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Passionately committed to improving the lives of patients by discovering, developing and commercializing first-in-class targeted therapies that advance patient care

November 2020

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; Ardelyx's expectation regarding the potential approval of its NDA for tenapanor for the control of serum phosphorus in chronic kidney disease (CKD) patients on dialysis and the expected timing thereof; the commercial potential for tenapanor for the control of serum phosphorus in CKD patients on dialysis, including Ardelyx's expectation regarding the rate of adoption and use of tenapanor, if approved; Ardelyx's expectations regarding the size of the patient population and the size of the market for tenapanor in CKD patients on dialysis, and the potential growth thereof; 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 November 5, 2020, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

Ardelyx Overview

- **Tenapanor: First-in-class product candidate** for the control of serum phosphorus in patients with chronic kidney disease (CKD) on dialysis
  - Three successful statistically significant Phase 3 studies
  - NDA Accepted September 2020
  - PDUFA Date – April 29, 2021
- **Large target market**
  - ~2.7M phosphate binder prescriptions written per year in U.S.[1]
  - Accessible with U.S. specialty-focused commercial organization
  - Ex-U.S. commercialization through select collaborations
- **Discovery platform** fuels additional pipeline programs
  - RDX013: novel approach for hyperkalemia
  - RDX020: novel approach for metabolic acidosis
- **Cash of $185M**[2] supports operations into first half of 2022

1. IQVIA 2019 (Retail); Adding estimate for Rxs through dialysis organization specialty pharmacies
2. Cash, cash equivalents and short-term investments as of September 30, 2020

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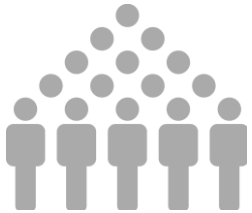
Delivered on Promises: 2020 in Review

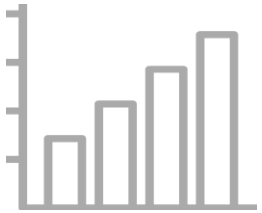
- ✓ **Submission of NDA** for tenapanor, June 2020
- ✓ **Filing and Acceptance of NDA** for tenapanor
- ✓ **PDUFA date set** for April 29, 2021
- ✓ **AMPLIFY Phase 3** results presented at ASN 2020
- ✓ **PHREEDOM Phase 3** results presented at ASN 2020
- ✓ **BLOCK Phase 3** results presented at ASN 2020
- ✓ **NORMALIZE 18-month Extension study** interim results reported June 2020
- ✓ **Kyowa Kirin presented results from Phase 2 trials** in Japan at ERA-EDTA and ASN 2020
- ✓ **"Advancing the Science of Phosphate Absorption"** Spotlight at ASN 2020
- ✓ **Enhanced organizational commercial-readiness** with hiring of CCO and CFO

Well-Established Hyperphosphatemia Market



>550K

U.S. Dialysis Patients[1]



3-4%

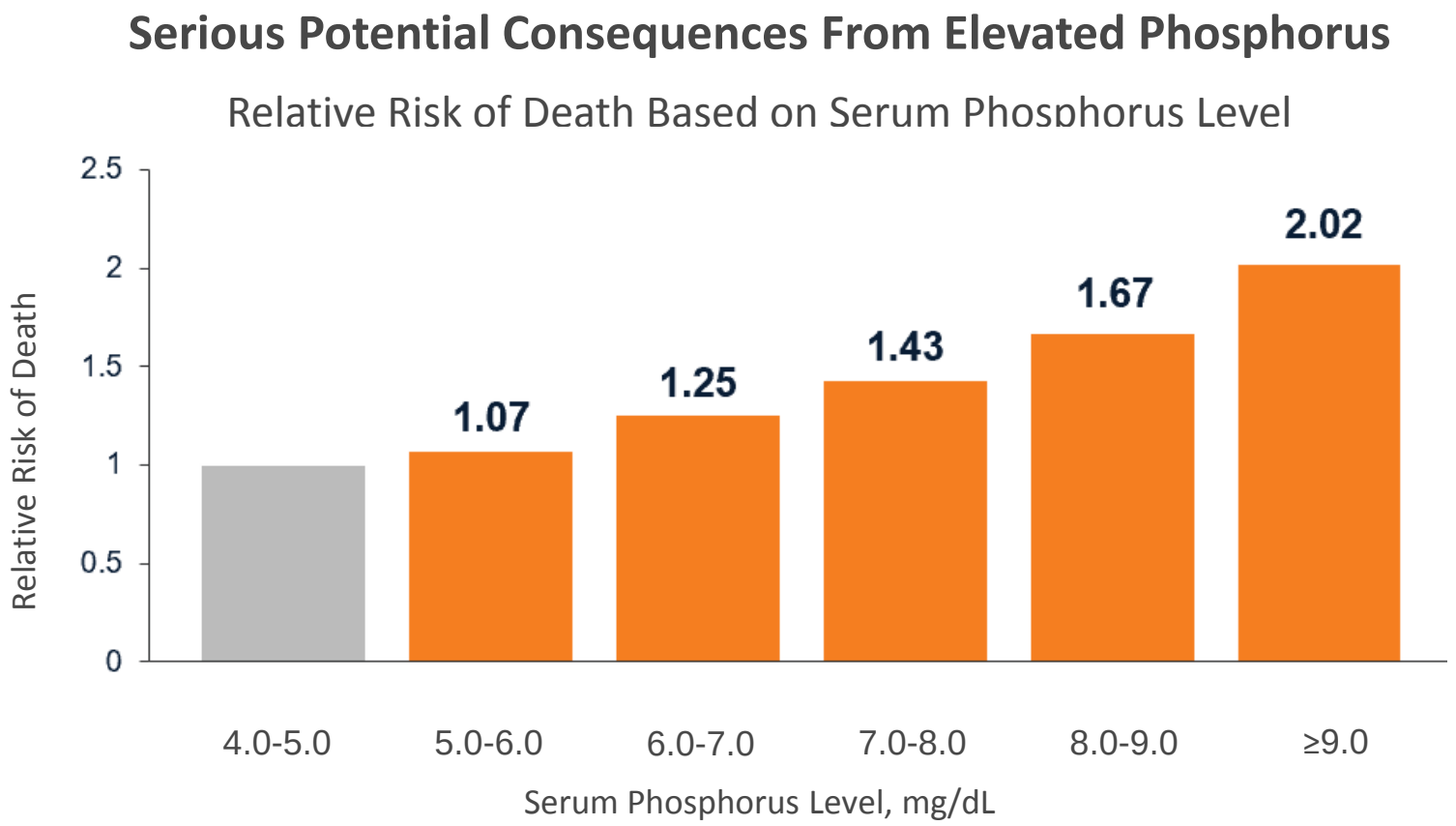
Annualized Growth Rate of U.S. Dialysis Population[1]

