



## MANAGEMENT CALL TO DISCUSS PHASE 3 ADPKD STUDY DESIGN

January 3, 2019

# Forward-Looking Statements

This presentation contains certain “forward-looking” statements that are made pursuant to the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. All statements, other than statements of historical or present facts, are forward-looking statements, including statements regarding our future financial condition, business strategy, and plans and objectives of management for future operations. In some cases, you can identify forward-looking statements by terminology such as “believe,” “will,” “may,” “estimate,” “continue,” “aim,” “assume,” “anticipate,” “contemplate,” “model,” “intend,” “target,” “project,” “should,” “plan,” “expect,” “predict,” “could,” “possible,” “seek,” “goal,” “potential,” “hypothesize,” “likely” or the negative of these terms or other similar terms or expressions that concern our expectations, strategy, plans, or intentions. These statements are based on our intentions, beliefs, projections, outlook, analyses, or current expectations using currently available information, are not guarantees of future performance, and involve certain risks and uncertainties. Although we believe that the expectations reflected in these forward-looking statements are reasonable, we cannot assure you that our expectations will prove to be correct. Therefore, actual outcomes and results could materially differ from what is expressed, implied, or forecast in these statements. Any differences could be caused by a number of factors including but not limited to: the success, cost, and timing of our product development activities and clinical trials; our ability to advance our NRF2 activators and other technologies; our ability to obtain and maintain regulatory approval of our product candidates, and limitations and warnings in the label of an approved product candidate; our ability to obtain funding for our operations, including funding necessary to complete further development and commercialization of our product candidates; our plans to research, develop, and commercialize our product candidates; the commercialization of our product candidates, if approved; the rate and degree of market acceptance of our product candidates; the size and growth potential of the markets for our product candidates, and our ability to identify target patient populations and serve those markets, especially for diseases with small patient populations; the success of competing therapies that are or may become available; our expectations regarding our ability to obtain and maintain intellectual property protection for our product candidates; the ability to license additional intellectual property relating to our product candidates and to comply with our existing license agreements; our ability to contract with third-party suppliers and manufacturers and their ability to perform adequately; our ability to attract collaborators with development, regulatory, and commercialization expertise; our ability to attract and retain key scientific or management personnel; our ability to grow our organization and increase the size of our facilities to meet our anticipated growth; the accuracy of our estimates regarding expenses, future revenue, capital requirements, and needs for additional financing; and regulatory developments in the United States and foreign countries.

Additional factors that could cause actual results to differ materially from our expectations can be found in our Securities and Exchange Commission filings. Moreover, we operate in a very competitive and rapidly changing environment. New risk factors emerge from time to time, and it is not possible for our management to predict all risk factors, nor can we assess the effects of all factors on our business or the extent to which any factor, or combination of factors, may cause actual results to differ materially from those contained in, or implied by, any forward-looking statements. All forward-looking statements included in this presentation are expressly qualified in their entirety by these cautionary statements. The forward-looking statements speak only as of the date made and, other than as required by law, we undertake no obligation to publicly update or revise any forward-looking statements, whether as a result of new information, future events, or otherwise.

