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Analyst Day

November 12, 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

Today's Agenda – Welcome!

Progress and Momentum	Mike Raab – CEO, Ardelyx
Impact of Tenapanor	German Hernandez, MD, FASN, FACP – El Paso Kidney Specialists, Texas Tech University
Market Perspective	Jennifer Robinson – President, Spherix Global Insights
Favorable Access Environment	Douglas Paul, PharmD, PhD – VP and Partner, MME
Planning for Commercial Success	Susan Rodriguez – CCO, Ardelyx
Advancing the Ardelyx Pipeline	Jeff Jacobs, PhD – CSO, Ardelyx & David Rosenbaum, PhD – CDO, Ardelyx
Financials and Partnering Strategy	Justin Renz – CFO, Ardelyx
Summary & Closing Remarks	Mike Raab – CEO, Ardelyx
Q&A	All

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

Impact of Tenapanor

German Hernandez, MD, FASN, FACP

El Paso Kidney Specialists

Clinical Associate Professor of Medicine,

Texas Tech University Health Sciences Center

Hyperphosphatemia Management is Important and Extremely Challenging

- Hyperphosphatemia management is extremely important, but an area where we have had limited success
- Elevated phosphorus is a strong predictor of cardiovascular morbidity and mortality
- A large percentage of patients are unable to consistently achieve target phosphorus levels
- Despite our best efforts and best efforts of patients, we are limited by the currently available therapies
  - Inherent limitations implicit to binding mechanism of action
- Enthusiasm for highly needed new approaches based on evolving science and new understanding of phosphate absorption

Tenapanor Represents a Significant Advancement

Tenapanor, a first-in-class, non-binder, phosphate absorption inhibitor, represents significant advancement

- Targets primary pathway of phosphate absorption
- Approach that inhibits absorption of phosphorus addresses many of the inherent challenges with binding mechanism

Impressive results with my patients and positive feedback from my patients in tenapanor clinical trials

- Efficacy
- Tolerability
- Dosing & Administration

Tenapanor Likely to Become My Go-To Hyperphosphatemia Treatment

- Tenapanor likely to become my go-to medication for hyperphosphatemia management
- Majority of patients could benefit from tenapanor
- Incident patients
- Prevalent patients
- High unmet need combined with novel, advanced approach likely to have positive impact on speed of adoption

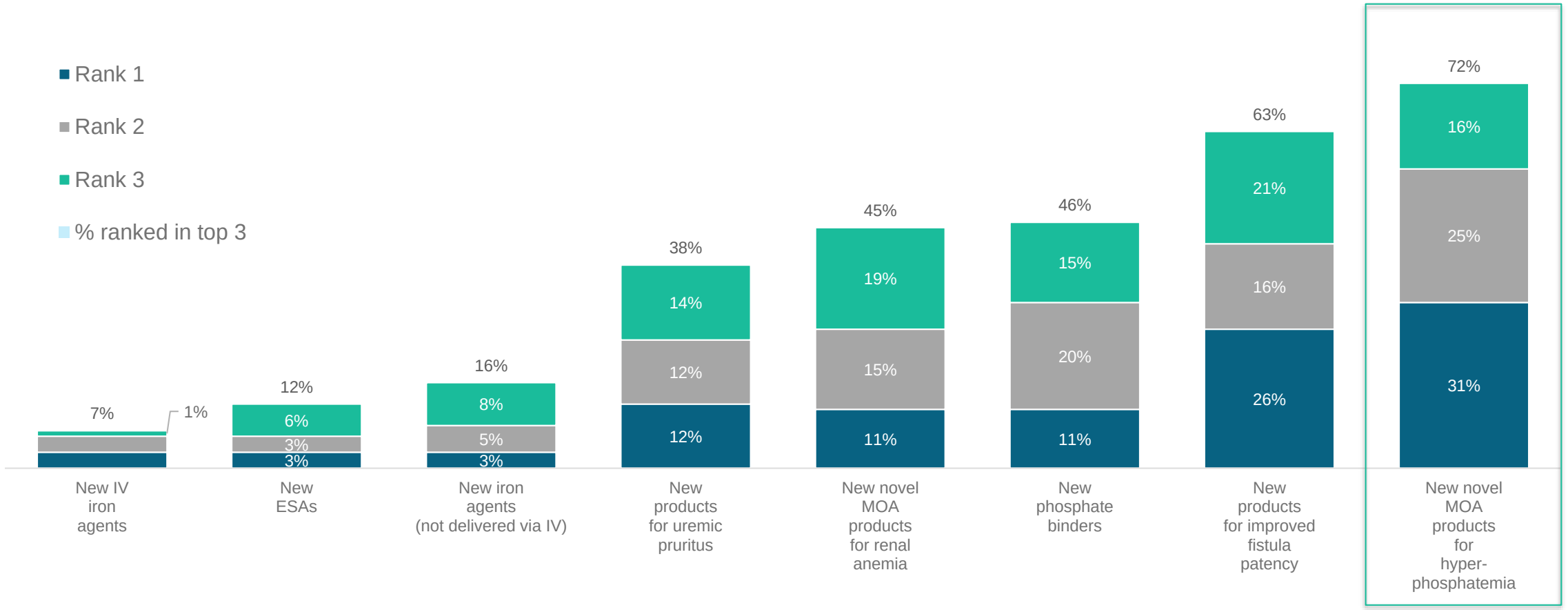
Jennifer Robinson
President, Spherix Global Insights

Hyperphosphatemia: One of the Highest Unmet Needs for Dialysis Patients

In a recent, independent study evaluating treatment patterns in dialysis patients, nearly three-quarters of the participating US nephrologists identified new, novel MOA products as the greatest unmet need for dialysis patients.

Rank Order of Unmet Need in Dialysis

(Percent of respondents)



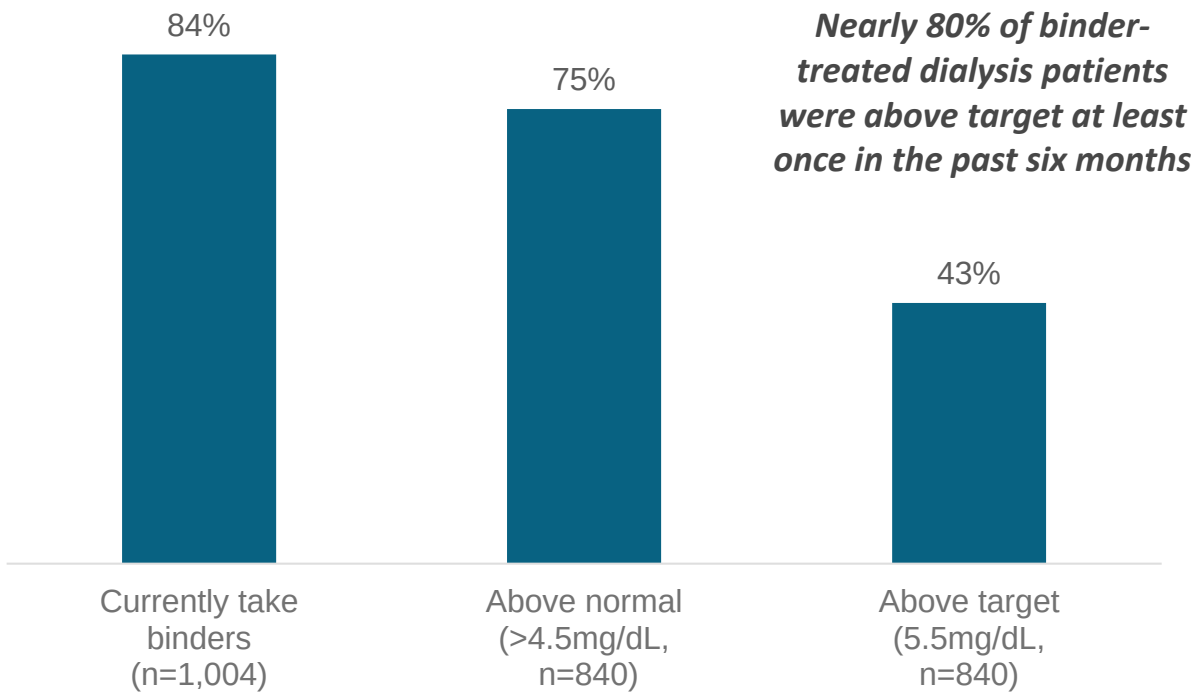
n=177 US nephrologists

Tenapanor Can Capitalize on a Significant Market Opportunity

There are over half a million dialysis patients in the US, the vast majority of whom take phosphate binders. Few patients are able to achieve and maintain target levels.

Treatment Rates and Most Recent Phosphorus

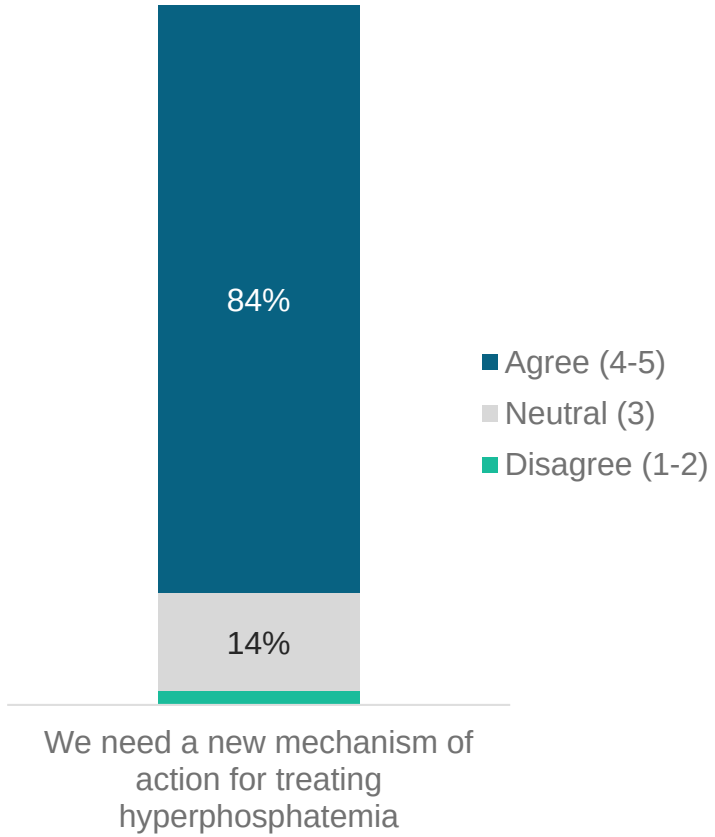
% of patients



Nearly 80% of binder-treated dialysis patients were above target at least once in the past six months

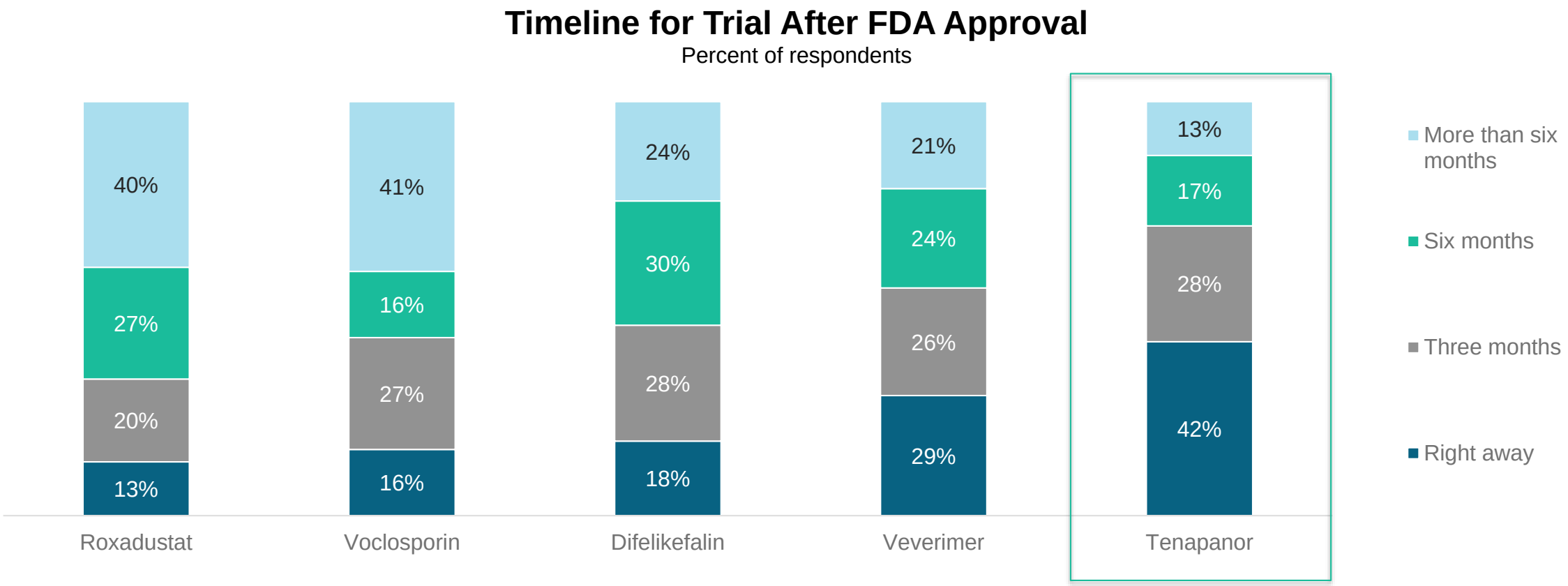
Statement Agreement

% of respondents



n=177 US nephrologists; n=1,004 patient records

Adoption of Tenapanor Anticipated to be Swift



Timeline for Trial: RealTime Dynamix Anemia (roxadustat in ND), RealTime Dynamix: Bone and Mineral (tenapanor); Special Topix: Renal Pipeline Opportunities (voclosporin, veverimer, difelikefalin)