~2.7M

U.S. Phosphate Binder Prescriptions[2]

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. IQVIA 2019 (Retail); Adding estimate for Rxs through dialysis organization specialty pharmacies

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

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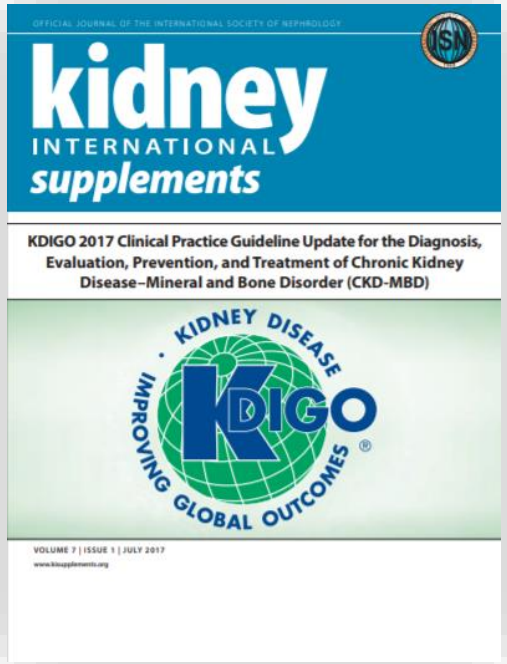
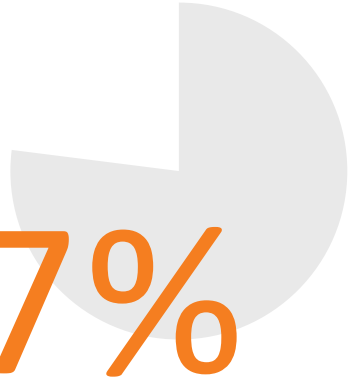
It is Well Recognized that the Majority of Patients are Unable to Consistently Maintain Target Phosphorus Levels Despite Active Management with Currently Available Therapies



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)



77%

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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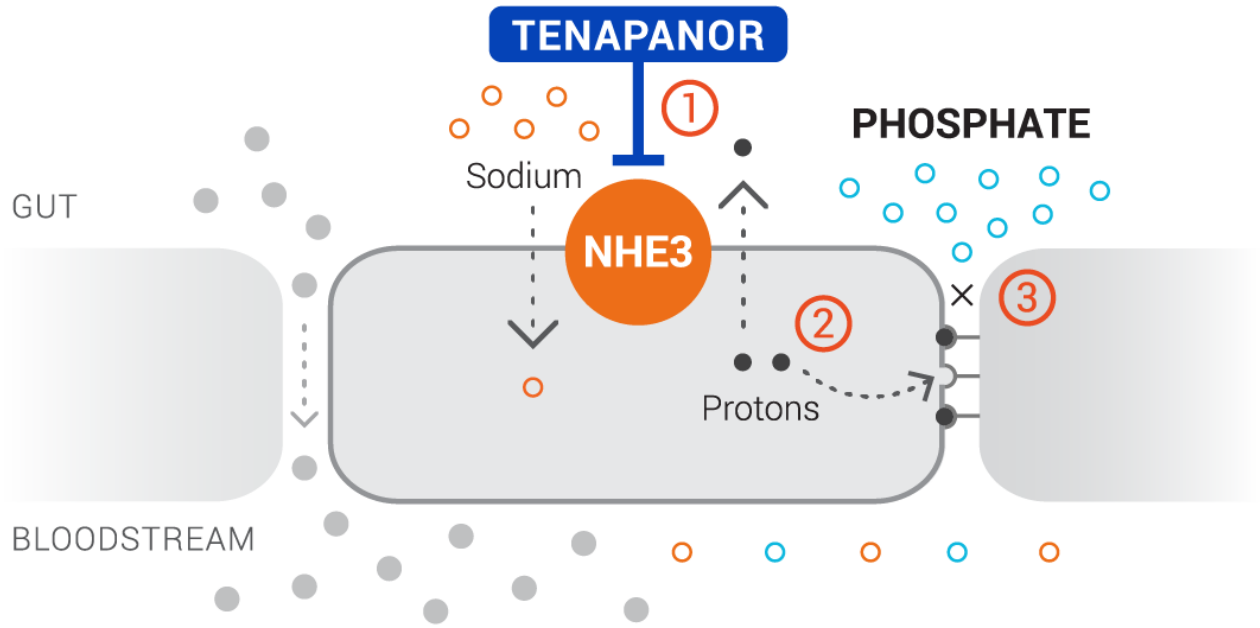
Tenapanor Clinical Development Program

Tenapanor: A First-In-Class Phosphate Absorption Inhibitor

TARGETS
primary pathway of phosphate absorption

BLOCKS
paracellular absorption of phosphorus*

DOSED
as one pill twice per day†



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

* 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.† In clinical trials, dosing is 1 pill BID

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Tenapanor Clinical Data Package is Robust

