ARDELYX®

BREAKTHROUGH SCIENCE FOR **BETTER HEALTH**

June 2019

NASDAQ: ARDX

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 future development plans for its product candidates and the expected timing thereof; the commercial potential for Ardelyx's product candidates; Ardelyx's ability to establish collaborations in the future; the potential for Ardelyx to receive milestone and royalty payments from its collaborators; 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 Annual Report on Form 10-Q filed with the Securities and Exchange Commission on May 7, 2019, and its future current and periodic reports to be filed with the Securities and Exchange Commission.

- Developing first-in-class, innovative medicines
- Lead product candidate, tenapanor, with $500-700M market opportunity in hyperphosphatemia alone.
- Opportunity for specialty renal U.S. commercial organization; Established partnerships in select ex U.S. geographies
- Seasoned management team with clinical and commercial cardiorenal expertise
- Operating runway through early 2021

A Cardiorenal Biotech Company

It’s the patients in need that motivate and inspire us to be relentless and work hard everyday. They push us to maintain a clear focus on scientific and clinical integrity with a commitment to medical innovation so that we can deliver exceptional medicines.

FOCUSED ON ADVANCING TENAPANOR TO REACH PATIENTS

HYPERPHOSPHATEMIA (HP)

- Novel non-binder approach to managing phosphorus
- Statistically significant phosphate reduction in first Phase 3 study
- Second Phase 3 study PHREEDOM enrolled. Topline Results 4Q19
- Third Phase 3 combo study AMPLIFY on track. Results 3Q19
- $500-700M commercial opportunity

IBS-C

- NDA accepted for review with PDUFA date September 12, 2019
- Evaluating potential partnering opportunities
- 11M people with IBS-C estimated in the U.S. alone

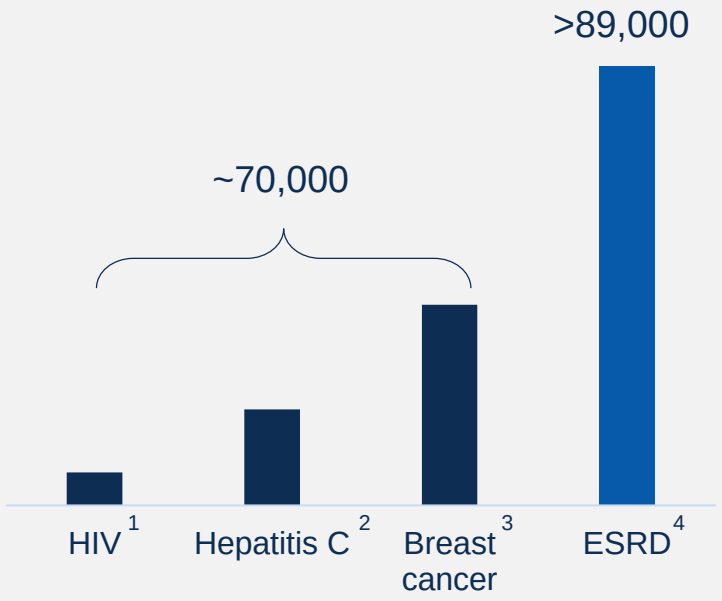
EX-U.S. COLLABORATIONS

- Japan: Kyowa Hakko Kirin for cardiorenal diseases
  - $30M upfront, up to $55M in total development milestones and 8.5B yen in commercialization milestones, high-teen royalties
- China: Fosun Pharma for HP and IBS-C
  - $12M upfront, $113M in milestones, mid-teen to 20% royalties
- Canada: Knight for HP and IBS-C
  - CAD 25M in upfront payment & milestones, double-digit royalties