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Learn from Our Experience,
Profit from Our Thinking.®

DOUG PAUL, PHARMD

VP and Partner, MME

SINCE 2001,
MME has developed value-based marketing strategies for large and emerging bio/pharmaceutical clients

>40 PROFESSIONALS

located in Oxford, MS;
Montclair, NJ

>125 LAUNCHES

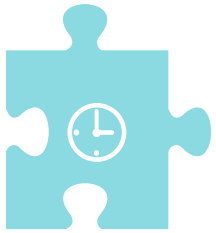
Completed US and EU launch projects in the last 3 years

We help clients identify, frame, communicate, and capture value

AREAS OF EXPERTISE INCLUDE:
biotech, market access, launch strategies and product line extensions, orphan drugs and hospital, providing:

Unique combination of manufacturer and customer perspectives combined with solid academic theory

Strategy development and tactical execution to support informed decision making



Assessment and planning of opportunities and competitive situations at every stage of the product life cycle

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THE UNIVERSAL TRUTH:

If the value of a product is uncertain or unclear,

PRICE will be the major issue in selling.

If the value is clear, the price will not matter.

MME CHECKLIST FOR SUCCESS

- ❑ **Is there criticality and unmet need?**
- ❑ Will physicians write prescriptions for the product and advocate for use by the patients?
- ❑ Will patients take the product?
- ❑ Will payors cover the product?

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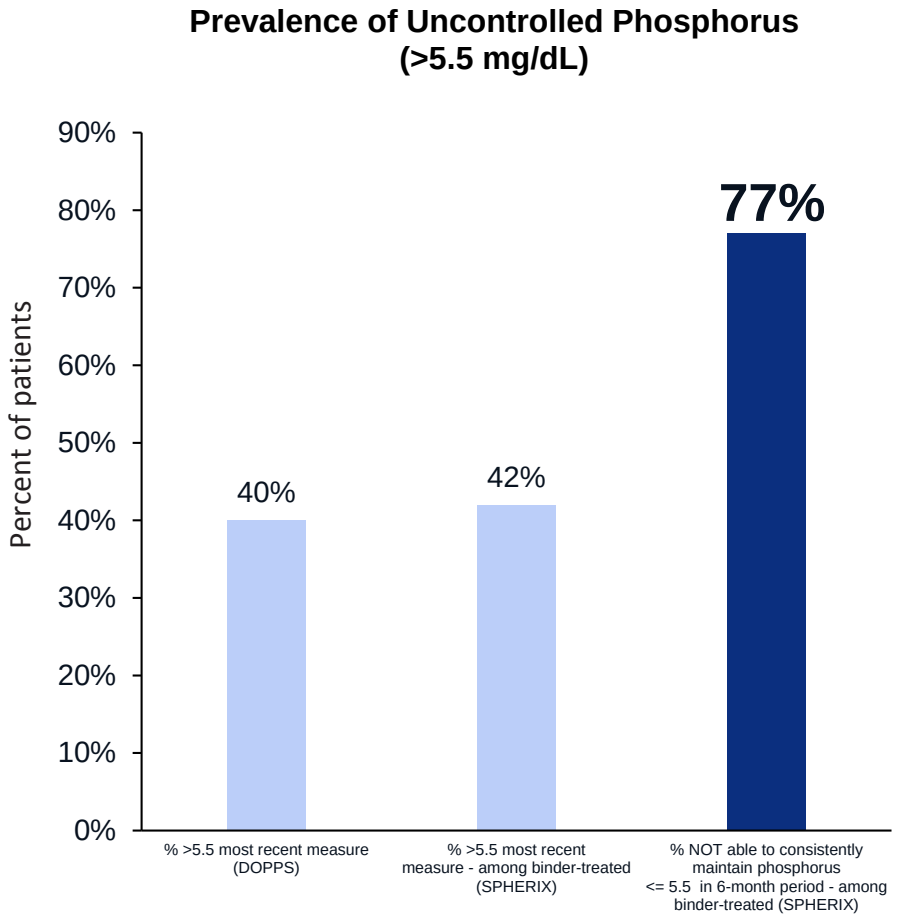
IS THERE A CRITICALITY AND UNMET NEED?

CRITICALITY

- Hyperphosphatemia is an independent predictor of morbidity and mortality in patients with CKD on dialysis in a disease state where mortality is high (annual mortality rate of 17% among patients on dialysis)*#

UNMET NEED

- Despite treatment with phosphate binders, the only class of medication for hyperphosphatemia, many patients have phosphorus levels >5.5 mg/dL
  - Approximately 40% of patients have phosphorus >5.5 mg/dL in any given month
  - **77%** of phosphate binder-treated patients are unable to consistently maintain phosphorus <=5.5 mg/dL in a 6-month period



*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.

There is no morbidity or mortality data for tenapanor.

US-DOPPS Practice Monitor, April 2020; http/://dopps.org/DPM

Spherix RealWorld Dynamix Dialysis 2019

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MME CHECKLIST FOR SUCCESS

- [x] Is there criticality and unmet need?
- [ ] **Will physicians write prescriptions for the product and advocate for use by the patients?**
- [ ] Will patients take the product?
- [ ] Will payors cover the product?

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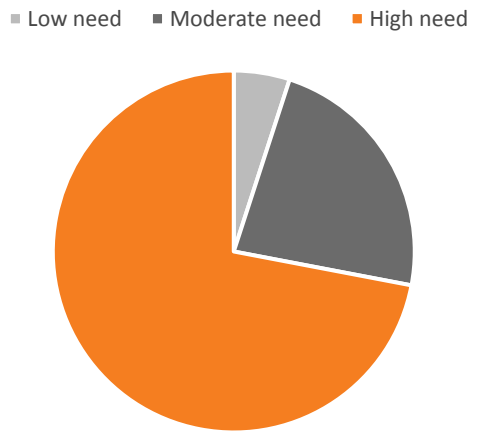
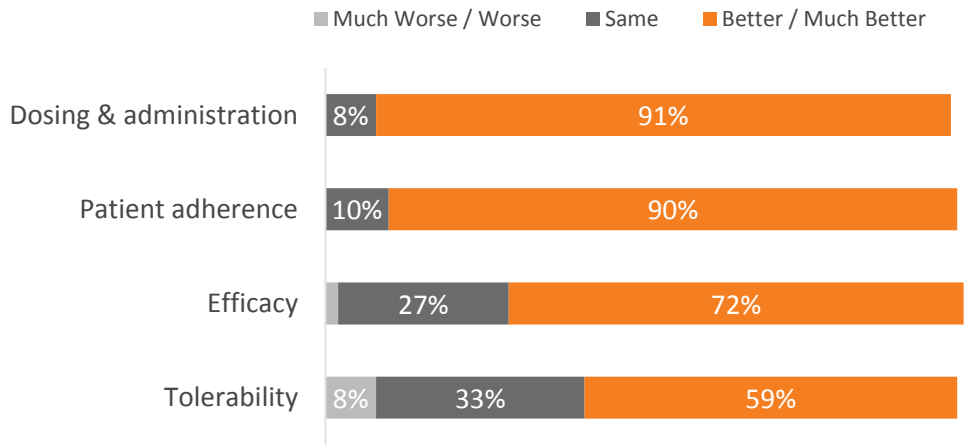
WILL PHYSICIANS WRITE PRESCRIPTIONS FOR THE PRODUCT & ADVOCATE USE TO THE PATIENT?

- Use of oral drugs to treat of hyperphosphatemia is already standard of care in the market
- Will physicians write for tenapanor specifically?
  - Novel mechanism to address unmet need
  - Tenapanor "wins" with physicians on key attributes

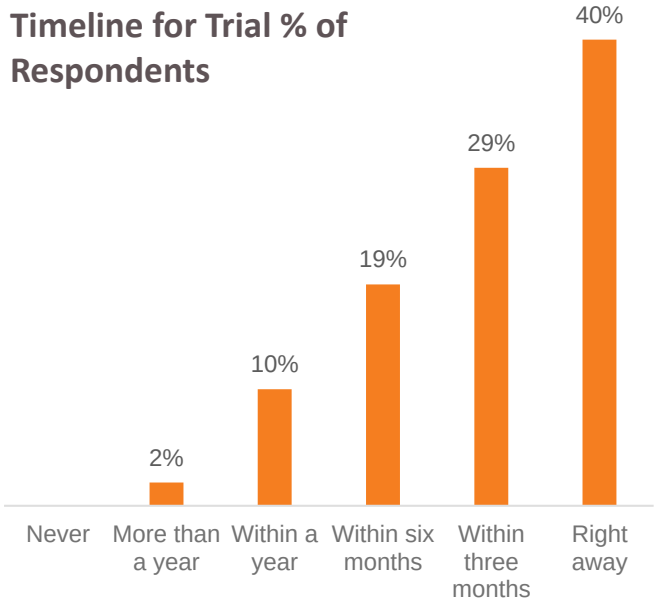
How Much of a Need for New Treatments?



How Does Tenapanor Compare to Phosphate Binders?*



Timeline for Trial % of Respondents



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

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).

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MME CHECKLIST FOR SUCCESS

- ☑ Is there criticality and unmet need?
- ☑ Will physicians write prescriptions for the product and advocate for use by the patients?
- ☐ **Will patients take the product?**
- ☐ Will payors cover the product?

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WILL PATIENTS TAKE THE PRODUCT?

- **Use oral drugs to treat hyperphosphatemia is already standard of care in the market**
  - Taking an average of 8 “large” tabs/day with side effects
- **Novel approach is valued due to shortcomings in binder class of therapy**
  - Patients constantly reminded by physicians they are not in range and persistently counseled on dietary restrictions and therapy compliance
  - Tenapanor will be one “small” tab BID
  - Physicians perceive tolerability profile to be similar or better to current treatments[1]
- **The market has historically had to overcome branded copays**
  - Ardelyx will have a robust copay assistance program and benevolent patient assistance program implemented by an experienced team

1. Source: Ardelyx market research study conducted by Hawk Partners, December 2019. How do you believe Product X would compare to phosphate binders on each of the following? (n=205). 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

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MME CHECKLIST FOR SUCCESS

- ☑ Is there criticality and unmet need?
- ☑ Will physicians write prescriptions for the product and advocate for use by the patients?
- ☑ Will patients take the product?
- ☐ **Will payors cover the product?**

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MANAGED CARE: MATCH THE PROBLEM TO THE SOLUTION

How do you make the decision?

Problem	Solutions
	

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MANAGED CARE: MATCH THE PROBLEM TO THE SOLUTION

Do prices change the way you make the decision?

Problem	Solutions
	

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MANAGED CARE: MATCH THE PROBLEM TO THE SOLUTION

What about now?