BLOCK
Phase 3 – Short Term

Primary and Secondary Endpoints met

PHREEDOM
Phase 3 – Long-Term

Primary and Key Secondary Endpoints met

NORMALIZE
PHREEDOM Extension

Initial Analysis Demonstrates Increased % of Patients Achieving Goal

AMPLIFY
Phase 3 – Short Term

Primary and Key Secondary Endpoints met

PDUFA Date: April 29, 2021

BLOCK: Statistically Significant Pivotal Monotherapy Phase 3 Results

DESIGN

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

n=219

Primary Endpoint: Difference in change in serum phosphorus between pooled tenapanor-treated patients and placebo-treated patients in the efficacy analysis set from the end of the 8-week treatment period to the end of the 4-week randomized withdrawal period

EFFICACY

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

Secondary analyses: At the end of the 8-week open label treatment period, tenapanor-treated patients in the efficacy analysis set (n=80) achieved a mean decrease in serum phosphorus from baseline of 2.56 mg/dL

SAFETY

Well tolerated

8-week open-label treatment period:

- 39% diarrhea
- Only adverse event ≥5%
- Mostly mild to moderate
- Stool form and frequency changes, on average, remained in normal range for healthy individuals
- 8% discontinuation due to diarrhea

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

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AMPLIFY: Statistically Significant Pivotal Phase 3 Results with Tenapanor and Binders

DESIGN

To evaluate tenapanor and phosphate binders (two distinct MOAs) when used in combination
n=235

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

EFFICACY

Primary endpoint statistically significant difference in reduction of serum phosphorus levels (p=0.0004) compared to binders alone at week 4

~2 times more patients achieved the serum phosphorus treatment goal of <5.5 mg/dL with tenapanor and phosphate binders vs phosphate binders alone (P≤0.0097)

Secondary analyses: Statistically significant reduction (p-values≤0.0027) in FGF23 levels

SAFETY

Favorable tolerability

Well tolerated: 4% of patients in tenapanor arm discontinued vs. 2% in the binder arm

- 43% diarrhea; single adverse event with a placebo-adjusted rate >3%
- Mostly mild-to-moderate
- 3% severe diarrhea
- Transient: median resolution 4 days after onset
- Resulted in treatment discontinuations in 3 out of 116 patients

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PHREEDOM: Statistically Significant Pivotal Long-term Monotherapy Phase 3 Results

DESIGN

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

n=564

Primary Endpoint: Difference in change in serum phosphorus between 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

EFFICACY

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

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 an SAE
- Diarrhea only adverse event >5% (52%)
  - Vast majority mild to moderate; 5% severe diarrhea

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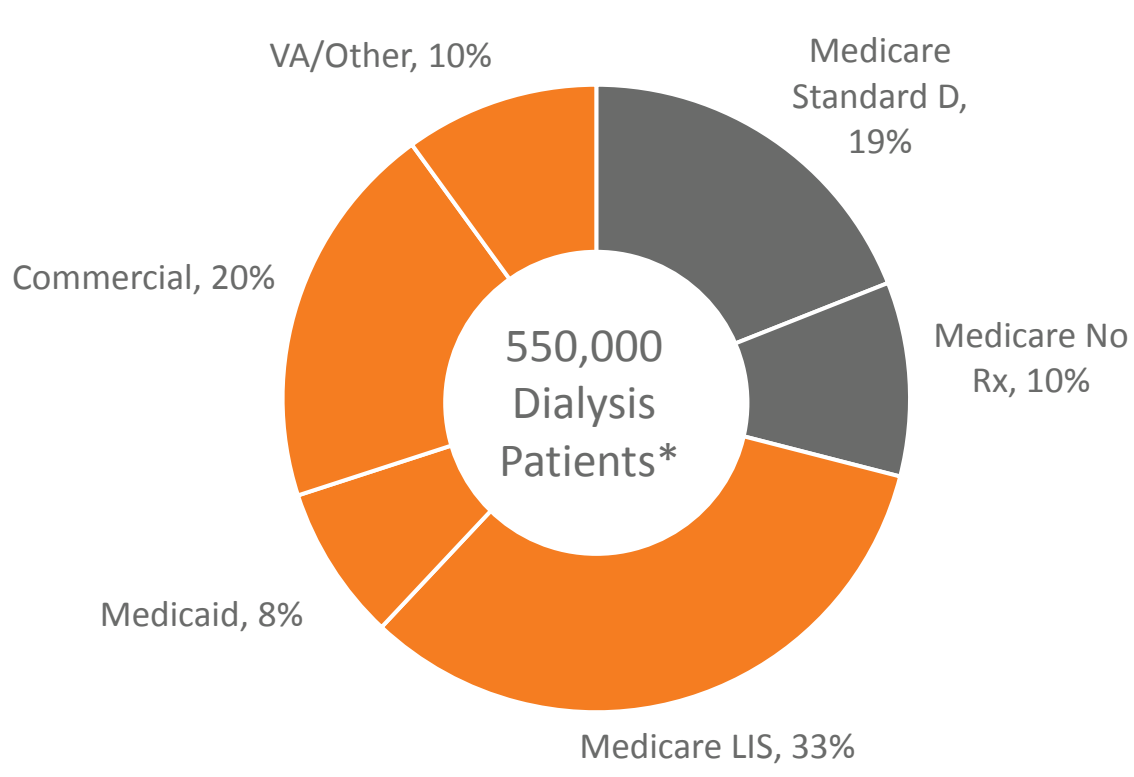
Tenapanor Commercialization: Disrupting and Restating the Hyperphosphatemia Market

Favorable Payor Landscape for Hyperphosphatemia Rx Therapies

1. 62% Medicare / 38% Commercial, Medicaid, Other

2. Tenapanor Launch Landscape: 70% Access and Affordability Potential



*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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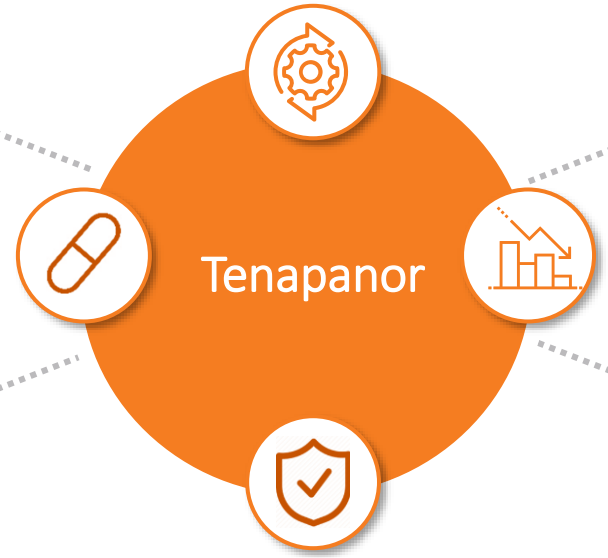
Tenapanor Product Profile is Compelling