End-Stage Renal Disease (ESRD) Patients on Dialysis

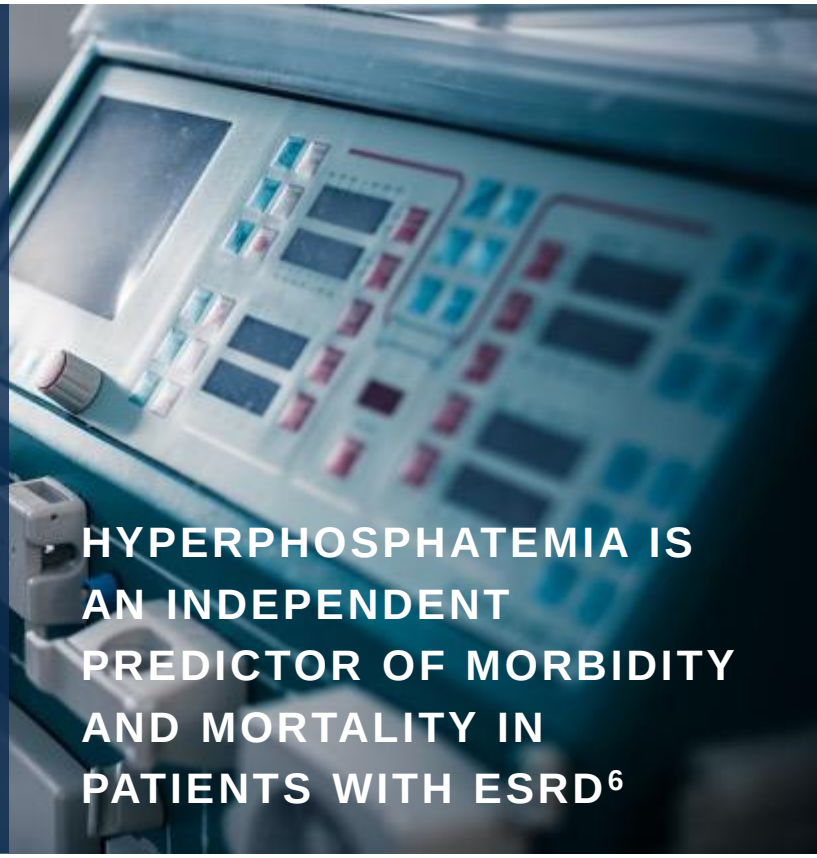
REQUIRE OUR ATTENTION

More ESRD patient deaths in the U.S. each year than breast cancer, HCV and HIV combined



95%

of ESRD patients need phosphate control[5]



HYPERPHOSPHATEMIA IS AN INDEPENDENT PREDICTOR OF MORBIDITY AND MORTALITY IN PATIENTS WITH ESRD[6]

1. CDC HIV in the United States 2014 (~6,700)
2. CDC Hepatitis C 2016 (~18,000)
3. ACS Breast Cancer Facts & Figures 2017-2018 (~41,000)
4. National Kidney Foundation, ESRD in the U.S. 2016
5. Savica, V Nephrol Dial Transplant 2006 21: 2065-2068
6. Emmett M Dialysis & Transplantation. 2006

~1 OUT OF 2 PATIENTS IS NOT COMPLIANT
with their hyperphosphatemia treatments[1]

2 OUT OF 3 PATIENTS NOT AT TARGET
based on serum phosphorus levels tested at any point in time[2]

NO CHANGES TO TREATMENT APPROACH SINCE INTRODUCTION OF PHOSPHATE BINDERS IN 1970s

Control of serum phosphorus limited by poor compliance and adherence to phosphate binder treatment

1. Fissel 2016
2. DOPPS Practice Monitor, December 2015. www.dopps.org/DPM

PILL BURDEN AND DOSE:

The #1 Challenge for Patients with Hyperphosphatemia

POTENTIAL TO IMPROVE COMPLIANCE THROUGH CONVENIENT DOSING

One week dose of today's SOC[1]

One week dose of tenapanor[2]

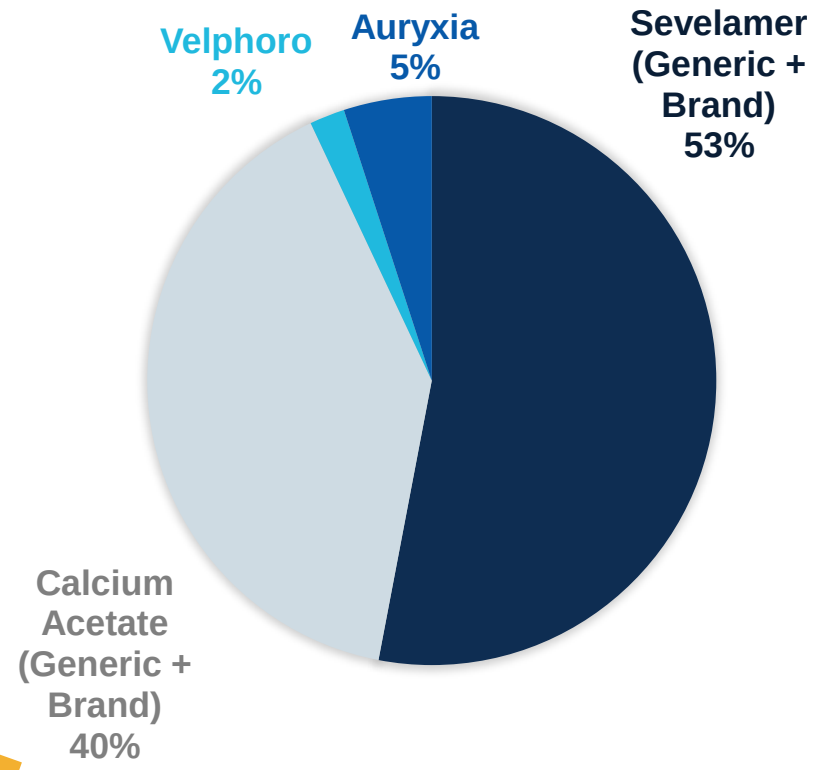
1. 800mg of Renvela (sevelamer carbonate) up to three times per day with meals per package insert
2. Investigational small molecule currently in Phase 3 development. Target dose 10-30 mg BID. (10 mg shown here)

HP Patients and Physicians Ready for the FIRST NON-BINDER TREATMENT OPTION

New evidence from three randomized controlled trials supports a more general recommendation to <u>RESTRICT CALCIUM-BASED PHOSPHATE BINDERS</u> in hyperphosphatemic patients across all severities of CKD.[1]