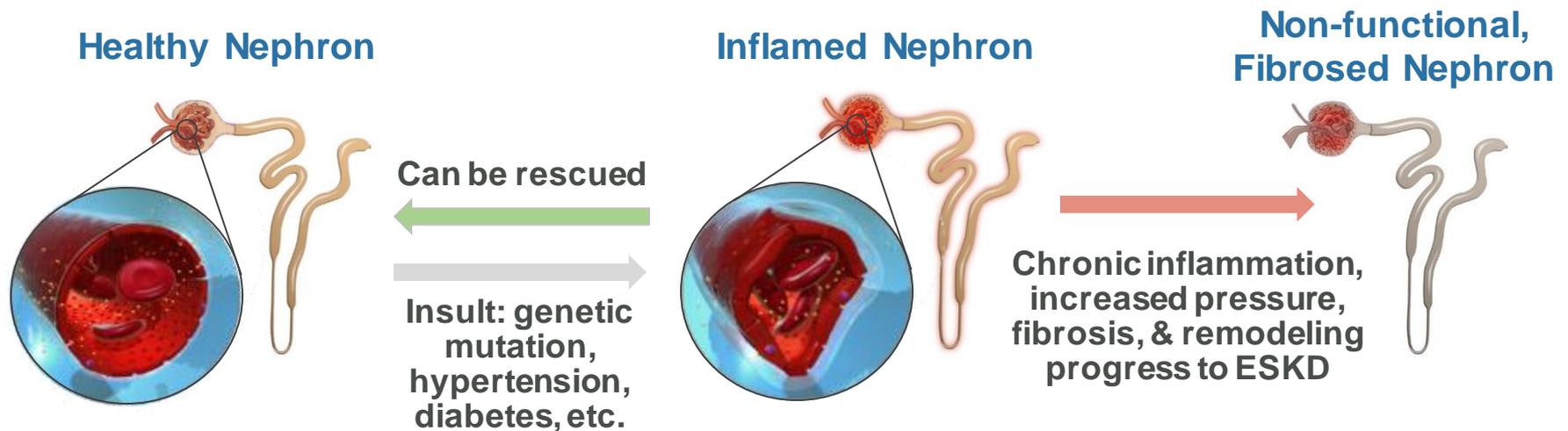
# A New Paradigm for Treating Chronic Kidney Disease



Bardoxolone (Bard) increases kidney function (GFR) by resolving inflammation

In preclinical models, Bard:

- Acutely increases glomerular filtration surface area<sup>1</sup>
- Reduces fibrosis and remodeling long-term, leading to structural improvement of the kidney<sup>2</sup>



# Overview of Autosomal Dominant Polycystic Kidney Disease (ADPKD)



ADPKD is the most common hereditary form of chronic kidney disease (CKD)

Cysts formation blocks filtration and causes inflammation and fibrosis

Mitochondrial dysfunction, impaired fatty acid oxidation, and oxidative stress are hallmarks of ADPKD

Approximately 116,000 diagnosed ADPKD patients in the US<sup>1</sup>

Approximately 50% of ADPKD patients progress to end-stage kidney disease (ESKD) by 60 years of age<sup>2</sup>

FDA recently approved tolvaptan for the treatment of ADPKD based on placebo-corrected retained estimated glomerular filtration rate (eGFR) of 1.27 ml/min<sup>3,4</sup>



# PHOENIX ADPKD Phase 2 Results: Significant eGFR Improvement in Patients Actively Declining on SOC



Enrolled 31 patients with ADPKD and treated for 12 weeks

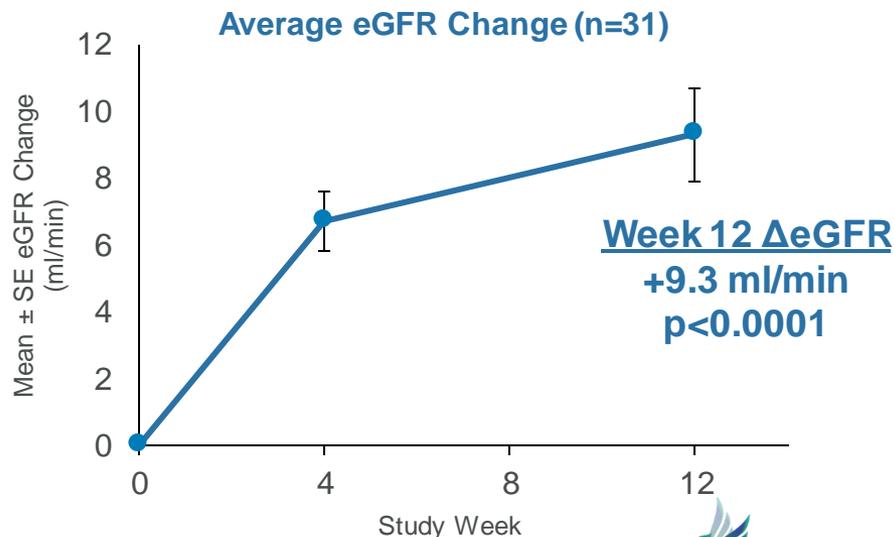
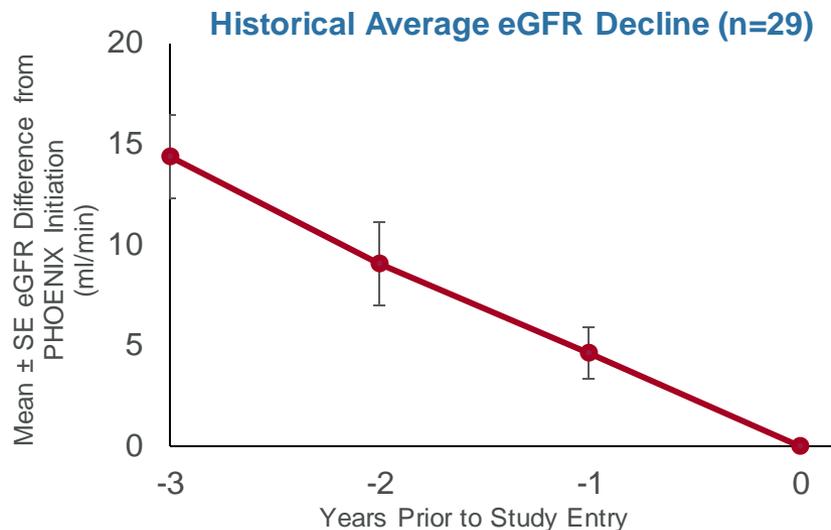
Baseline characteristics:

- Mean age of 47 years old
- Mean eGFR of 48 ml/min
- 81% of patients were on ACEi or ARB
- Representative of ADPKD population

Average annual eGFR loss prior to study of ~4.8 ml/min

Large, statistically significant increase in eGFR after 12 weeks of treatment

- High response rate with all but one patient showing improvement
- No change in urinary albumin excretion





# Available Data Support 300 Patient ADPKD Study

Observed significant 9.3 ml/min on-treatment eGFR change vs. baseline at Week 12

Prior one-year duration trials demonstrated:

- Correlation between Week 12 and Week 48 eGFR change
- Significant retained eGFR benefit after one year of treatment and four-week washout

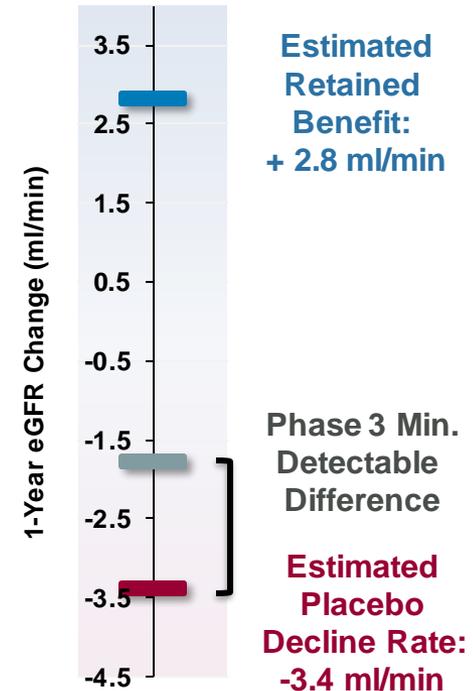
Phase 3 modeling<sup>1</sup> assumes:

- Phase 2 retained eGFR benefit of 9.3 ml/min is sustained through Week 48
- 30% (2.8 ml/min) of on-treatment eGFR change is retained after withdrawal
- Placebo loss of 3.4 ml/min based on several recently published ADPKD trials

Potential placebo-corrected retained benefit of 6.2 ml/min

At 300 patients, the Phase 3 is powered to detect a placebo-corrected retained benefit of 1.6 ml/min

## FALCON Phase 3 Modeled Retained eGFR



# Completed End-of-Phase 2 Interaction with FDA During 4Q 2018



Agreed to same eGFR-based retained benefit approval endpoints for ADPKD as previously recommended for Alport syndrome

- One-year, placebo-corrected retained eGFR data could support accelerated approval
- Two-year, placebo-corrected retained eGFR data could support full approval