MOA

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



Dosing and Administration

- One small 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

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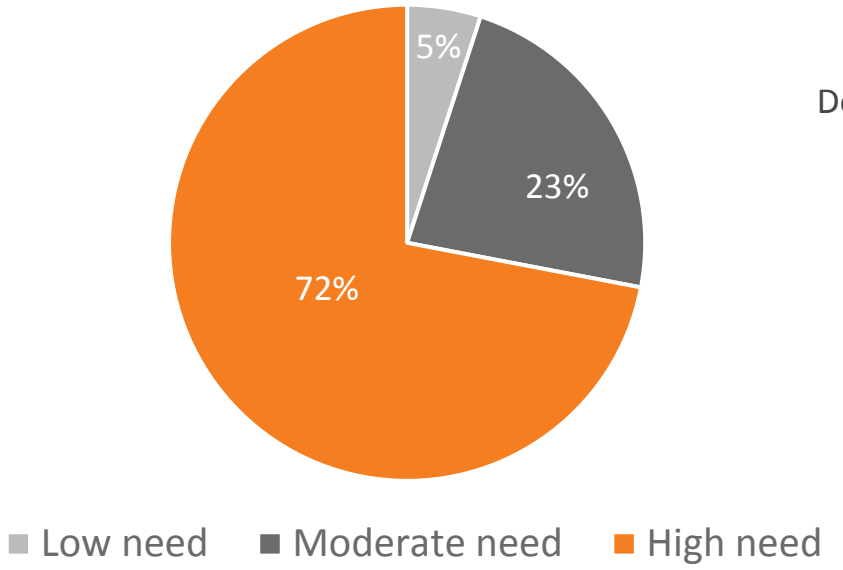
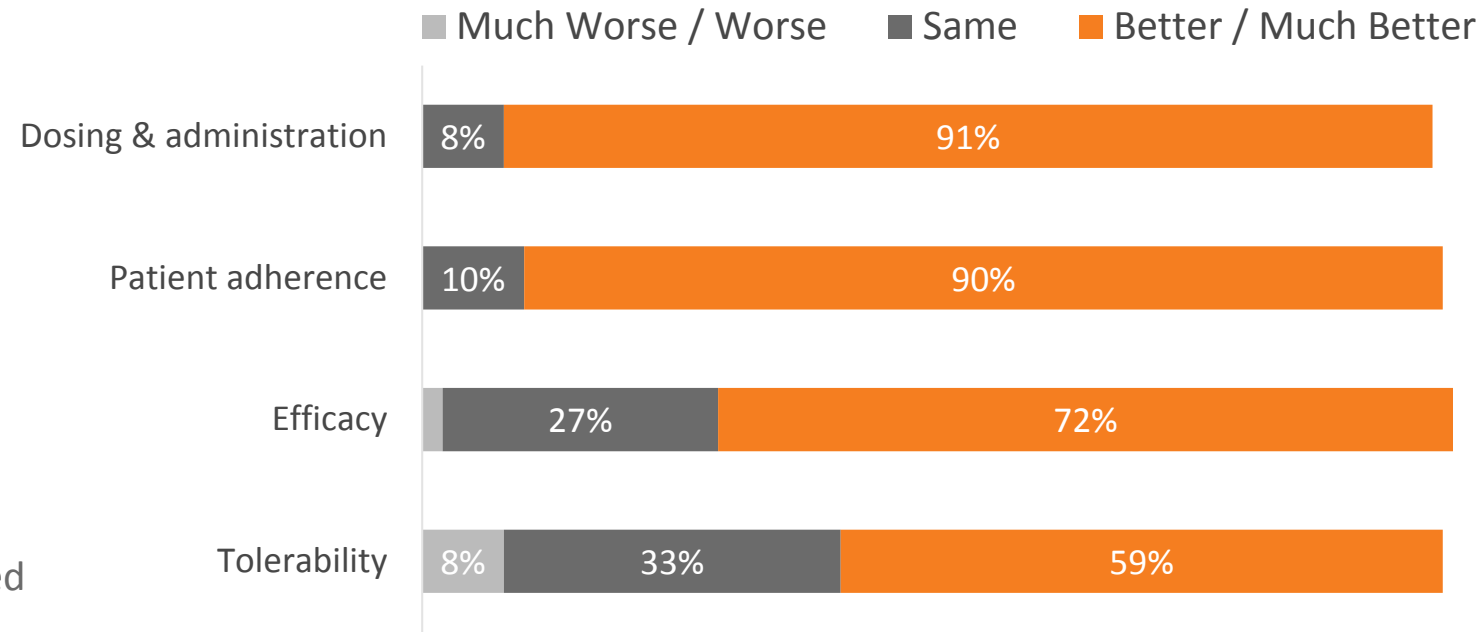
Market Research Reflects That Nearly 3 Out of 4 Nephrologists See a High Need for New Treatments and Expect Tenapanor to Provide an Improvement Compared to Phosphate Binders

How Much of a Need for New Treatments?