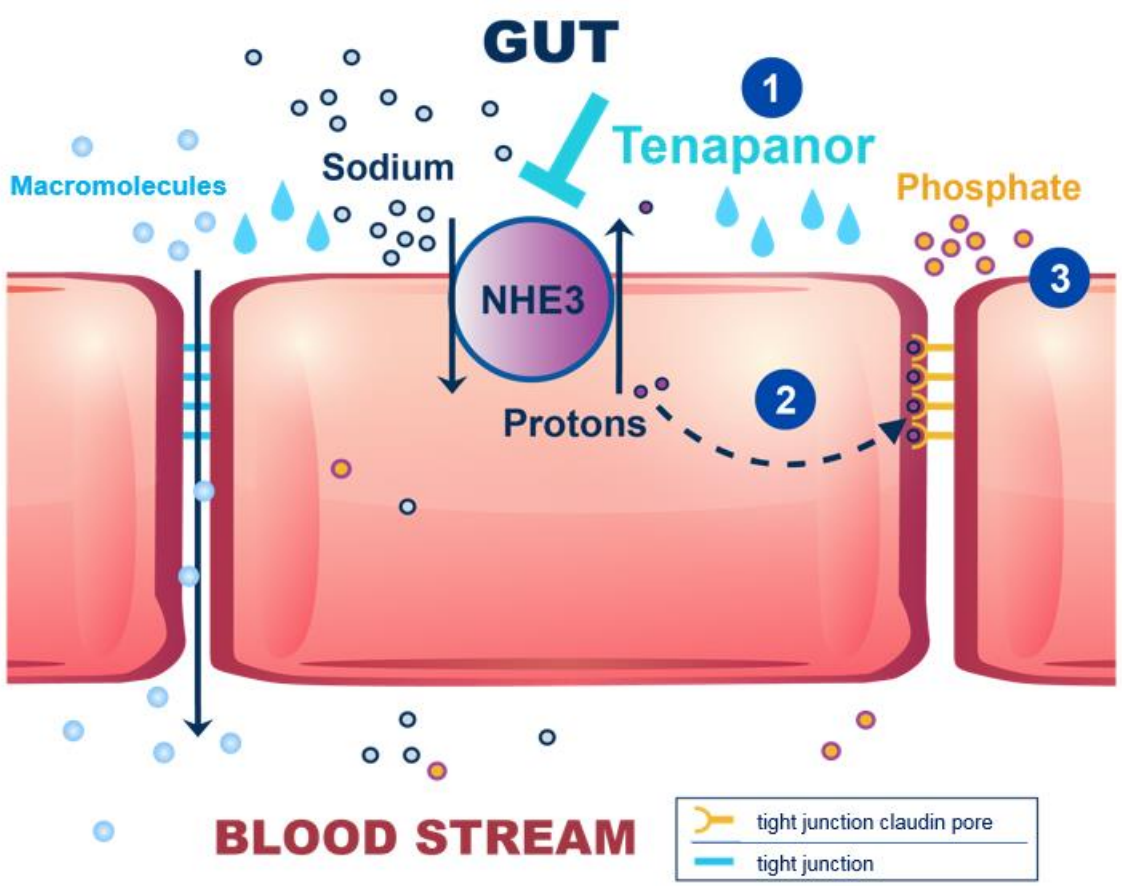
BINDERS REMAIN THE ONLY TREATMENT OPTION TODAY[2]

TRx Unit Market Share



1. 2017 KDIGO CKD-MBD Guideline Update; Kidney International (2017) 92, 26–36
2. IQVIA binder TRx Market Share 12 months through November 2018

FIRST-IN-CLASS TREATMENT FOR ESRD PATIENTS WITH HYPERPHOSPHATEMIA



1. Tenapanor inhibits NHE3 which transports luminal sodium in exchange for cellular protons
2. Cellular proton retention reduces tight junction permeability to phosphate
3. Reduced tight junction phosphate permeability results in reduced paracellular absorption of luminal phosphate

Paracellular transport is quantitatively the most important mechanism of phosphate absorption in the GI tract

Selective NHE3 Inhibition in the GI tract blocks paracellular transport of phosphate via tight junctions

Clinical and preclinical data suggest GI NHE3 inhibition has no overall effect on absorption of nutrients or other ions

TENAPANOR EFFICACY

Demonstrated in First Phase 3 HP Study[1]

ROBUST TREATMENT EFFECT IN RESPONDERS[2]

- 2.56 mg/dL mean change in serum phosphorus levels in responder population (baseline to end of 8-week treatment period)