Problem	Solutions
	

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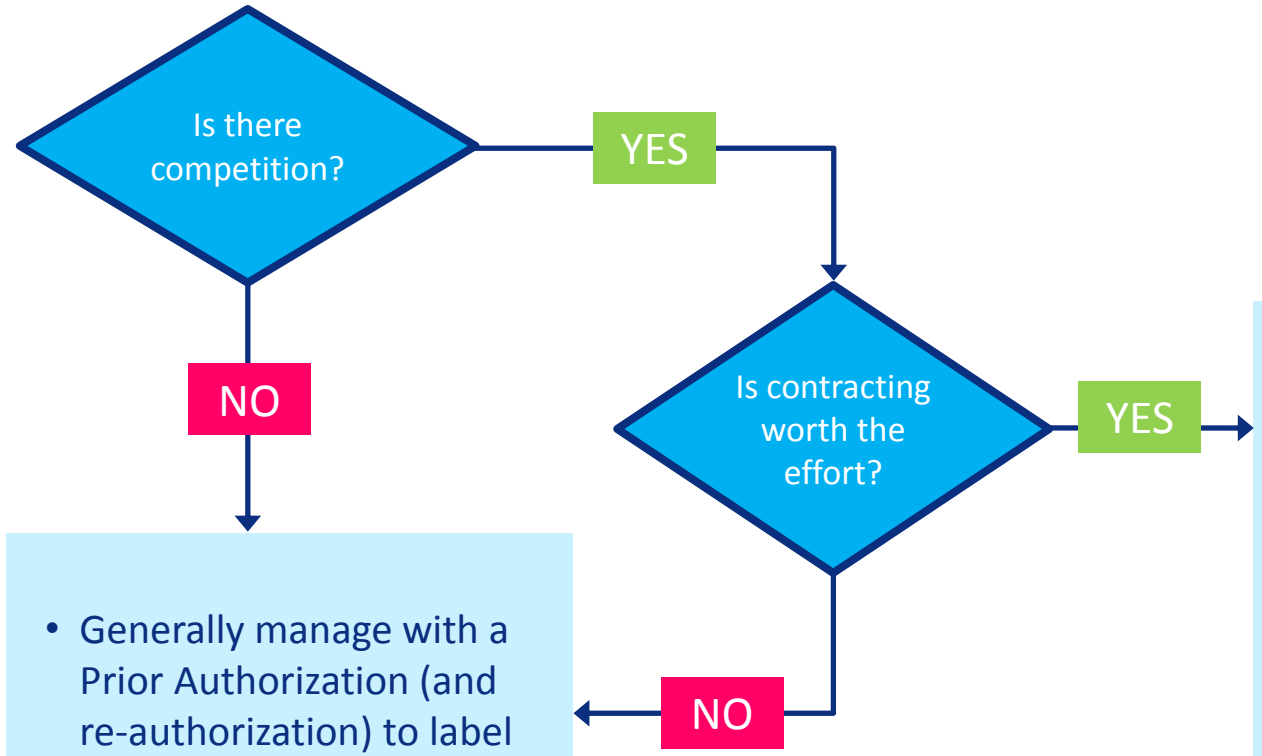
OVERSIMPLIFIED MANAGED CARE DECISION TREE FOR SPECIALTY PRODUCTS



- Opportunity for contracting
- Preferred options
- Manage with a Prior Authorization (and re-authorization) to label and potentially manage with step-therapy
- Manage site of care

- Generally manage with a Prior Authorization (and re-authorization) to label
- Manage site of care

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WILL PAYORS COVER THE PRODUCT?

- Tenapanor represents disruptive technology in a market heavily treated with oral therapies and patients still not meeting nationally recognized and accepted clinical targets
  - Recall up to 80% of patients are not consistently in range
- Ardelyx will have comprehensive hub service support, robust copay assistance program, and benevolent patient assistance program implemented by an experienced team

MME CHECKLIST FOR SUCCESS

- ☑ Is there criticality and unmet need?
- ☑ Will physicians write prescriptions for the product and advocate for use by the patients?
- ☑ Will patients take the product?
- ☑ Will payors cover the product?

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Commercialization Plan: Disrupting and Restating the Hyperphosphatemia Market

Susan Rodriguez

Chief Commercial Officer

Commercialization Plan – Restating the Hyperphosphatemia Market

- Hyperphosphatemia Market Dynamics – Ripe for Restatement
- Tenapanor First-in-Class Product Proposition
- Priming the Market – Ardelyx Strategy and Initiatives
- Tenapanor Launch Strategy, Plan and Mobilization

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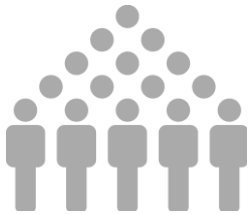
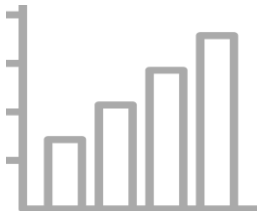
Well-Established Hyperphosphatemia Market



>550K

U.S. Dialysis Patients[1]



3-4%

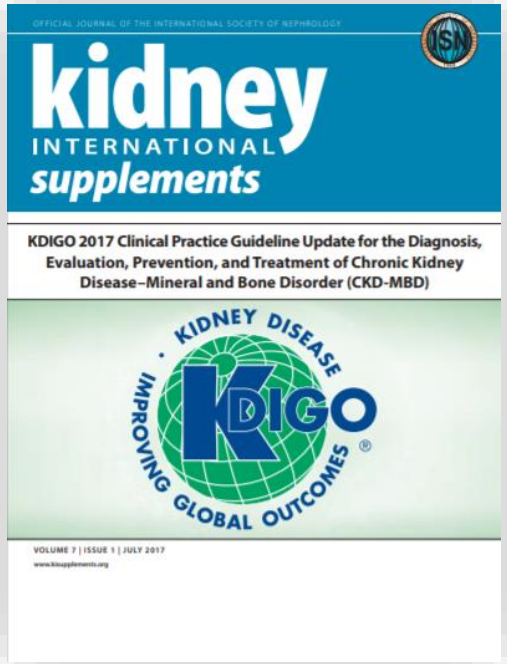
Annualized Growth Rate of U.S. Dialysis Population[1]

~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

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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Currently Available Therapies Rely on the Binder Mechanism of Action that has Inherent Limitations

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

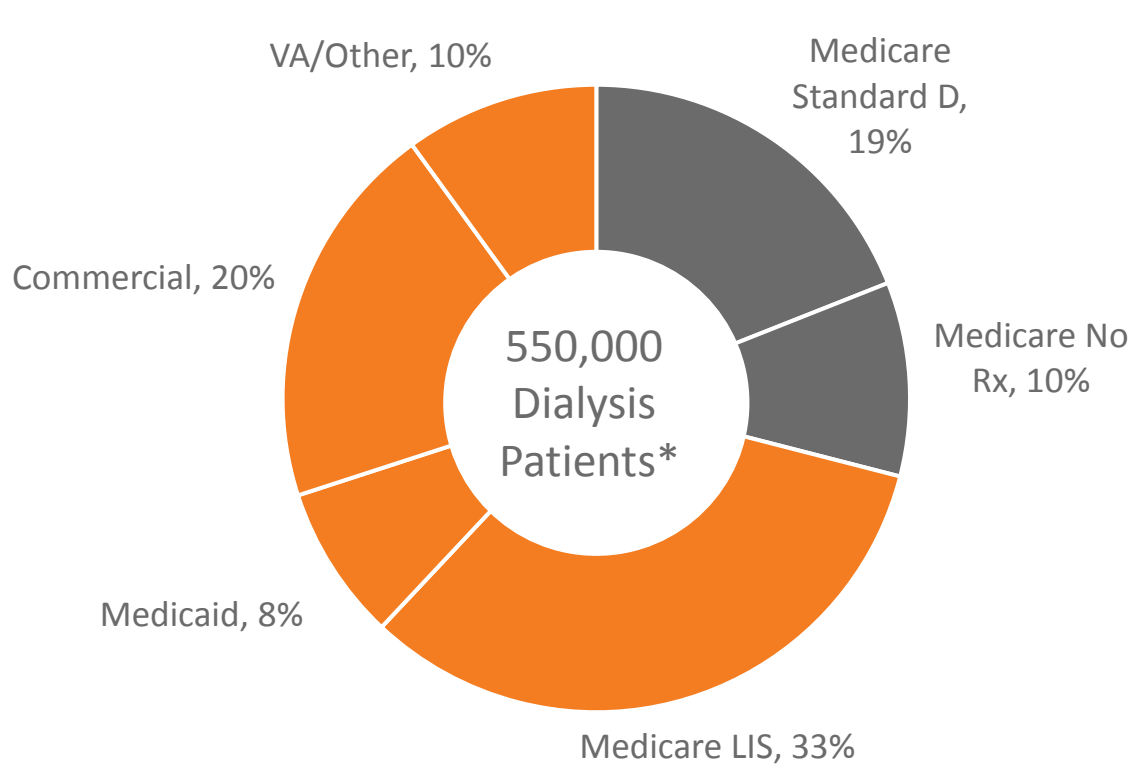
- Constipation
- Vomiting
- Nausea
- Diarrhea

Challenges Achieving and Maintaining Effective Phosphate Control

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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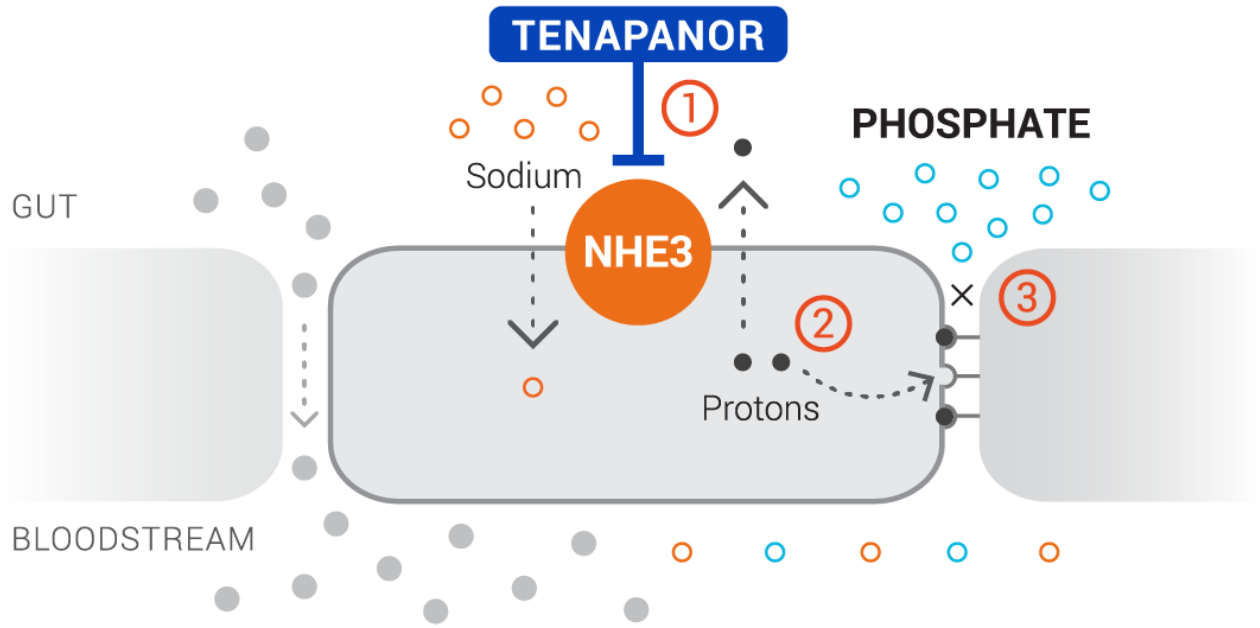
Tenapanor First-In-Class Product Proposition