How Does Tenapanor Compare to Phosphate Binders?*



*Physician perceptions of tenapanor relative to phosphate binders based on tenapanor product profile. There have been no head-to-head studies comparing tenapanor to phosphate binders

Source: Ardelyx market research study conducted by Hawk Partners, December 2019. A14. How much of a need is there for new treatments for hyperphosphatemia? (n=205) . D2. How do you believe Product X would compare to phosphate binders on each of the following? (n=205)

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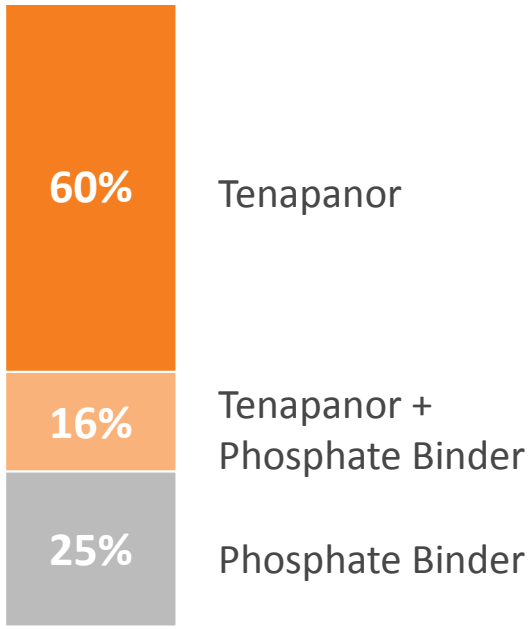
The Majority of Nephrologists Expect to Use Tenapanor as First Line Therapy

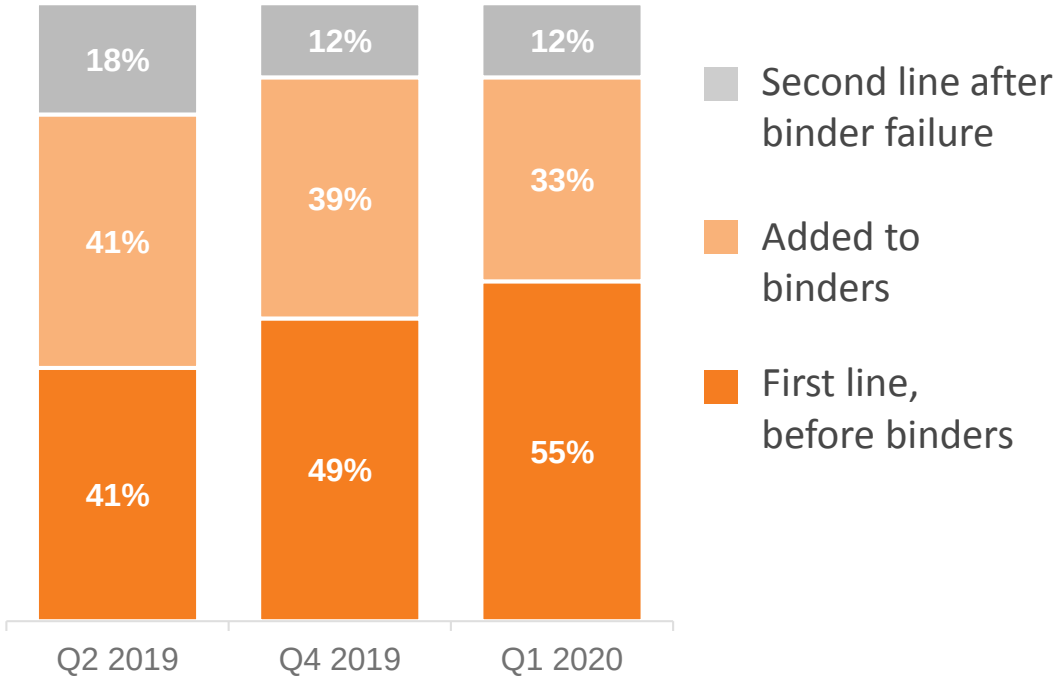
Most Likely First Line Hyperphosphatemia Treatment[1]

% of respondents



Tenapanor Anticipated Line of Therapy[2]

% of respondents



1. 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)
2. 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)

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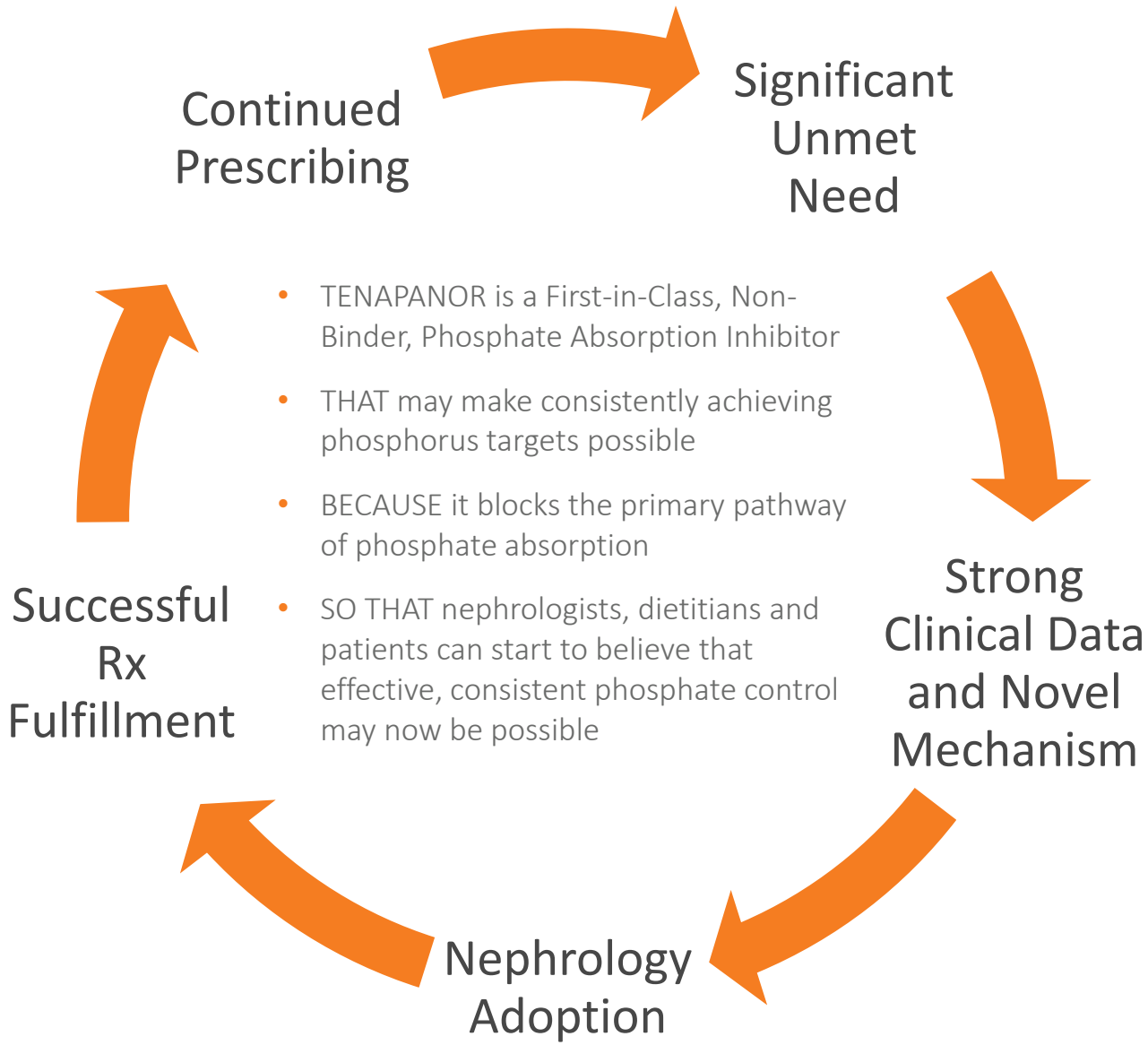
Commercial Strategic Priorities