STATISTICALLY SIGNIFICANT RESULTS*

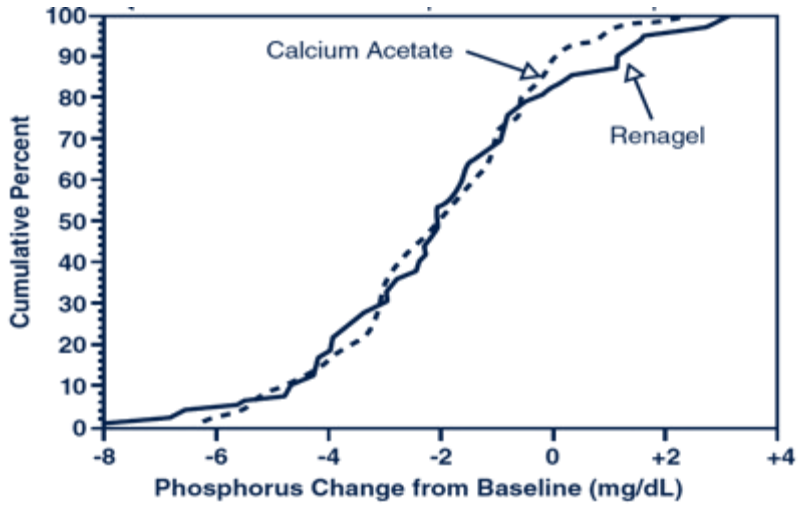
- 1.01 mg/dL mean delta between placebo and tenapanor (95% CI -1.44, -0.21)
- Primary endpoint: -0.82 mg/dL LS mean; p=0.01

FAVORABLE TOLERABILITY

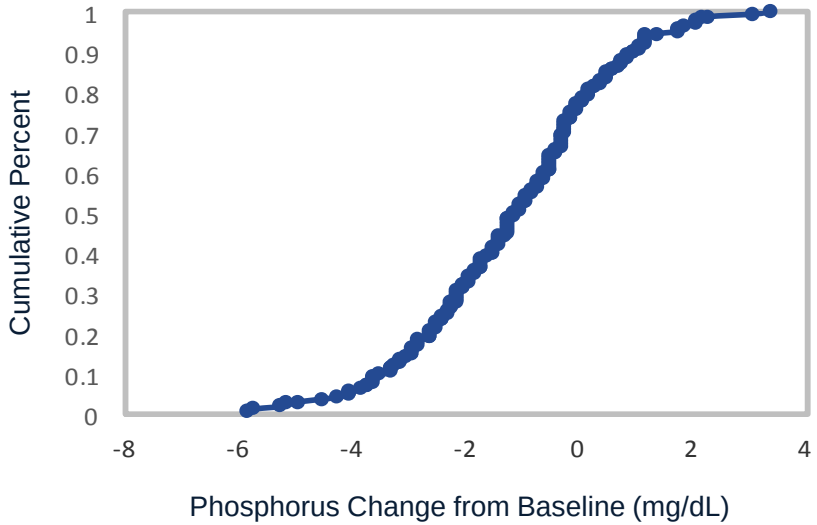
- No discontinuations due to diarrhea in placebo-controlled randomized withdrawal period

*Serum phosphorus level from end of 8-week treatment period to end of 4-week randomized withdrawal period for tenapanor vs placebo in responders

Renagel Package Insert Data[3]
(sevelamer n=81; Calcium Acetate n=83)



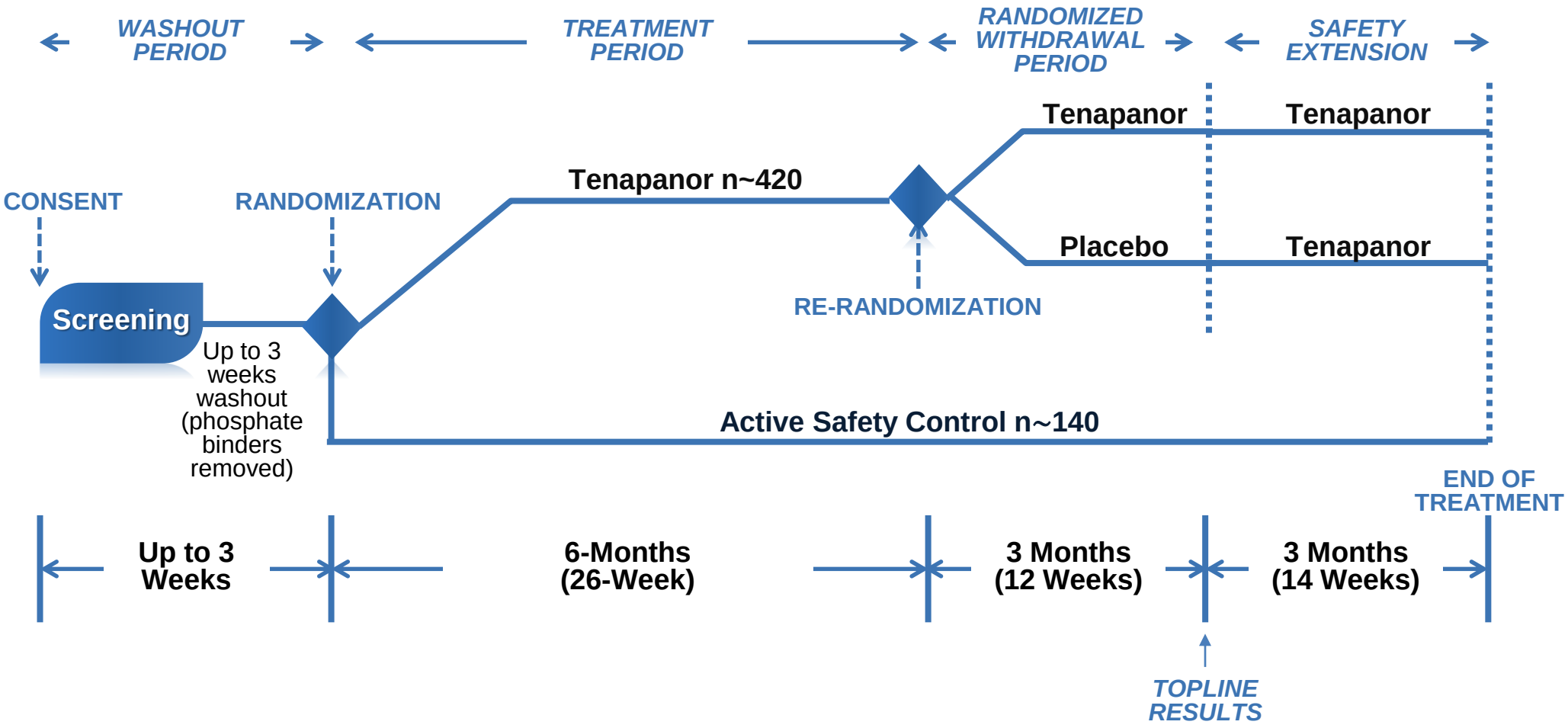
Tenapanor 1st Phase 3 Trial (n=164)[1,3]