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

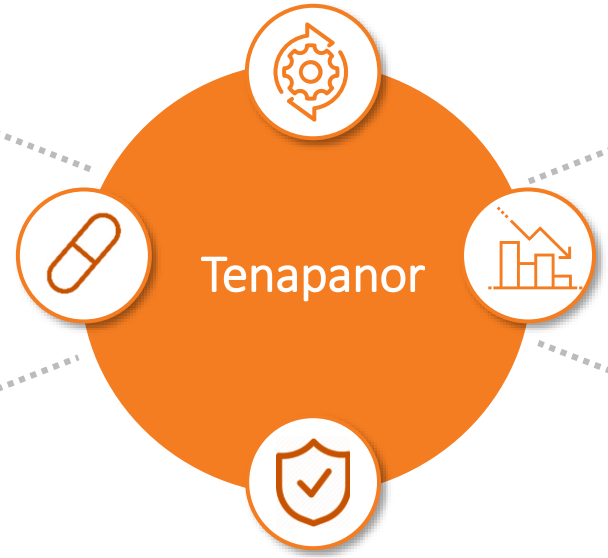
Primary and Key Secondary Endpoints met

PDUFA Date: April 29, 2021

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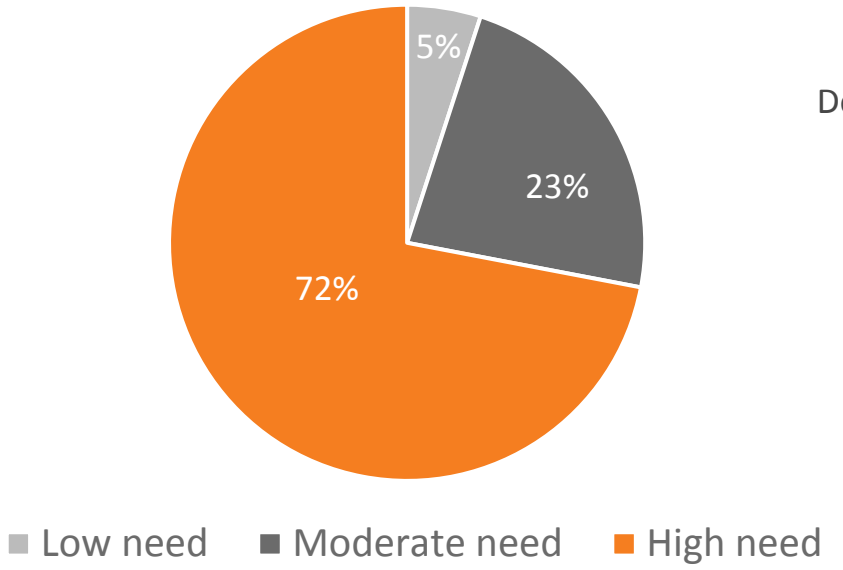
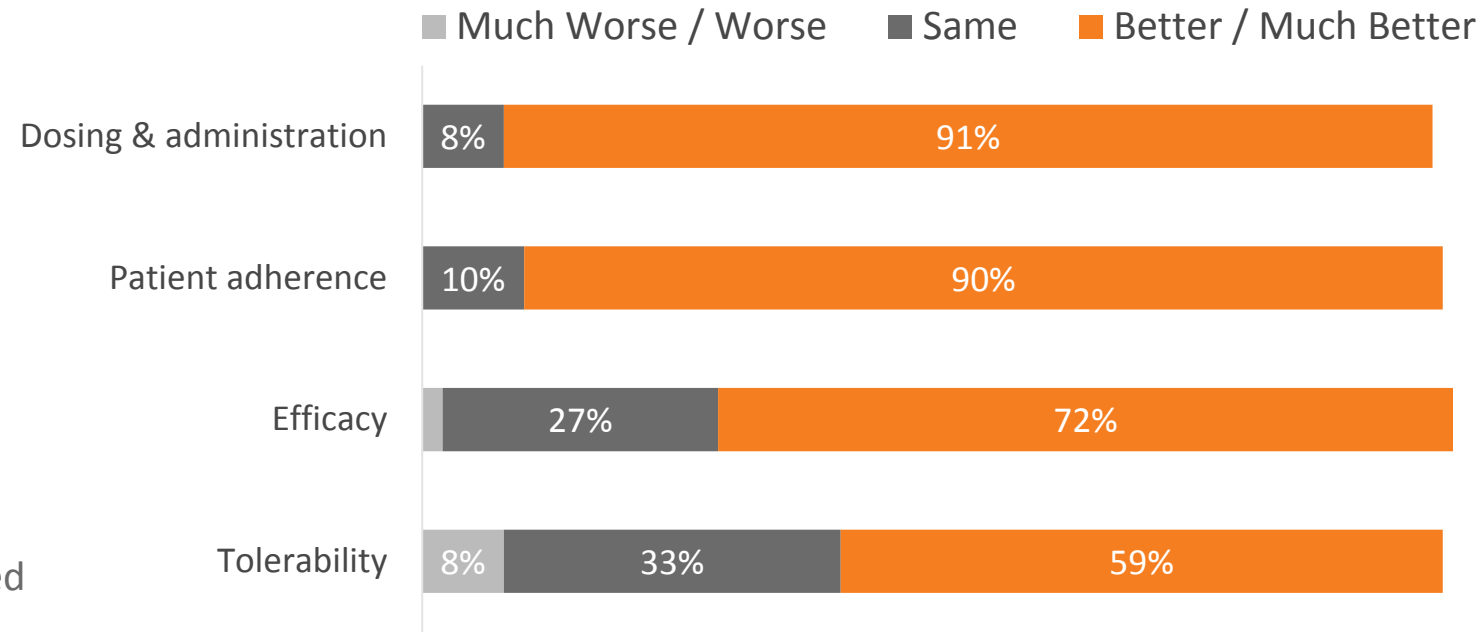
Market Research Reflects That Nearly 3 Out of 4 Nephrologists See a High Need for New Treatments and Expect Tenapanor to Provide an Improvement Compared to Phosphate Binders

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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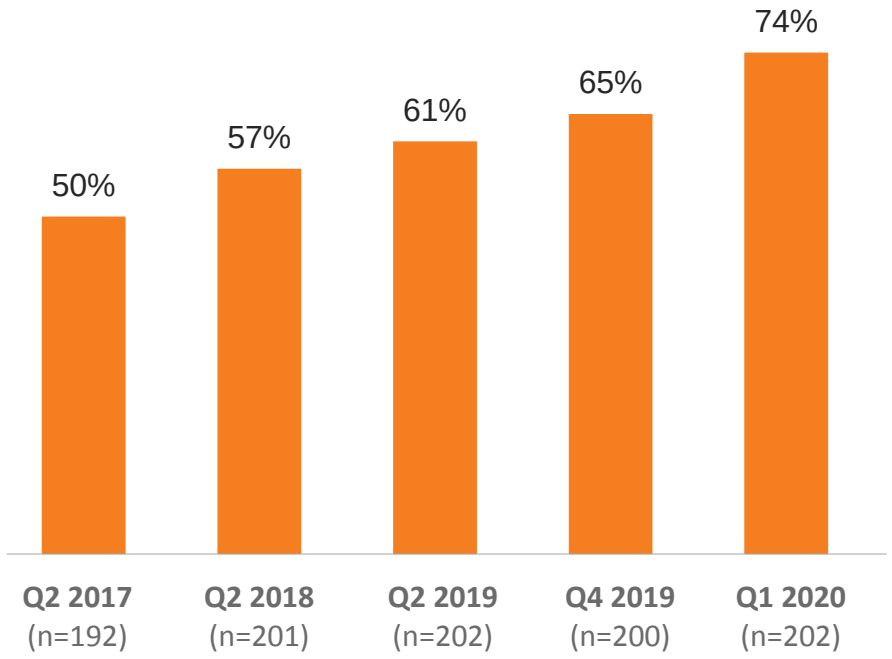
Nephrologists Report a High and Growing Anticipation for Tenapanor

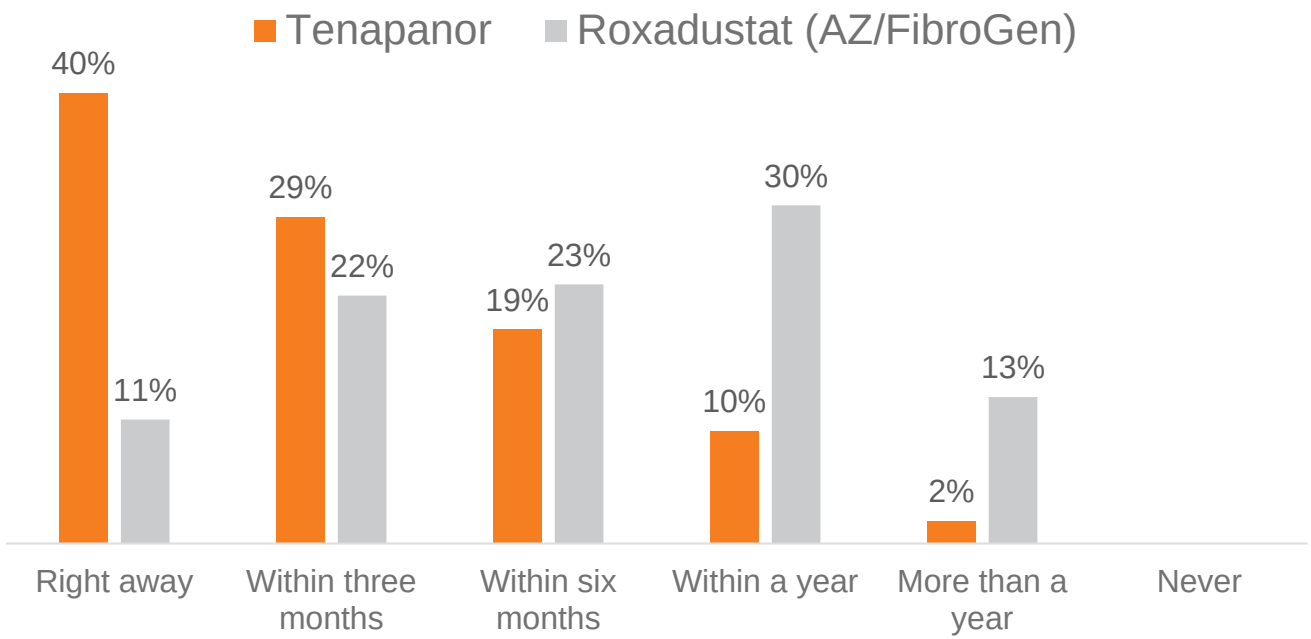
Interest in Tenapanor

% 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 setting?
*Excerpt from RealTime Dynamix: Bone and Mineral Metabolism, Q1 2020 (n=202)

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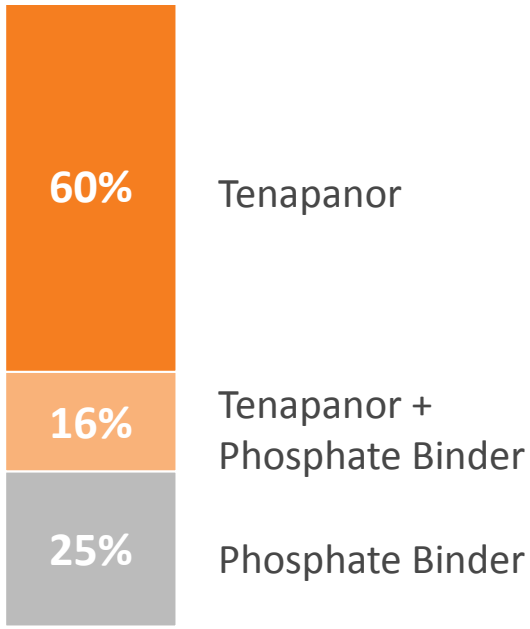
The Majority of Nephrologists Expect to Use Tenapanor as First Line Therapy

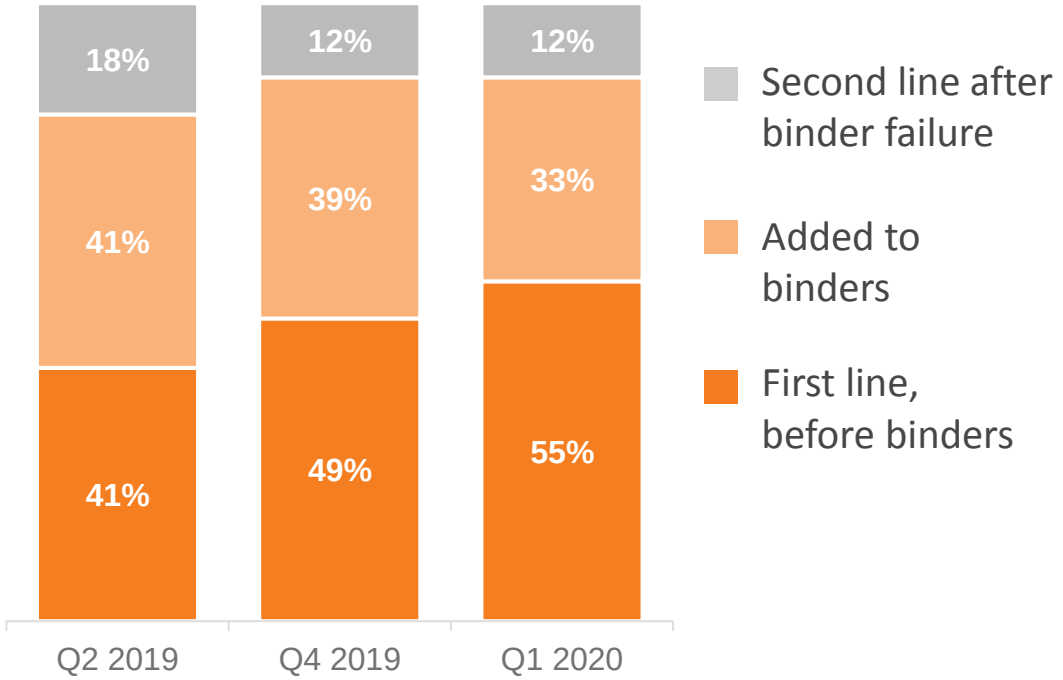
Most Likely First Line Hyperphosphatemia Treatment[1]

% 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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Payors Acknowledge Tenapanor Clinical Value Based on Disease Burden, Unmet Need, and Tenapanor Clinical Data Package

- Payors recognize unmet need and clinical value of tenapanor
- Tenapanor is most likely to be managed on a specialty or non-preferred tier
- No payors said tenapanor would be “non-formulary”

Precision Xtract I Tenapanor Value Proposition Development and Market Research with Payors – December 2019