- Establish foundational therapy positioning
- Drive strong nephrology demand
- Optimize patient access and affordability
- Leverage growing Ardelyx reputation as leader in advancing science and patient care



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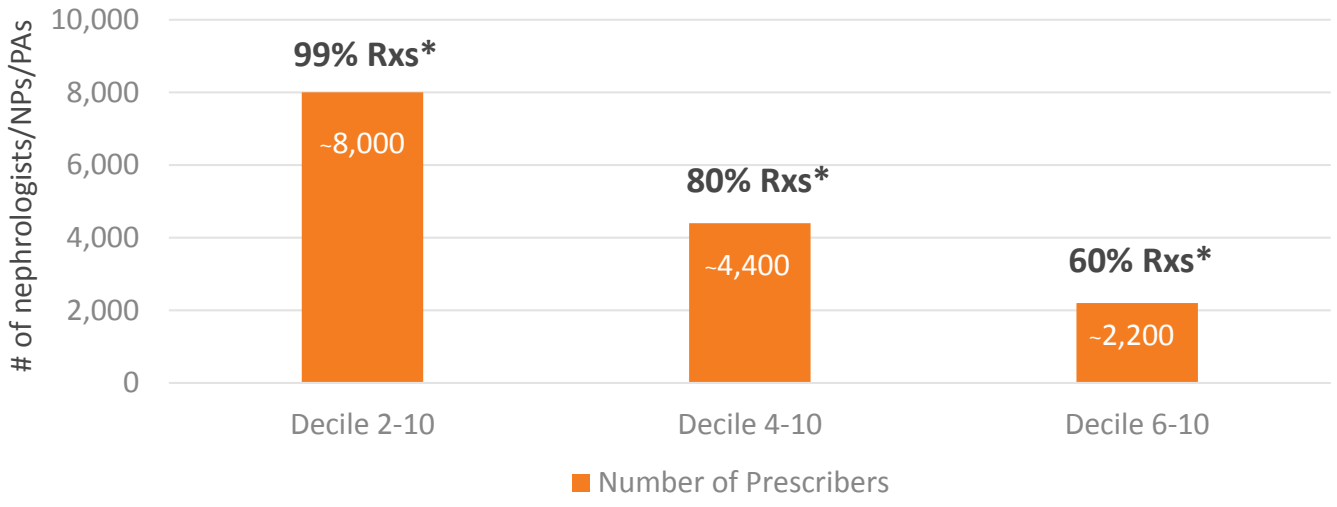
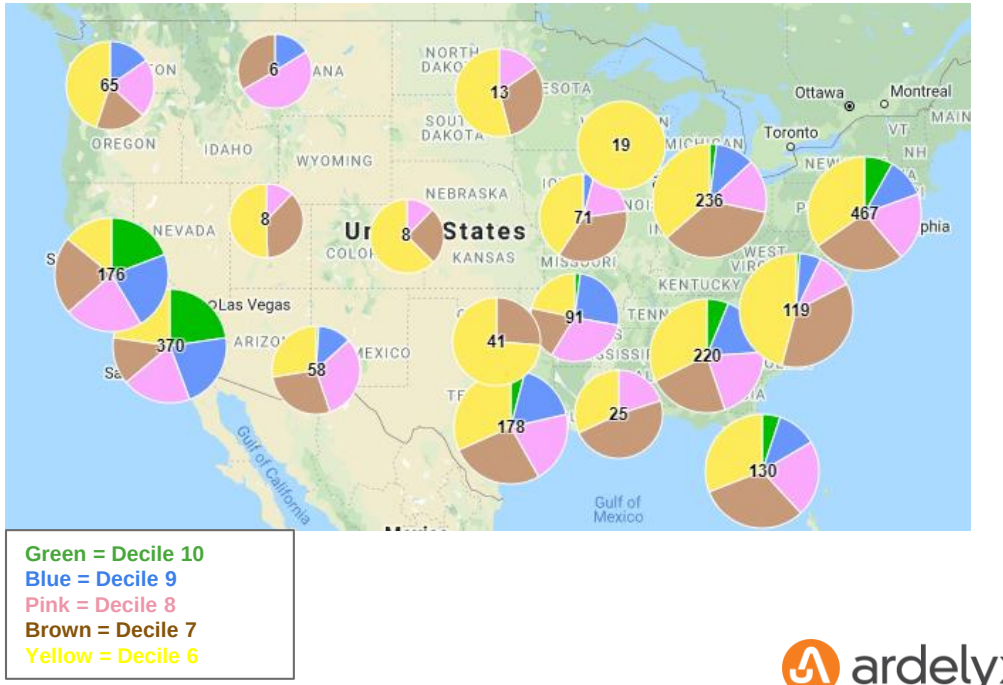
Strategic Imperatives – Drive Strong Nephrology Demand