1. Tenapanor is an investigational medicine; Phase 3 data reported February 2017
2. 49% (80 of 164) responders (serum phosphorus decrease of ≥ 1.2 mg/dL) in first Phase 3 trial
3. Renagel and tenapanor have not been evaluated in head-to-head studies

Tenapanor Second Phase 3 Registration Study Enrolled Topline Results in 4Q 2019

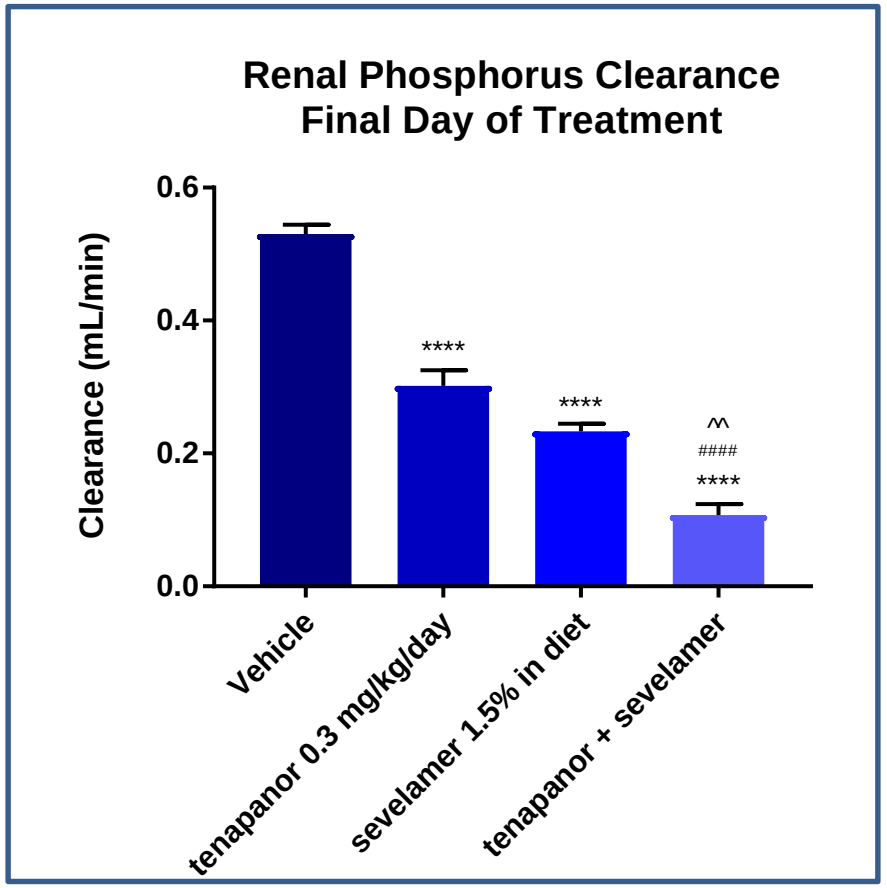
PHREEDOM TRIAL

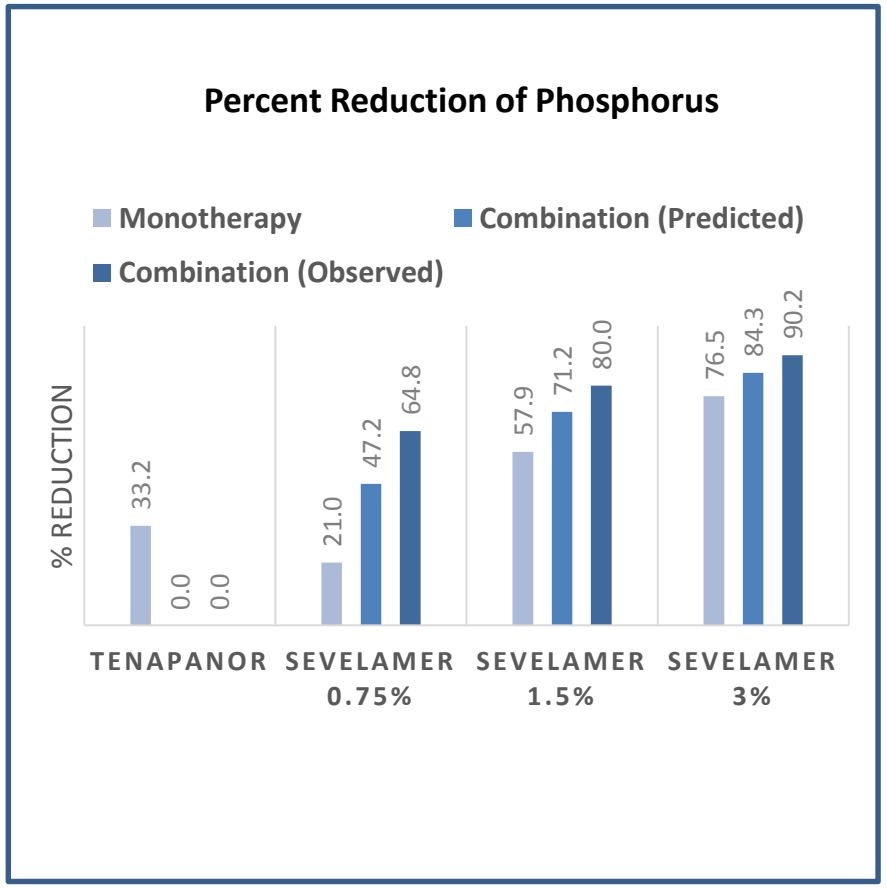


COMBINATION USE WITH BINDERS

Presented at ASN 2018

Tenapanor and sevelamer are synergistic in their reduction of Pi in rats





*Mean ± SEM data shown; One-way ANOVA; N=6/group; **** = p < 0.0001 compared to vehicle; #### = p < 0.0001 compared to tenapanor alone; ^^ = p < 0.05 compared to sevelamer alone*