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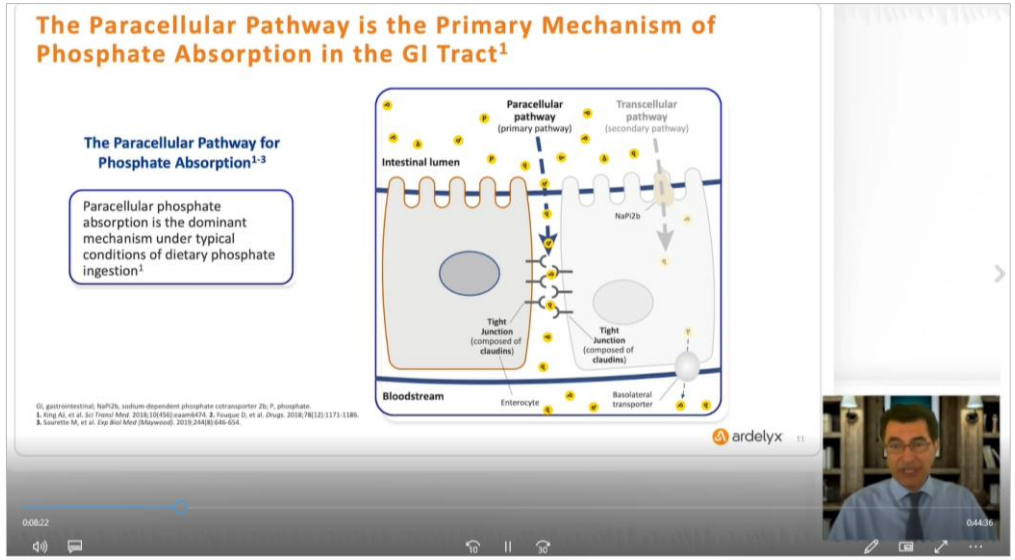
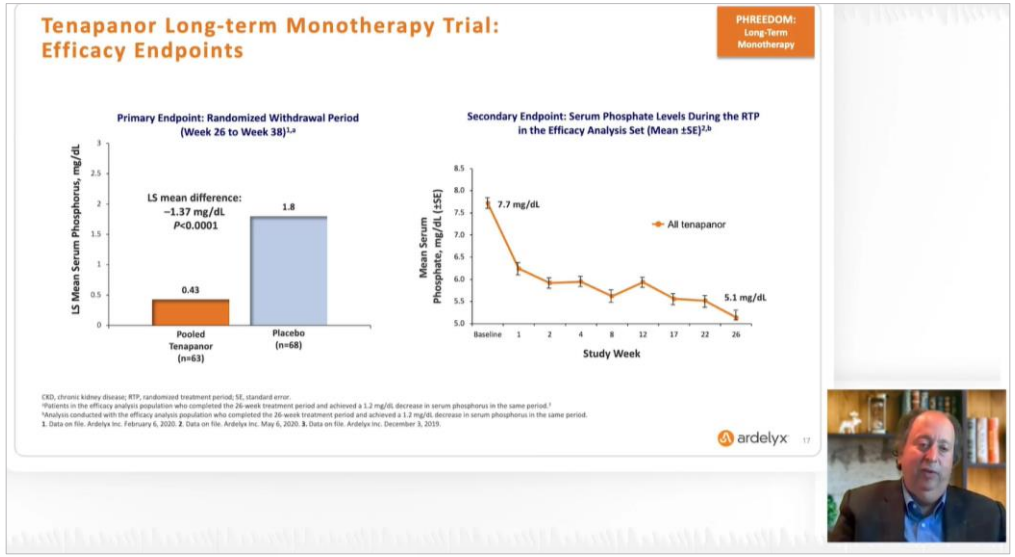
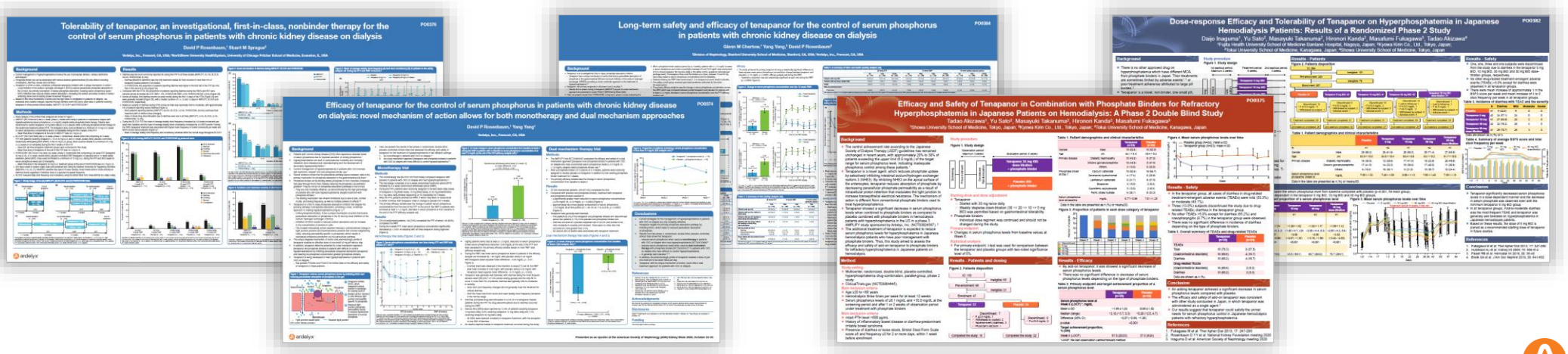
Priming the Market

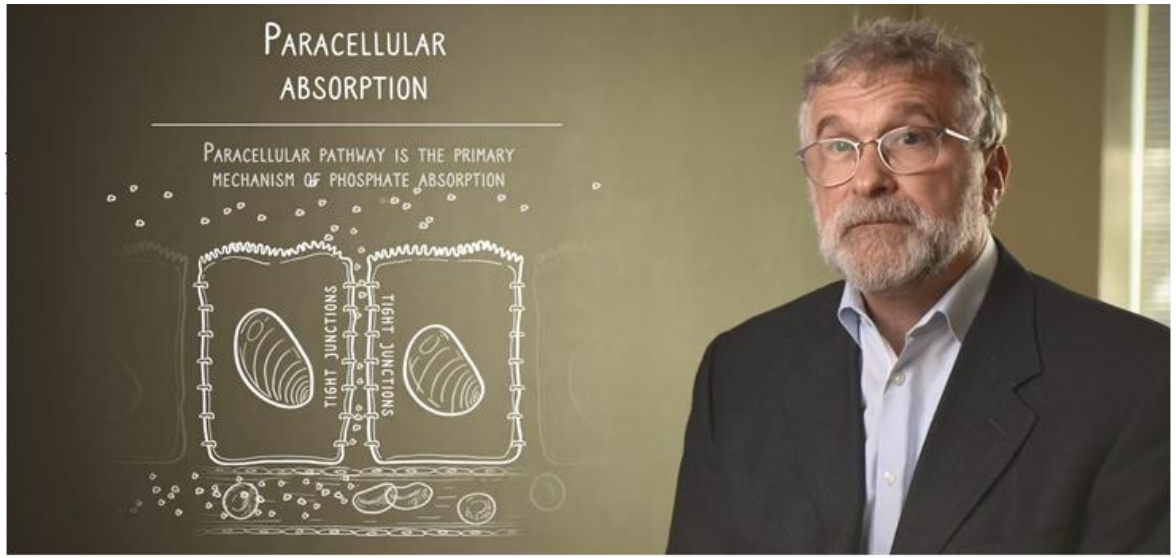
Ardelyx Highly Visible at ASN 2020 with Clinical Data and KOL Presentations



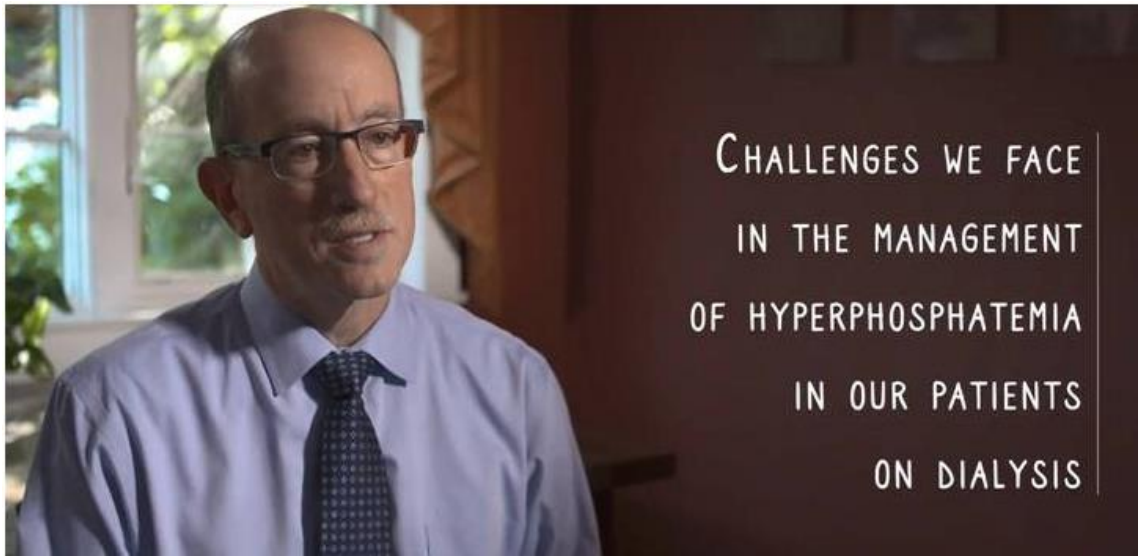




Ardelyx “Can We Do Better?” Disease Awareness Campaign Launched October 2020 Educating Nephrology Community on New Primary Pathway Science, Challenges in Managing Hyperphosphatemia, and Need to do Better



Dr. Stuart Sprague
Chief, Division of Nephrology and Hypertension at Northshore University Health System



Dr. Steven Fishbane
Chief of Nephrology, Northwell Health and Professor of Medicine, Zucker School of Medicine

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Multi-Channel Tactics for Ardelyx "Can We Do Better?" Campaign Launched in Q4'20 and Intensifying through 2021

- **Microsite**
  advancingphosphatecontrol.com
- **Media Placement**
  - Banner ads
  - Social media
  - Journal ads
  - Third party platforms
    - Doximity, Medscape
  - Email
  - Direct Mail
  - SEO/SEM
- **Speaker Webcasts**
- **Advertorials**

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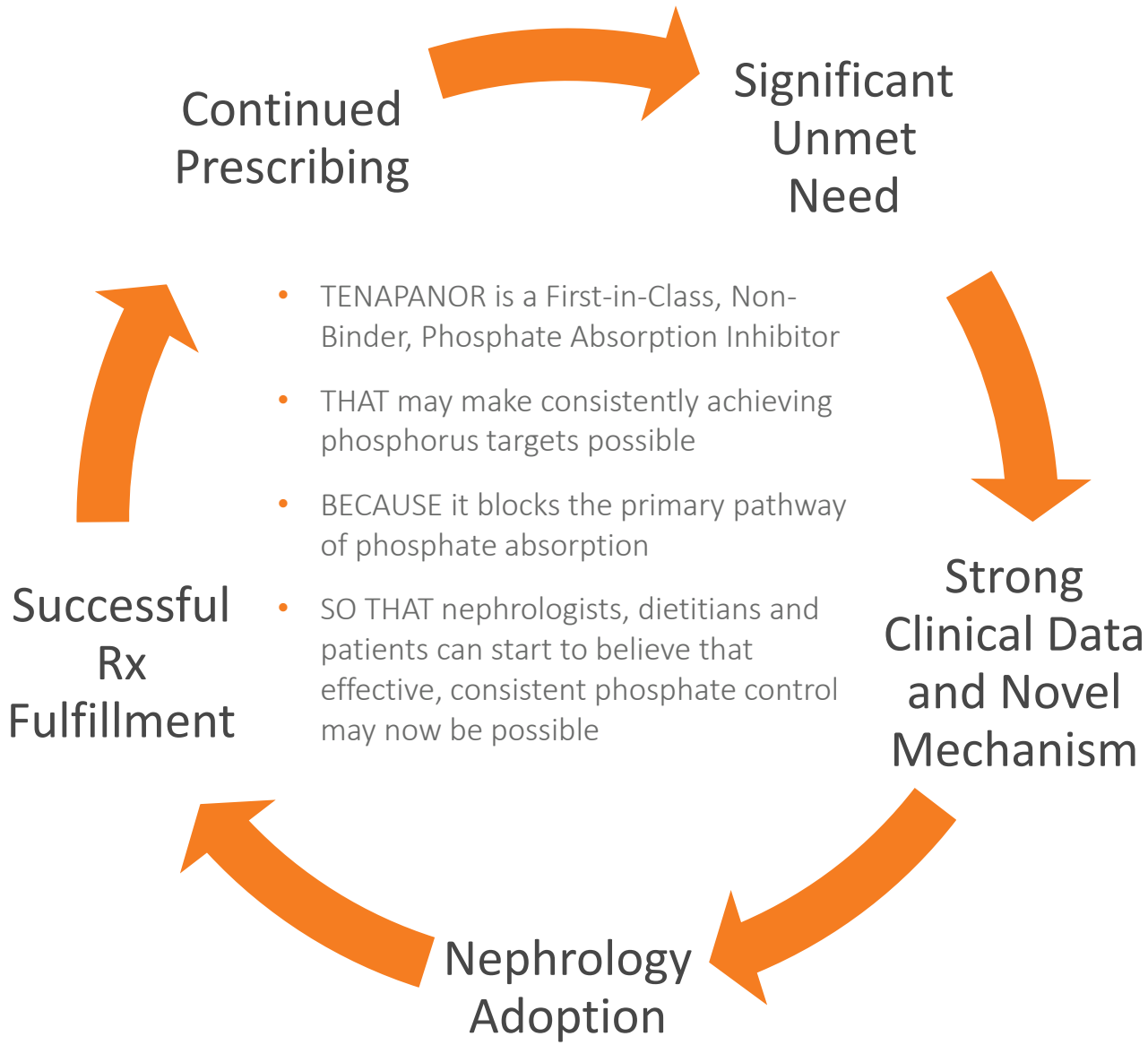
Tenapanor Launch Plan

