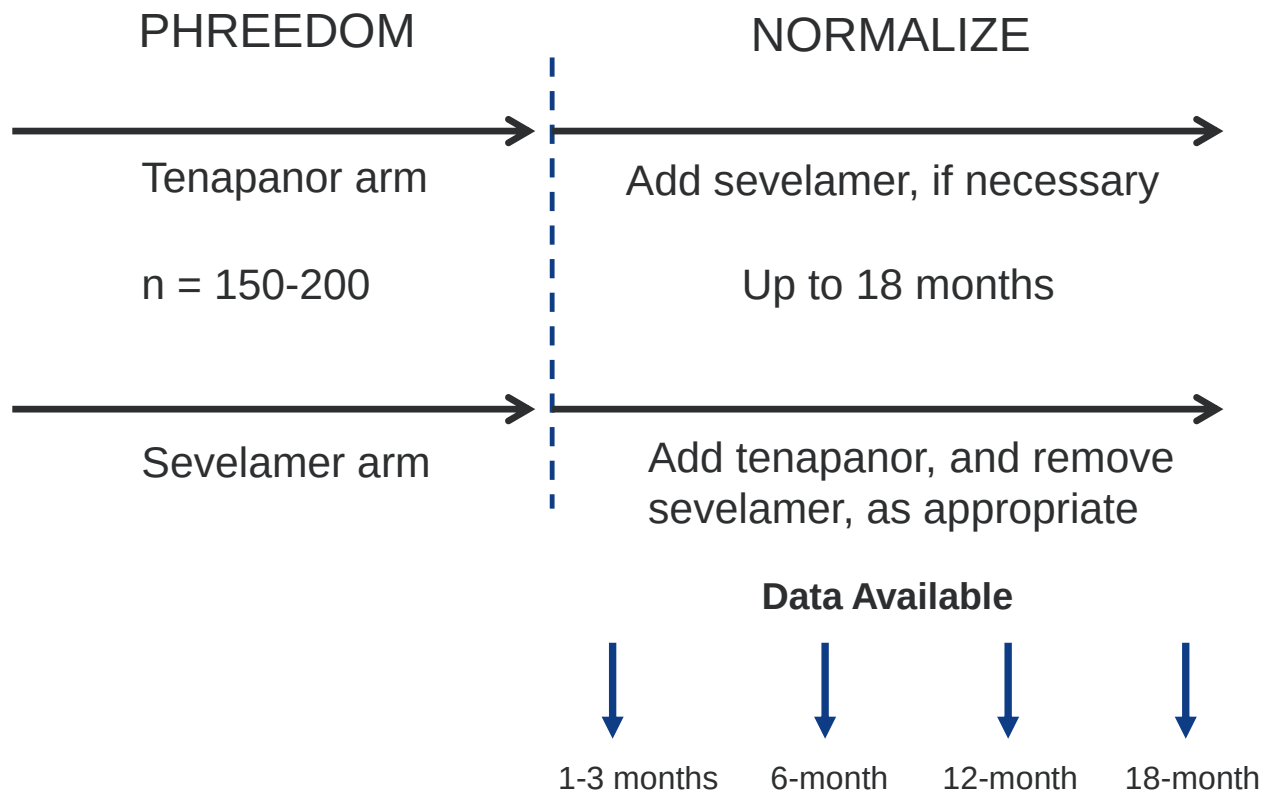
11/17/2019 Analysis

WHY NORMALIZE?

- To obtain real-world evidence regarding 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



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NORMALIZE: Patient Characteristics

- Expected to enroll up to 180 patients

- Currently 96% (116/121) of eligible patients have enrolled to date
  - 76 entered from the tenapanor arm
  - 40 entered from the active safety control arm (sevelamer)

- 73 patients have been evaluated who have >1 month of treatment (1-3 months)
  - 50 entered from the tenapanor monotherapy arm
  - 23 entered from the active safety control arm (sevelamer)

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NORMALIZE: Initial Results are Favorable to DOPPS

NORMALIZE

- 42% (31/73) patients treated for >1 month had serum phosphorus levels <4.6 mg/dL
- 71% (52/73) of patients treated for >1 month had serum phosphorus levels ≤5.5 mg/dL