COMBINATION USE WITH BINDERS

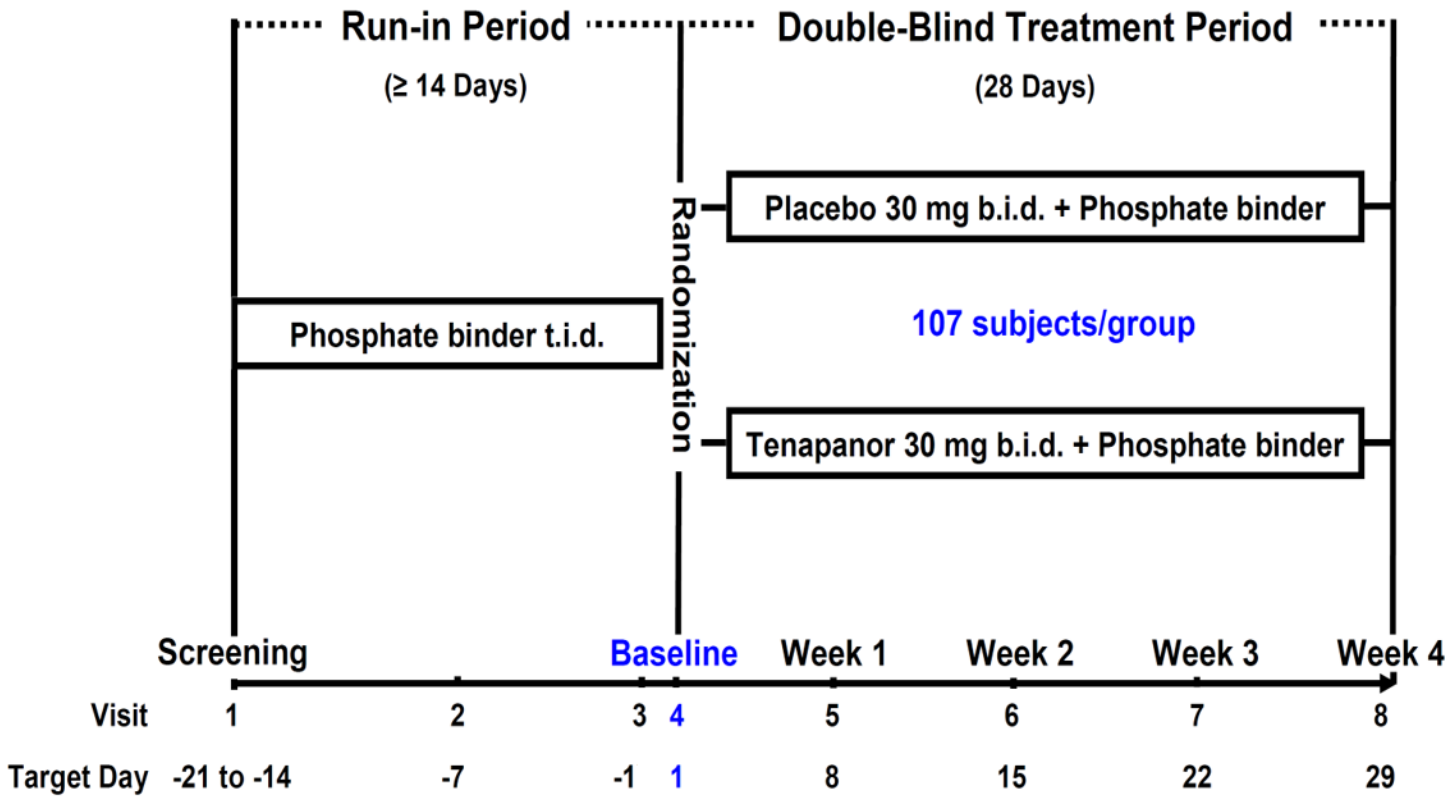
Tenapanor potential differentiation

- Efficacy / adherence & compliance a large issue
  - 65% of patients >4.5mg/dL[1]
- Only 11% of HD patients being treated with binders currently take more than one brand[2] (no efficacy benefit)
  - Manage side effects
  - Manage costs
- Tenapanor's effect is synergistic in rats when added to sevelamer
- Phase 3 combination study underway
- With successful results, tenapanor would be the first and only phosphate lowering therapy to be indicated for use in combination with binders

1 DOPPS Practice Monitor, United States, Serum Phosphorus, most recent, National Sample, Feb 2018 https://www.dopps.org/DPM/Files/phosphmgdl_c_overallTAB.htm
2 RealWorld Dynamix Dialysis 2017; Spherix; Slide 16

TEN-02-202: *AMPLIFY*

Tenapanor as Adjuvant Therapy to Phosphate Binders



Study Design

Randomized, double-blind and placebo controlled

30 mg bid starting dose that can be titrated to 20 mg or 10 mg