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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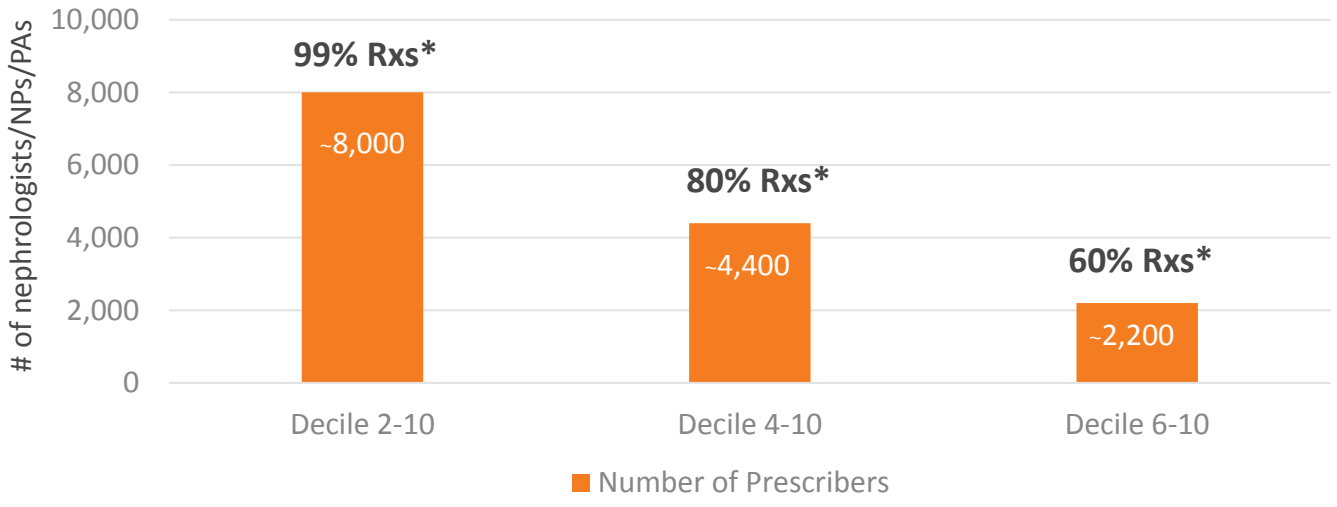
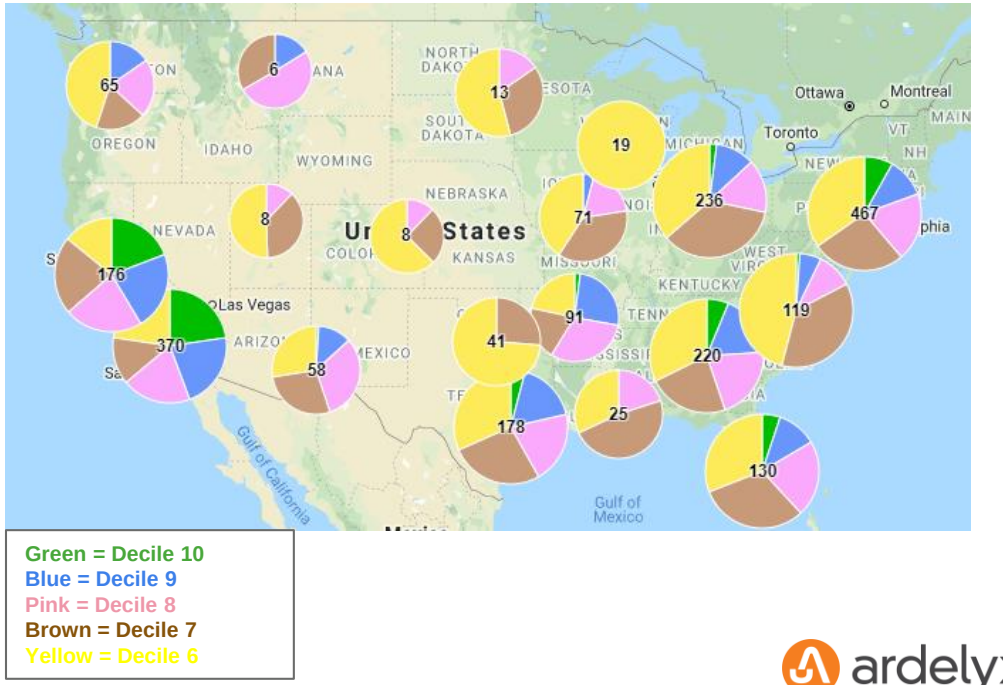
Strategic Imperatives – Drive Strong Nephrology Demand

- 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

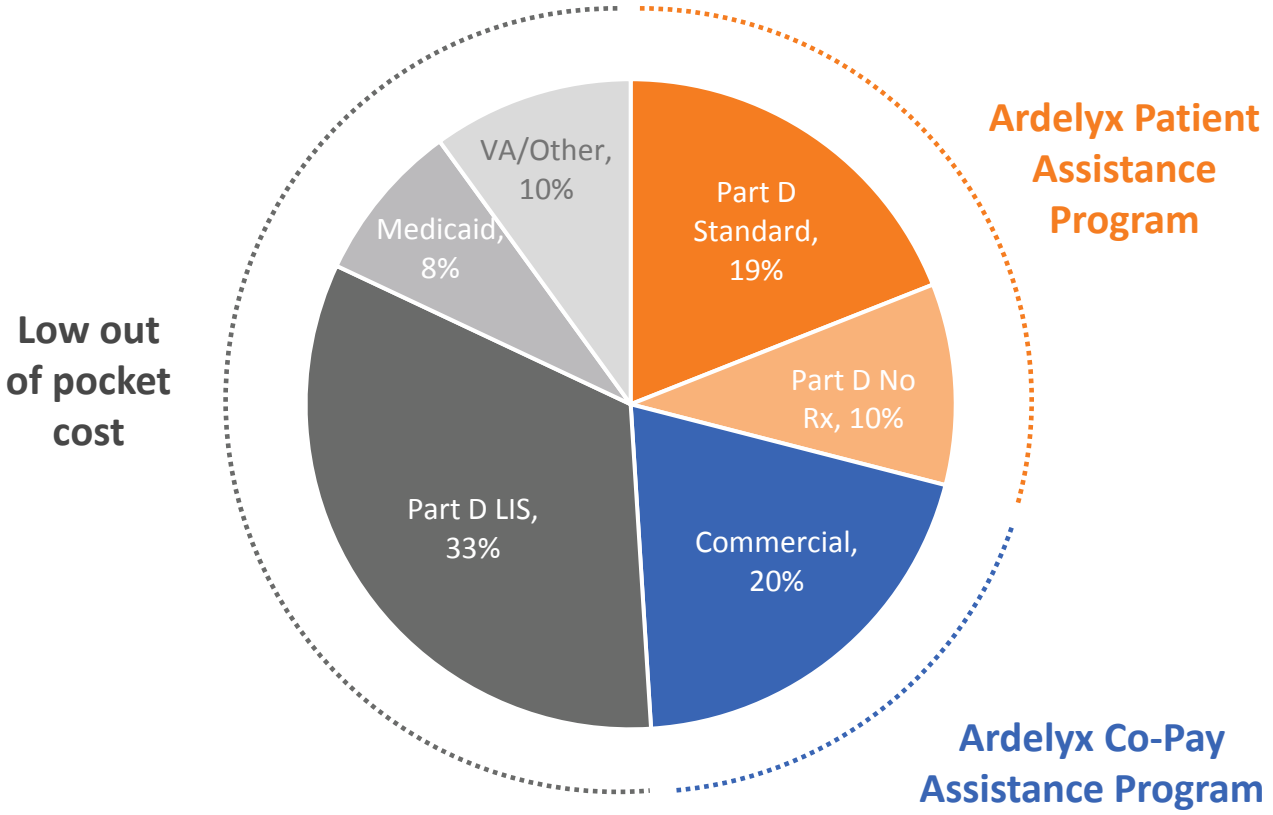




Source: IQVIA Targeting and Segmentation analysis. SAT score decile based on number of TRxs and quality of access. 12,571 nephrologists/nephrology NPs/PAs in total. Percentage of Rxs based on total from this group of 12,571

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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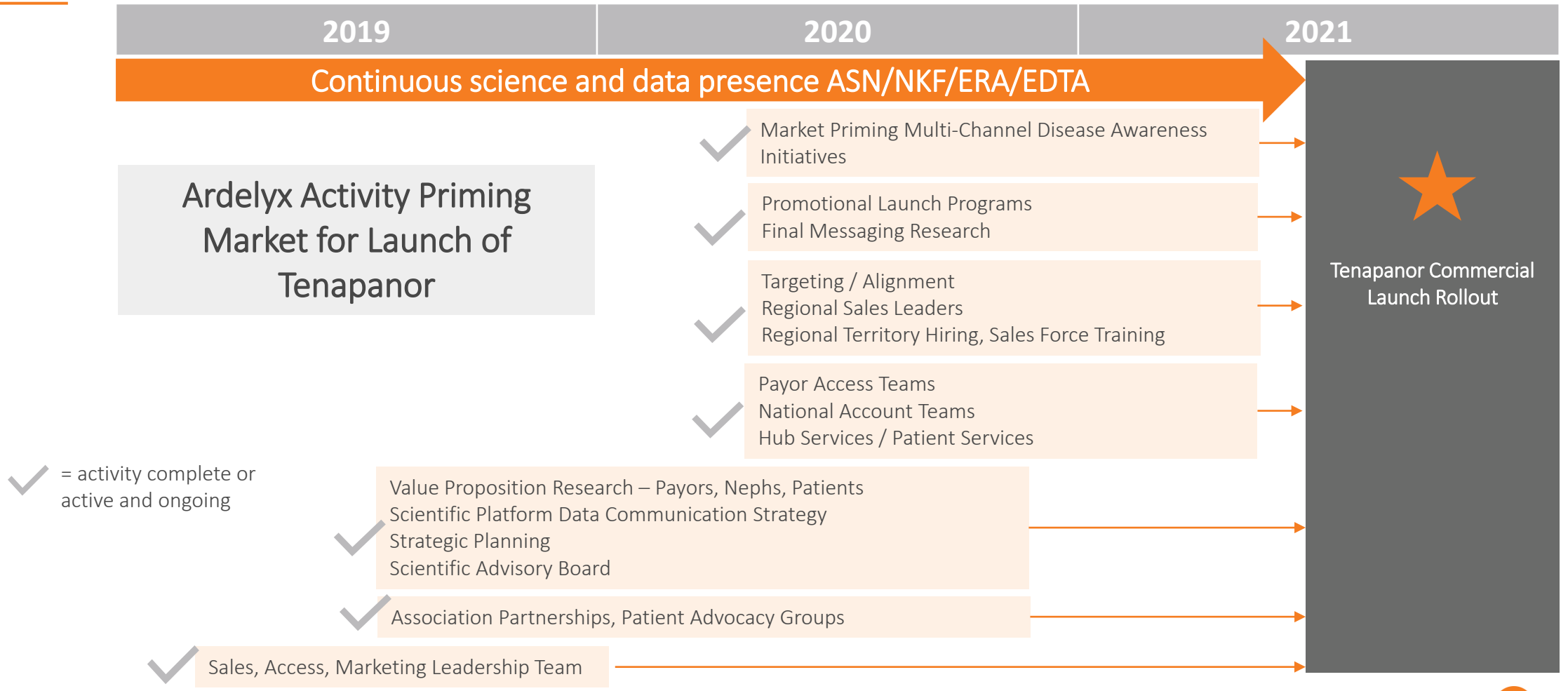
Ardelyx Commercial Presence Rapidly Expanding and Fully Mobilized for Q2 2021 Approval of Tenapanor



Ardelyx is Restating the Hyperphosphatemia Market

- ✓ Hyperphosphatemia market is ripe for restatement
- ✓ Favorable nephrologist response to tenapanor first-in-class product proposition with anticipated rapid adoption and broad-based use
- ✓ Ardelyx data communication strategies and disease awareness initiatives are priming the market for the successful launch of tenapanor
- ✓ Ardelyx mobilizing tenapanor commercial organization with robust launch strategy and tactical execution excellence