Dialysis Outcomes Practice Patterns Study (DOPPS) Practice Monitor – June 2019

- 29% of patients had a phosphorous level <4.6 mg/dL
- 56% of patients had a phosphorous level ≤5.5 mg/dL

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Closing remarks
Mike Raab, CEO

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

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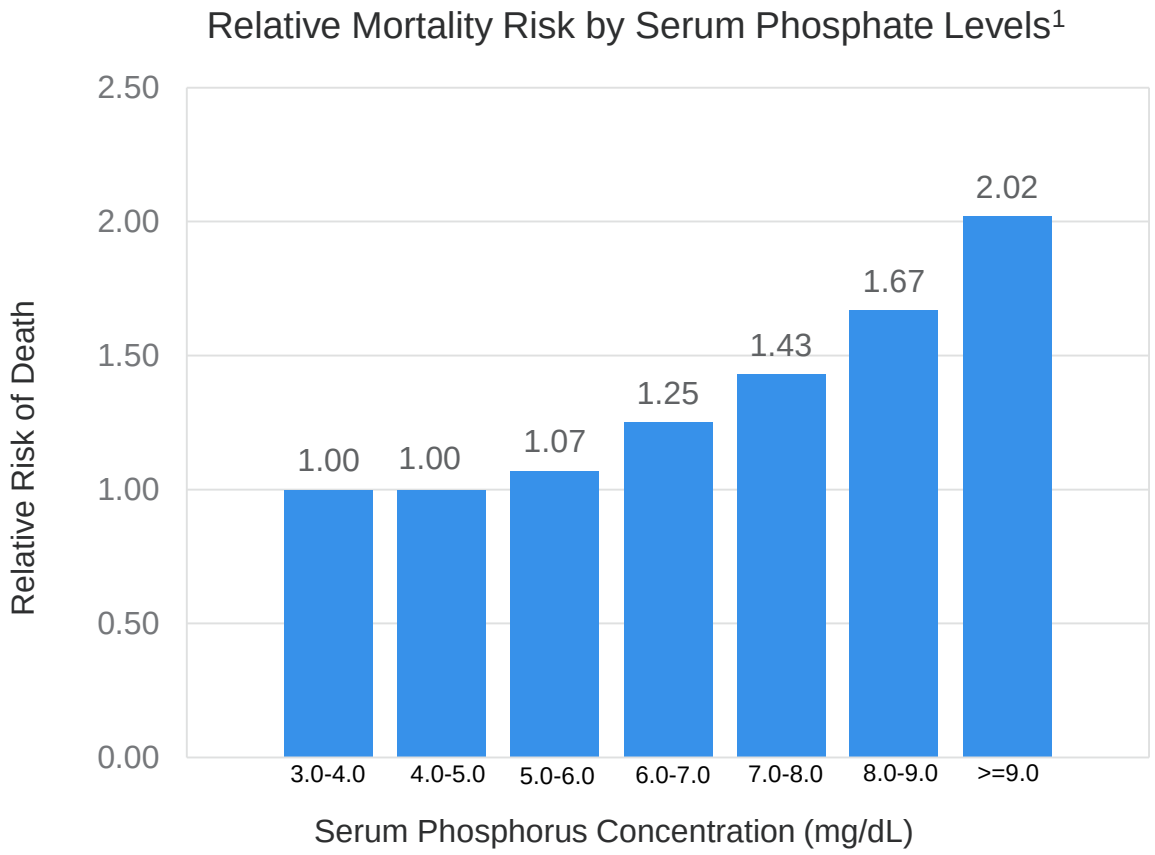
Phosphate Level is an Independent Predictor of Morbidity and Mortality in Patients on Dialysis[1]

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

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There is a High Unmet Need for Novel Hyperphosphatemia Treatments

Approximately 85% of dialysis patients require phosphate lowering treatment[1]

72%

of patients treated with binders had at least one phosphorus level >5.5 mg/dL in the past six months[1]