Key Inclusion Criteria

- 3 doses of phosphate binders/day, serum phosphorus ≥ 5.5 mg/dL and ≤ 10 mg/dL at screening and Day -1

Primary Endpoint

- Difference in change between tenapanor and placebo of serum phosphate levels from randomization to end of 4-week treatment period

Sample size calculation

- 85% power to detect a treatment difference of 0.5 mg/dL with a common standard deviation of 1.0 mg/dL using a two-sample t-test with a two-sided significance level of α=0.01

BRINGING TENAPANOR TO HP PATIENTS

Clear Path to Commercialization

- Data-driven, KOL-led market
- Specialized U.S. commercial organization targeting nephrologists
- Access outside the U.S. via strategic collaborations

KYOWA KIRIN FOSUN PHARMA 复星医药 Knight

- Highly experienced renal team

$500 – $700M

COMMERCIAL OPPORTUNITY

TENAPANOR IN IBS-C

NDA accepted for review

PDUFA date September 12, 2019

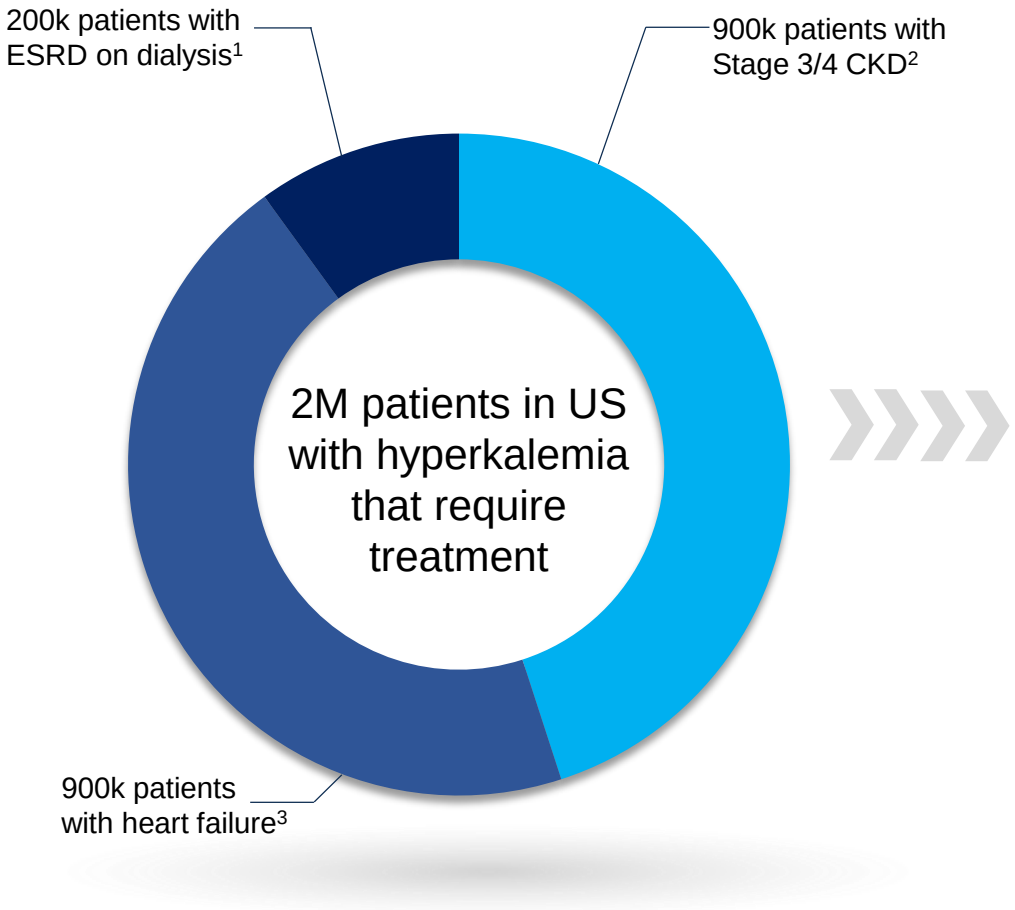
Advancing through strategic collaborations
Ex U.S. development and commercialization partnerships