- Hyperphosphatemia Rx market is driven by nephrologists
- Call universe of nephrologists highly concentrated. Sales force territories and targets aligned to optimize opportunity
- Commercial force of ~100 targeted at tenapanor opportunity – nephrologists, dialysis organizations, payors





Source: IQVIA Targeting and Segmentation analysis. SAT score decile based on number of TRxs and quality of access. 12,571 nephrologists/nephrology NPs/PAs in total. Percentage of Rxs based on total from this group of 12,571

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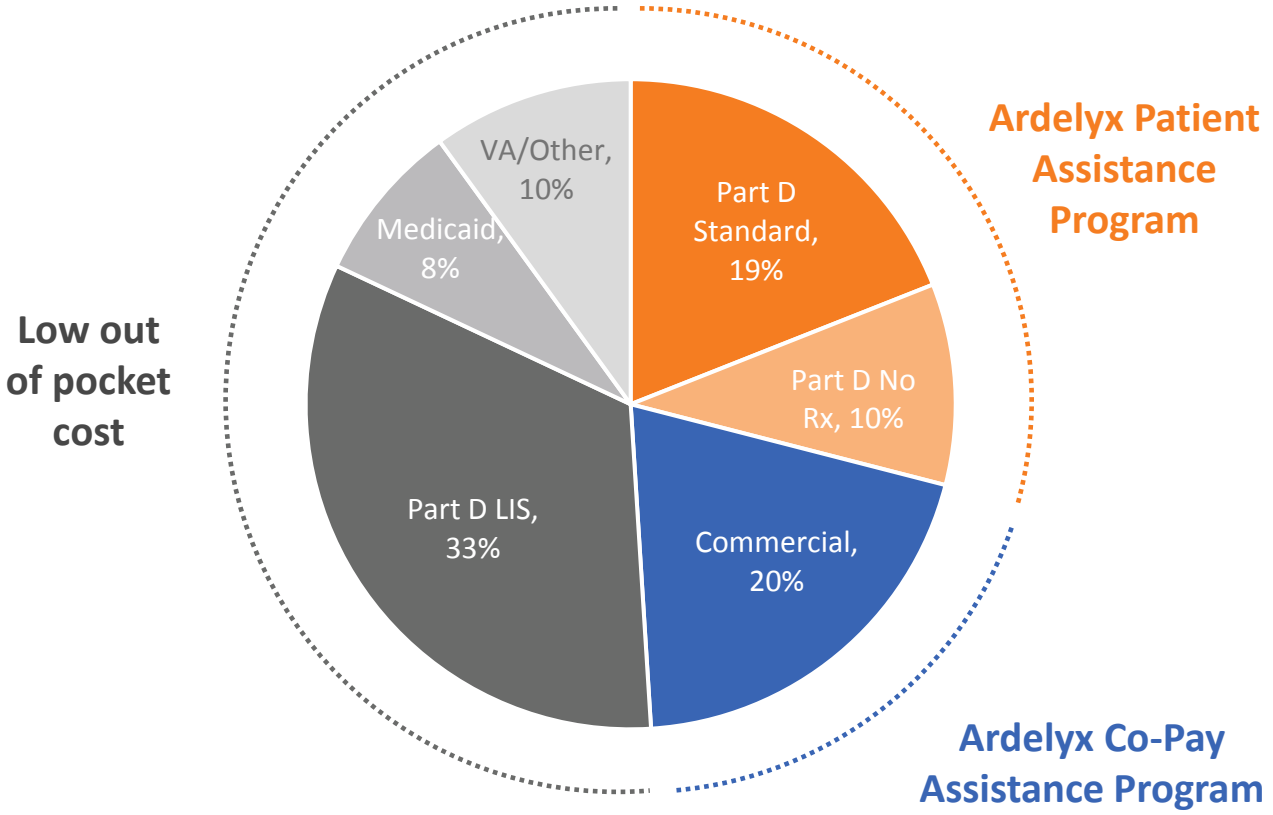
Our Goal is That All Patients Prescribed Tenapanor Will Be Treated with Tenapanor, and Affordability Across all Patients Will Be Optimized

- Targeted payor initiatives to secure access
- State of the art hub service to support prior authorization approvals
- Patient programs to optimize affordability



Payor Mix Estimates: Spherix RealWorld Dynamix Dialysis 2019 and USRDS 2018 Medicare Breakdown from 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.

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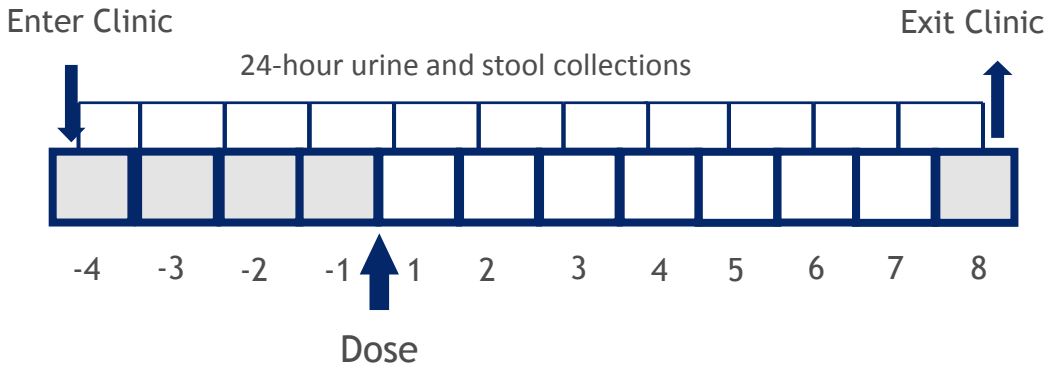
RDX013 for Hyperkalemia