SUB-OPTIMAL AND INCONSISTENT PHOSPHORUS CONTROL WITH PHOSPHATE BINDERS

1. Spherix RealWorld Dynamix, Dialysis 2018

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Inherent Limitations with Phosphate Binder Mechanism of Action

BIND DIETARY PHOSPHATE IN THE GUT

- MOA requires mealtime dosing
- Dosing frequency

LIMITED BINDING CAPACITY

- Number of pills
- Size of pills
- Formulation

POOR TOLERABILITY

- Constipation
- Bloating
- Nausea
- Diarrhea

Challenges with Efficacy and Patient Adherence

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Tenapanor Controls Phosphorus with One Small Pill Taken Twice Daily

One week dose of
Tenapanor
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

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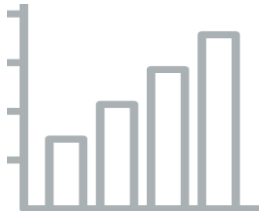
Significant Opportunity for Tenapanor in Hyperphosphatemia Market

>500K

U.S. Dialysis Patients[1]



3-4%

Annualized Growth Rate of U.S. Dialysis Population[1]

> $1B

Prescription Phosphate Binder Market[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

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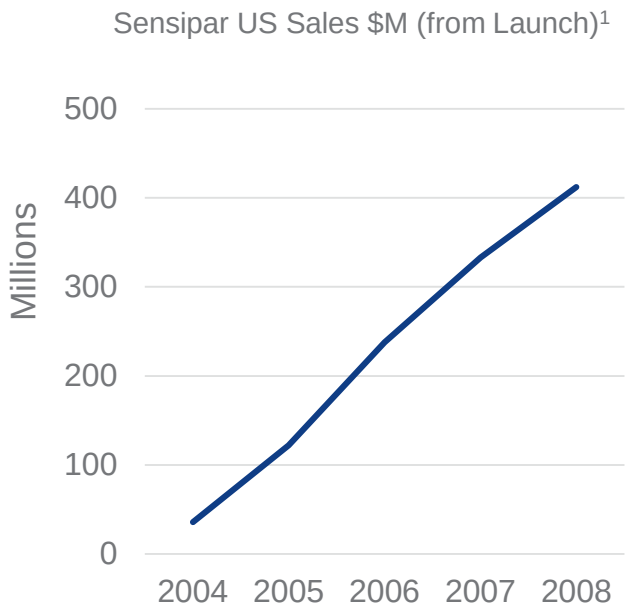
Ardelyx is Well-Positioned to Commercialize Tenapanor in the US

Historically, novel mechanisms in renal outperformed and built significant markets



Experienced Commercial Team with Cardiorenal Experience

ACTELION
A JANSSEN PHARMACEUTICAL COMPANY OF Johnson & Johnson
Akebia THERAPEUTICS
Baxter
KERYX BIOPHARMACEUTICALS, INC
precision diagnostics
QUESTCOR
relypsa
Roche
SANOFI GENZYME
Walgreens

Building Specialized US Commercial Organization

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

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

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2019 has been a Significant, Transformational Year

✓Kyowa Kirin Corporation initiated Phase 2 tenapanor trial in hyperphosphatemia in Japan

✓Publication of successful Phase 3 monotherapy trial for tenapanor in JASN

✓Established commercial team with highly talented, experienced leadership

✓Strengthened board with appointment of Geoff Block, M.D., luminary in cardiorenal medicine

✓Reported successful AMPLIFY Phase 3 trial of tenapanor in combination with binders

✓IBSRELA® (tenapanor) for IBS-C approved Sept 2019

✓Expanded partnership with Kyowa Kirin with new research collaboration and equity investment

✓Reported successful PHREEDOM Phase 3 results for tenapanor as monotherapy Dec 2019

✓Initial results from NORMALIZE support increasing number of patients achieve normal serum phosphorus levels with tenapanor.

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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+
- Ongoing market development and pre-commercial activities
- Expect tenapanor NDA submission for hyperphosphatemia mid-2020
- Expect tenapanor approval for hyperphosphatemia mid-2021
- Potential partnership for IBSRELA
- Advancing our cardiorenal franchise with RDX013
- Ongoing progress with our partners in Japan, China and Canada

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Thank you