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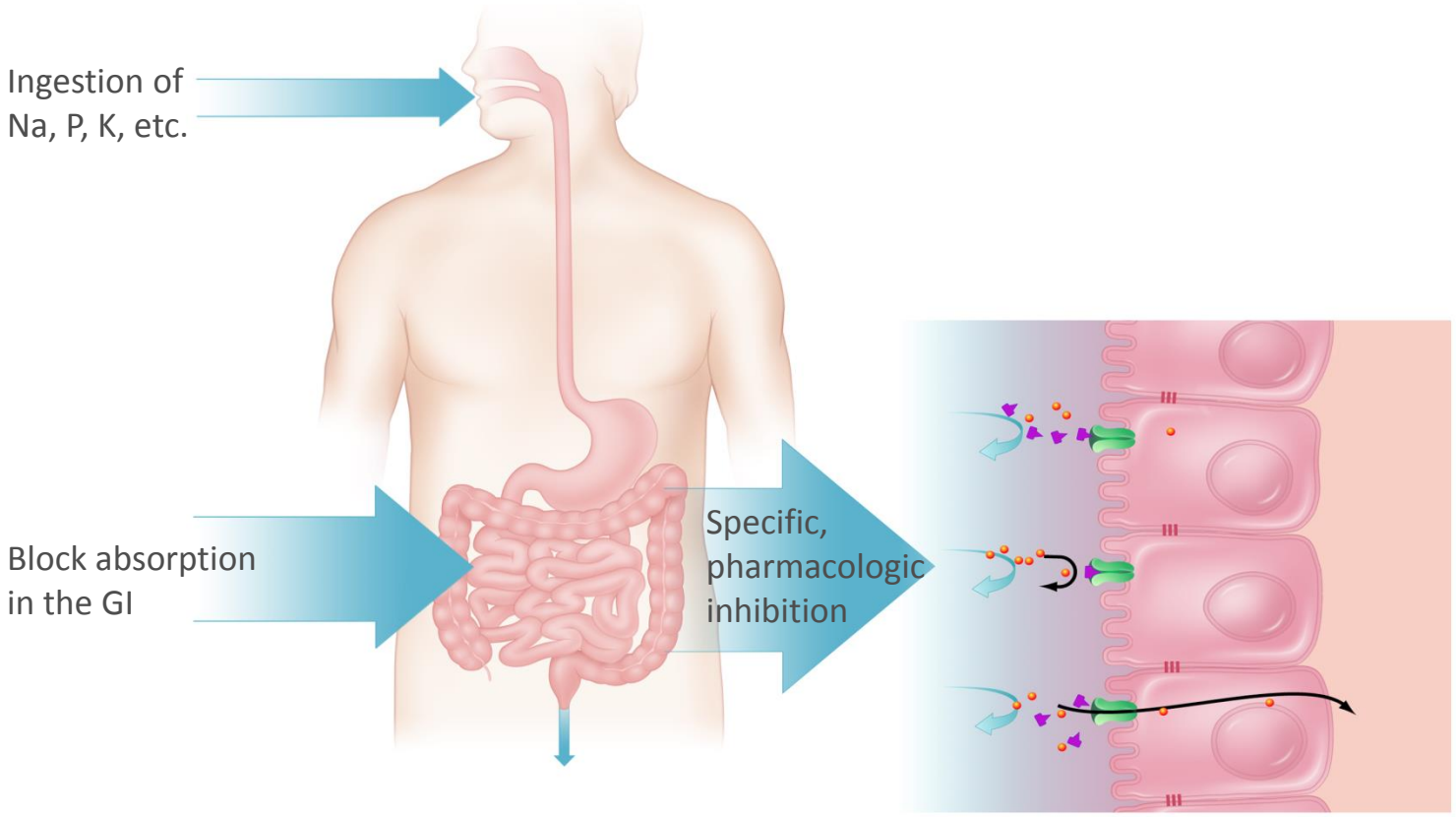
Ardelyx Research: Pioneering New Mechanisms in Transport Biology to Create First-In-Class Therapies

Jeff Jacobs Ph.D.

Chief Scientific Officer

Discovering New Mechanisms in Transport Biology to Treat Cardiorenal Diseases



Divert excess pathologic ions to the stool

Modulate GI transport processes to treat systemic physiology:

- Sodium
- Phosphate
- Potassium
- Acid-Base balance

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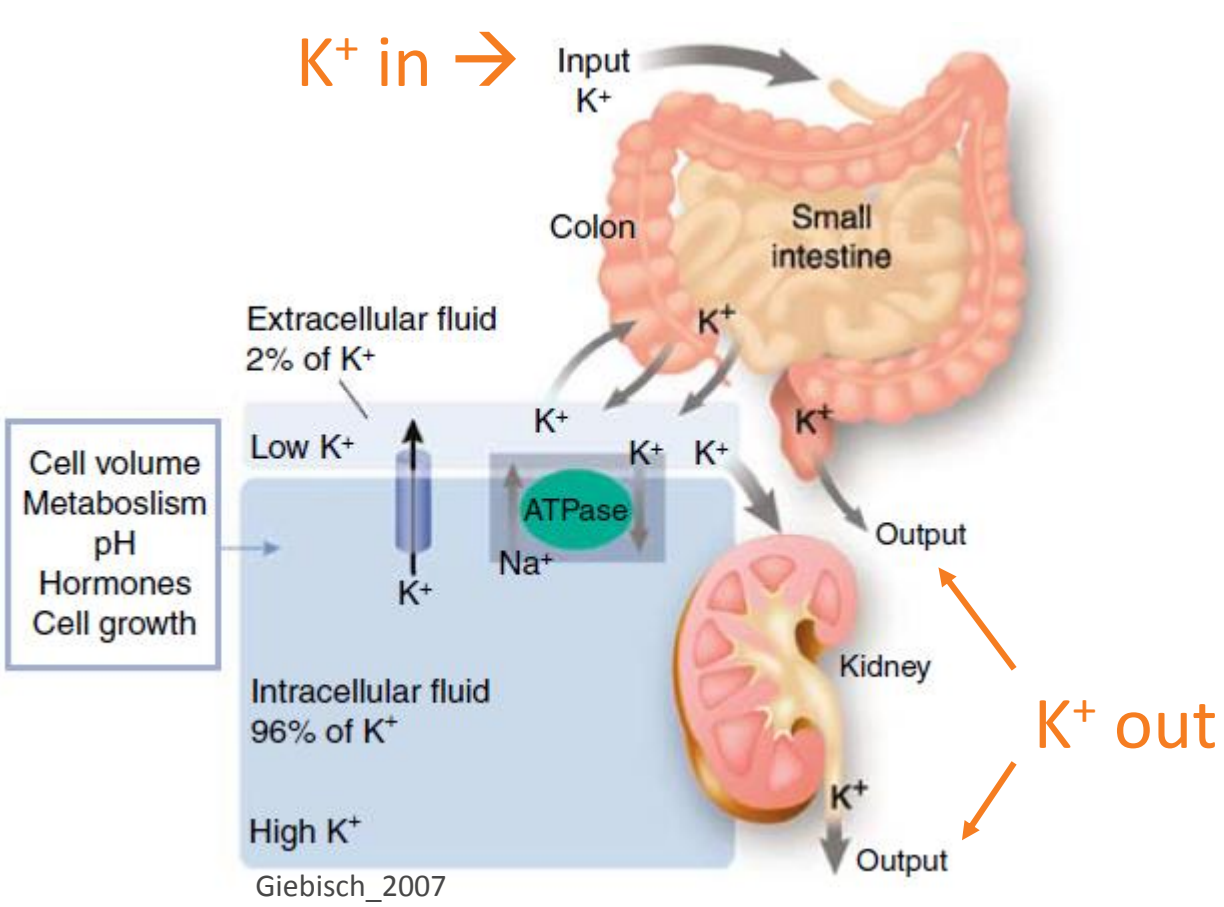
Advancing the Science of Hyperkalemia Treatments: The Ardelyx Journey



Giebisch_2007

- Potassium's exit from the body is mediated by both the kidney (primary) and the colon
- Targeting colonic K^+ secretion is required for management of hyperkalemia in ESRD or in CKD if maintaining RAAS blockade
- Ardelyx has pursued excellence in potassium management with two approaches:
  - Best-in-class potassium binder
  - First-in-class colonic potassium secretagogues

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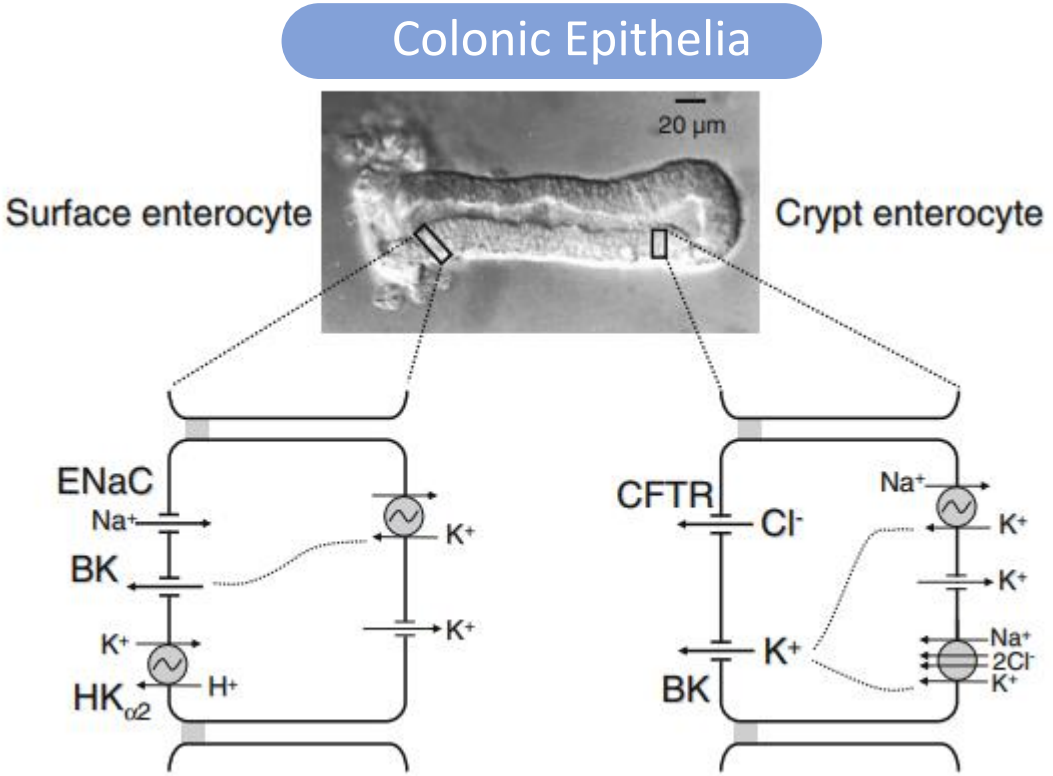
RDX013 is a Secretagogue That Greatly Increases Colonic K^+ Secretion



- The colon has a large capacity for K^+ secretion
- Colonic epithelial K^+ secretion is a two-step transport process:
  - Initial K^+ uptake over the basolateral membrane
  - Followed by K^+ channel-dependent exit into the lumen
- RDX013 amplifies colonic potassium secretion