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

RDX013-101: 112 Subject, Phase 1 Safety and Proof-of-Concept Study

- Double-blind, placebo-controlled, healthy volunteers (19-75 years old)
- 112 total: 8 groups x 14 subjects/group (12 treated and 2 placebo)
- Treatment: Different doses and dosing regimens
- 12 days/ 11 nights in phase 1 study unit; standardized meals
- Endpoints
  - Safety assessment: clinical and vital signs, hematology, blood chemistries, ECG, etc.
  - Pharmacodynamics: Change from baseline in stool potassium excretion



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RDX013: Generally Safe and Well Tolerated

- There were no treatment-related trends in terms of AEs
- The majority of TEAEs reported were mild in severity and resolved without treatment
- There were no deaths, severe TEAEs or SAEs reported during the study
- There were no treatment- or dose-related trends in the clinical laboratory evaluations, vital signs data, 12-lead ECG data, or physical examination findings during the study

RDX013: Comparable PD Response to Potassium Binders in Healthy Subjects at a Significantly Lower Dose

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]

[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 in CKD Patients with Hyperkalemia

RDX013-201: 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

RDX020: a first-in-class targeted agent for treating metabolic acidosis

RDX020: Discovery Program Targeting a Bicarbonate Exchange Inhibitor

Metabolic acidosis is a highly prevalent comorbidity in CKD, strongly correlated with disease progression and adverse outcomes

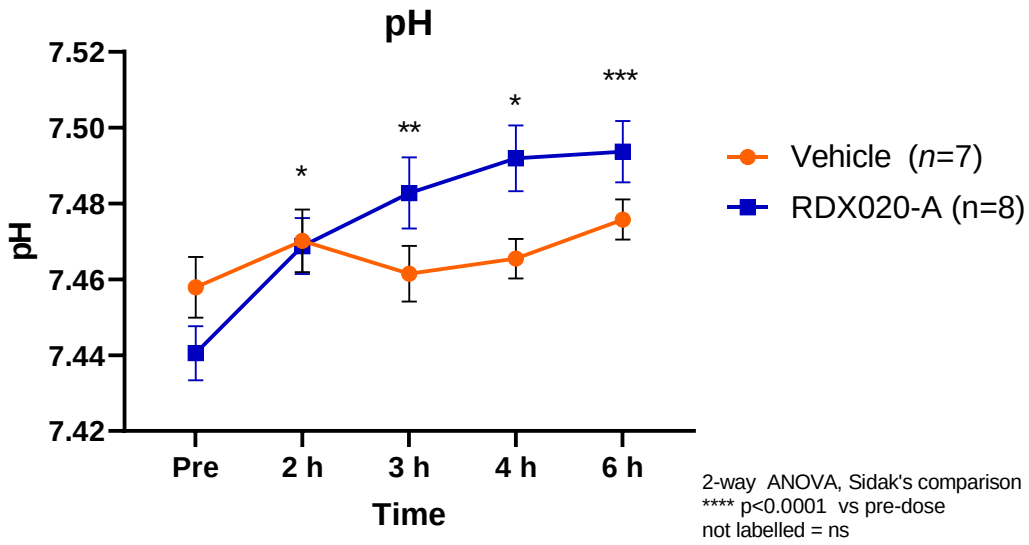
There are no approved treatments for metabolic acidosis

- Physicians utilize large quantities of oral alkali salts (~4-10 g/day as a starting dose)
- Treatment brings high sodium load; most CKD patients have sodium-sensitive comorbidities (hypertension, CVD, HF, edema)

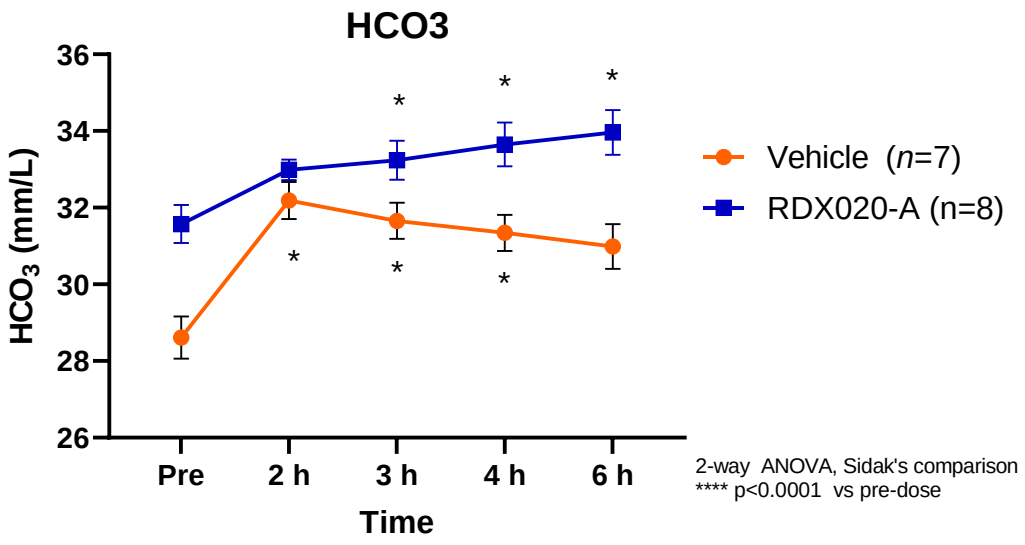
Ardelyx has successfully targeted intestinal bicarbonate exchange

- Ardelyx lead compounds are potent, selective and proprietary inhibitors
- RDX020 program has the potential to be a first-in-class treatment

RDX020: Lead Compound Shows Promising Pharmacodynamic Activity



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



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

Ardelyx bicarbonate secretion inhibitor modulated blood pH

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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Financials & Partnering Strategy

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

Maintaining flexibility in Europe

Key Financial Items

$185.5 MM

Cash and Investments of as of September 30, 2020

Cash runway into first half of 2022

~ $50 MM of debt- interest only until December 2021

~ 90.2 MM shares outstanding as of September 30, 2020

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Thank You