- China: Fosun Pharma
- Canada: Knight

U.S. - Additional partnerships being evaluated for commercialization opportunities

1. Lovell 2012

SIGNIFICANT HYPERKALEMIA MARKET WAITING TO BE TAPPED



THE POTENTIAL FOR RDX013

- Target Product Profile
  - Greatly improved pill burden
  - Improved efficacy in both acute and chronic settings
  - Exceptional safety
  - Administration alongside lifesaving drugs that can cause hyperkalemia (RAASi's, Entresto, Etc.)
- Build upon the market being created by Lokelma and Veltassa

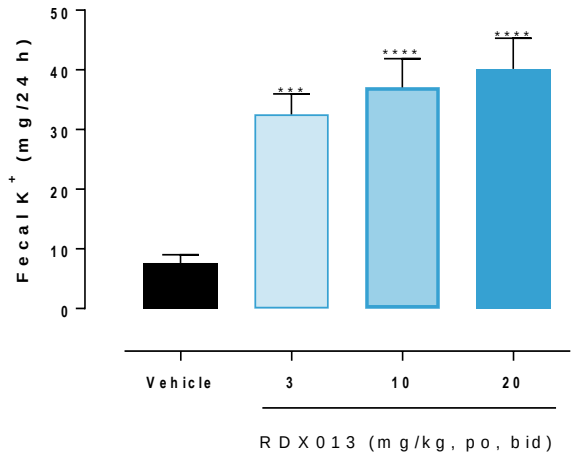
1. Independent Market Research, Spherix Global Insights
2. Einhorn LM, et al. Arch Intern Med. 2009 Jun 22;169(12):1156-62
3. Mozaffarian D, et al. Circulation. 2015 Jan 27;131(4):e29-322

RDX013 PROGRAM
Expanding Our Renal Footprint

RDX013 PROGRAM

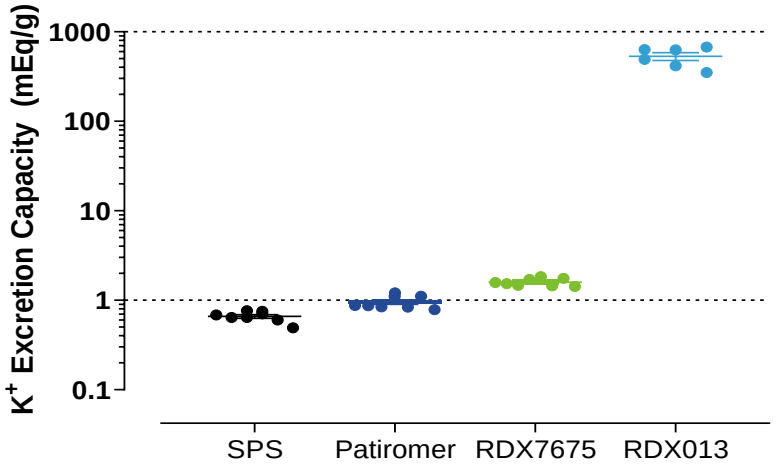
- Novel, oral potassium secretagogue program
- Convenient, small pill dosing
- Increases fecal potassium excretion; reduces serum potassium
- Allows optimal dosing of anti-hypertensives
- ~1000x improved *in vivo* efficiency vs binders

IN VIVO FECAL POTASSIUM EXCRETION



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

~1000x improved *In Vivo* Efficiency vs Binders*



*K+ binding capacity determined in mouse

- First-in-class cardiorenal medicine with a unique and differentiated MOA
- Significant market opportunity in cardiorenal alone: hyperphosphatemia
- Go-to-market approach with specialized U.S.-focused cardiorenal commercial organization
- Optimizing global patient access through strategic collaborations
- Seasoned management with proven track record

Breakthrough Science for **BETTER HEALTH**