Sorensen_2010

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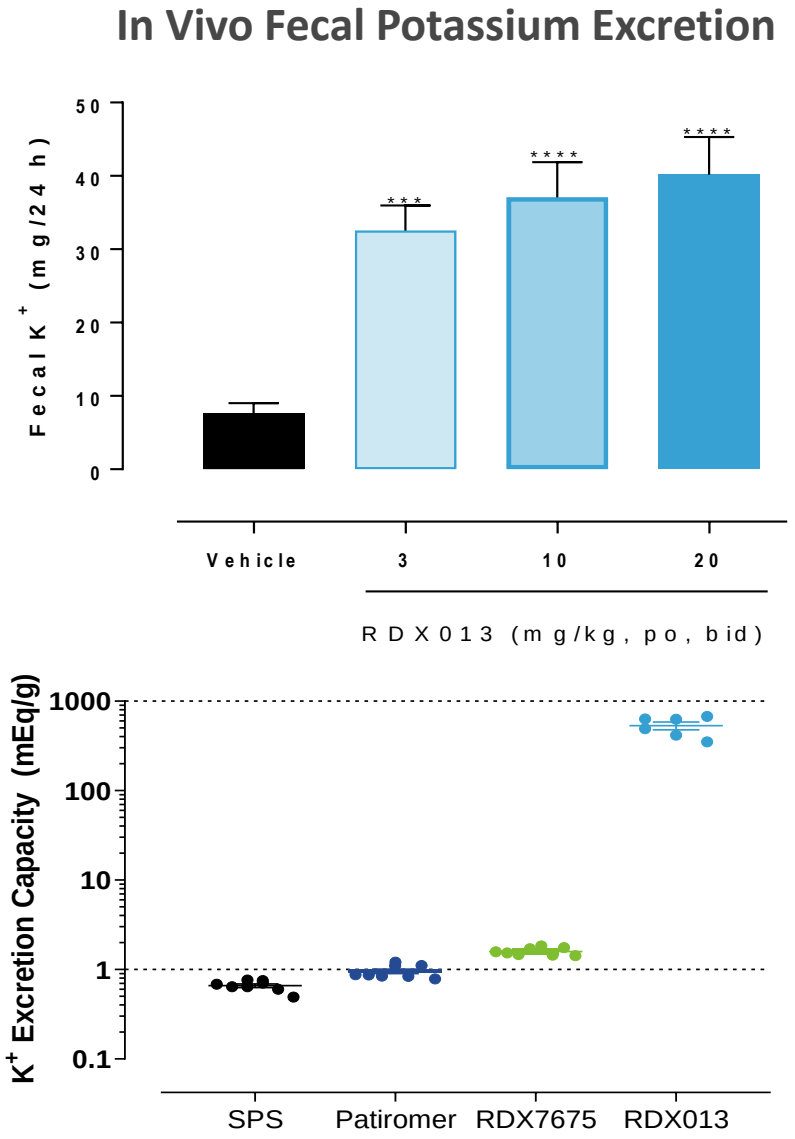
Expanding our Renal Footprint

- Novel, oral small molecule potassium secretagogue
- Small pill dosing
- Increases fecal potassium excretion; reducing serum potassium
- May allow for optimal dosing of RAAS inhibitors--foundational anti-hypertensive drugs
- ~1000x improved *in vivo* potency vs binders

*K^+ binding capacity determined in mouse



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

~1,000x

Improved In Vivo Potency vs Binders*

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RDX013 Has the Potential to Revolutionize the Treatment of Hyperkalemia

- Ardelyx insights in colonic potassium secretion have enabled the potential development of a potent potassium secretagogue
- RDX013 targets pharmacology that significantly amplifies natural secretion mechanisms in the gut
- The RDX013 secretagogue program offers a 21st century solution to the hyperkalemia problem, with potential for market-leading efficacy, tolerability and dosing profile

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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

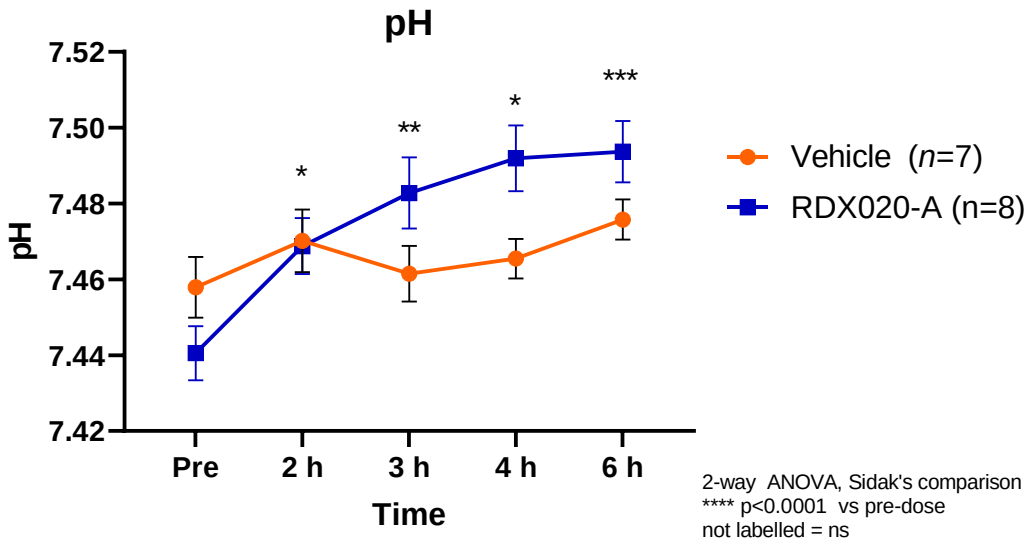
There are no approved treatments for metabolic acidosis

- 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)

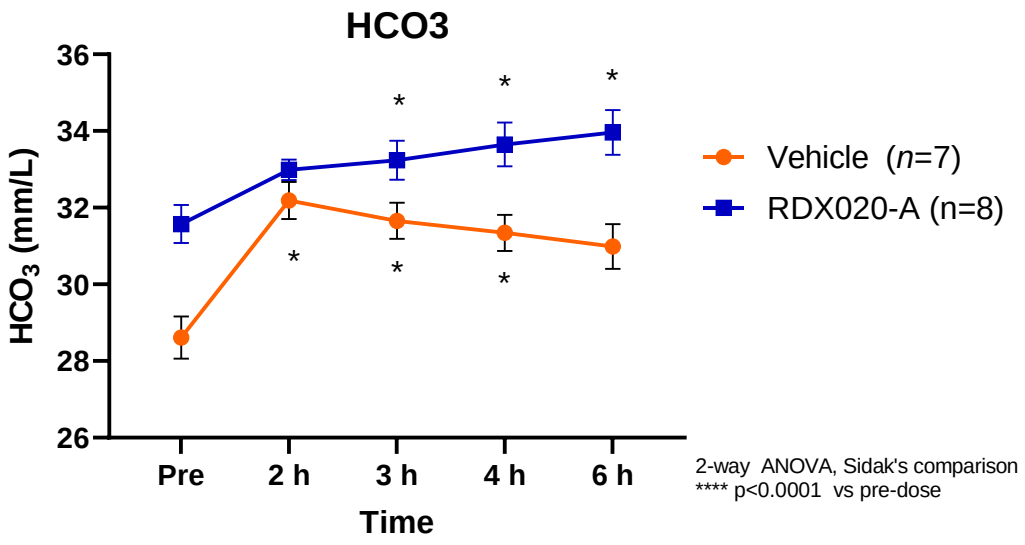
Ardelyx has successfully targeted intestinal bicarbonate exchange

- 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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Targeting Intestinal Bicarbonate Secretion to Treat Metabolic Acidosis

- Potent, selective and proprietary set of small molecule bicarbonate secretion inhibitors identified
- Compounds are active in rodent studies, with a dose-response profile and favorable PK properties
- Preliminary safety profiling indicate that lead compounds have minimal off-target activity and are well tolerated in vivo
- Potential to be a first-in-class therapeutic

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Advancing the Ardelyx Pipeline

David Rosenbaum Ph.D.

Chief Development Officer

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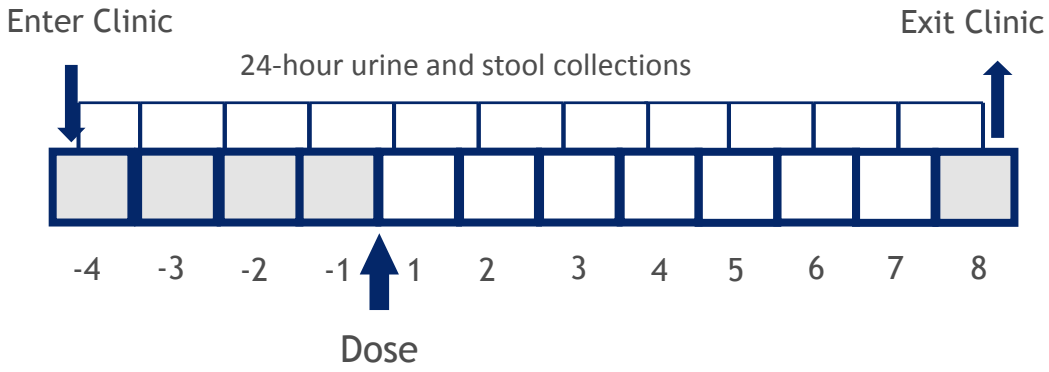
RDX013-101: Phase 1 Safety and Proof-of-Concept Study

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

Potassium Change from Baseline

Dose (mg/day)	N	Days of Treatment	Stool (mEq/day)	Fold Increase in Stool
Low Dose	12	3	9.96	1.83
Mid Dose	12	3	13.8	2.09
High dose	12	3	22.2	2.68

Dose response was observed

Administration	N	Days of Treatment	Stool (mEq/day)	Fold Increase in Stool
Once-a day	12	7	5.42	1.39
Twice-a-day	12	7	19.1	2.46

BID better than QD

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

Summary and Next Steps

- Clinical proof-of-concept achieved for RDX013
- Decreased urine potassium and increased stool potassium excretion
- Acceptable PK, safety, and tolerability in healthy subjects
- Data support moving forward with Phase 2 study evaluating RDX013 in hyperkalemic patients
- Phase 2 design based on regulatory interactions

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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

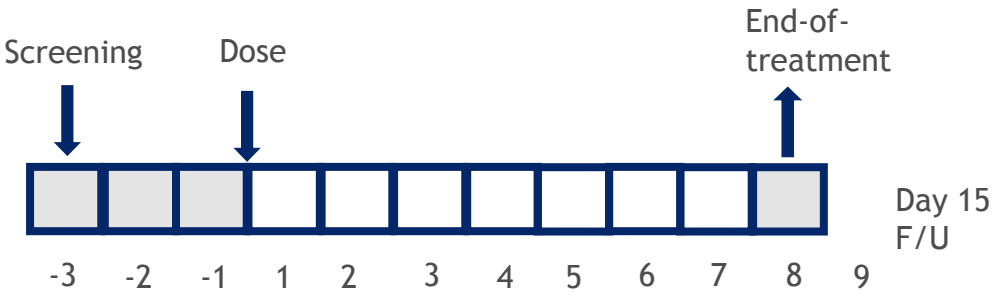
- sK value 5.1 to < 6.5 mmol/L at Screening
- Chronic kidney disease with eGFR ≥ 15 to < 60 mL/min/1.73m^2, most recent historical value (MDRD or CKD-EPI formula)

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

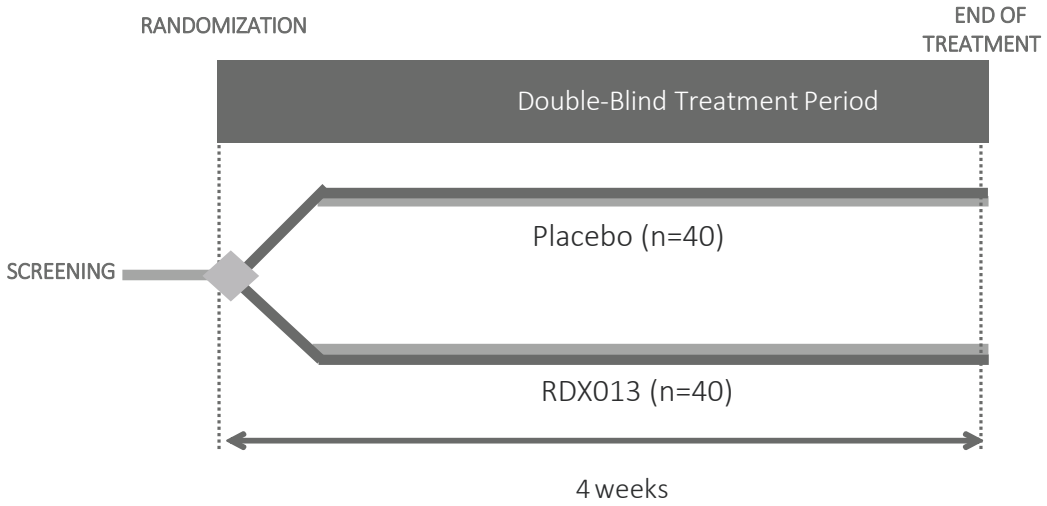
RDX013-201: Phase 2 Adaptive-Design Study

Part A: Dose Selection



- Part A, one-week treatment duration to determine the effect of RDX013 on serum potassium
- Based on Part A results, dose(s) will be selected to evaluate in Part B

Part B: Double-Blind Placebo-Controlled



- Part B, double-blind, placebo-controlled evaluating the difference between placebo and RDX013 in the change in serum potassium from baseline to week 4

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Financials & Partnering Strategy

Justin Renz

Chief Financial Officer

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

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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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24-Month View of Potential Milestones and Catalysts

- Initiate OPTIMIZE trial to inform on the integration of tenapanor into clinical practice
- Progress in market development and pre-commercial activities
- PDUFA date for tenapanor approval for hyperphosphatemia April 29, 2021
- If approved, launch tenapanor for the treatment of hyperphosphatemia
- Advance kidney and cardiovascular franchise with RDX013
- Advance RDX020 for metabolic acidosis
- Ongoing progress with partners in Japan, China and Canada
- Develop strategic plan to advance tenapanor in Europe

Q&A

Mike Raab

President & CEO