FDA again confirmed 4-week withdrawal period is appropriate for Bard

- Bard's maximum pharmacodynamic effect on eGFR occurs in two to four weeks
- Bard reaches sub-therapeutic concentrations within 4 weeks after withdrawal of drug
- After withdrawal of drug, retained eGFR stabilizes by week 4 in T2D CKD patients

FDA indicated that the sample size for FALCON will be sufficient to assess safety of Bard

- Large safety database with over 2,000 people having been exposed to Bard
- Bard well-tolerated without major safety signals in patient populations under study

Upon review of all preclinical toxicology and clinical pharmacology studies, FDA did not recommend any additional studies

Consistent guidance from FDA on endpoints provides confidence that CARDINAL and FALCON trial designs will support NDA submission and approval if successful



# FALCON is an International Phase 3 Trial of Bard for the Treatment of ADPKD



Pivotal Phase 3 will enroll 300 patients

- Randomized, double-blind, placebo-controlled international study
- Two-year total treatment duration
- Planning to enroll patients across approximately 60 sites in the US, Europe, and Australia

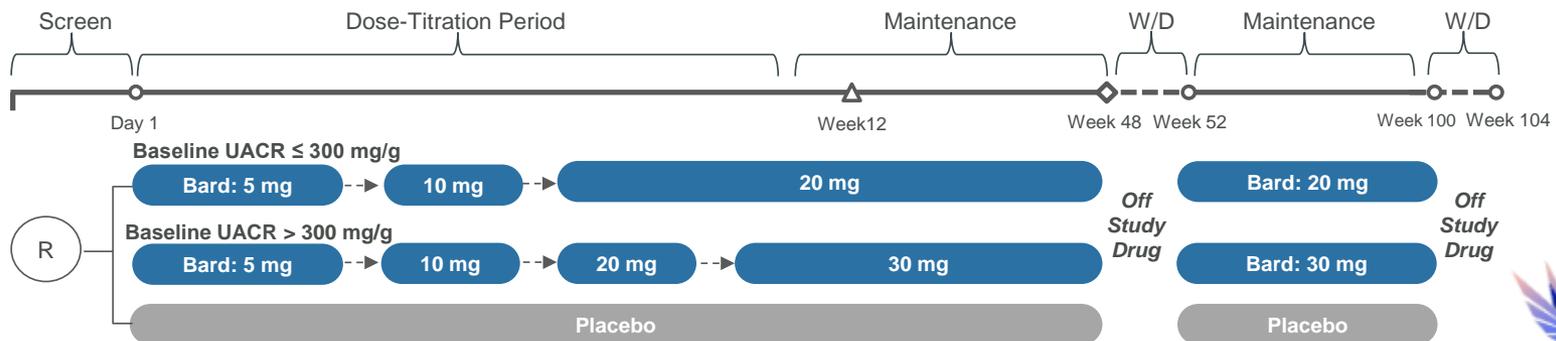
Broad eligibility criteria

- eGFR 30-90 ml/min
- Age 18-70 years old
- Tolvaptan use is allowed but not required

Retained eGFR benefit endpoints support approval

- Potential accelerated approval on retained eGFR after one year of treatment and drug withdrawal
- Potential full approval on retained eGFR after two years of treatment and drug withdrawal
- Conservatively powered to detect improvement in retained eGFR

Trial initiation expected mid-2019





# Recent CKD Highlights and Key Upcoming Milestones

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## **Bard in Alport syndrome**

Pivotal Phase 3 fully enrolled with data available in 2H19

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## **Bard in rare forms of CKD**

12-week data from ADPKD, IgAN, and T1D CKD already reported  
12-week data from FSGS cohort available in 1H19

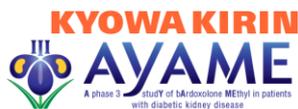
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## **Bard in ADPKD**

Pivotal Phase 3 trial design finalized  
Initiate enrollment mid-2019

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## **Partner Program: Bard in diabetic CKD**

Phase 3 AYAME trial underway, data available in 1H22  
Sponsored by KHK, Reata's licensee in Asia

## Q&A