



# Corporate Presentation April 2018

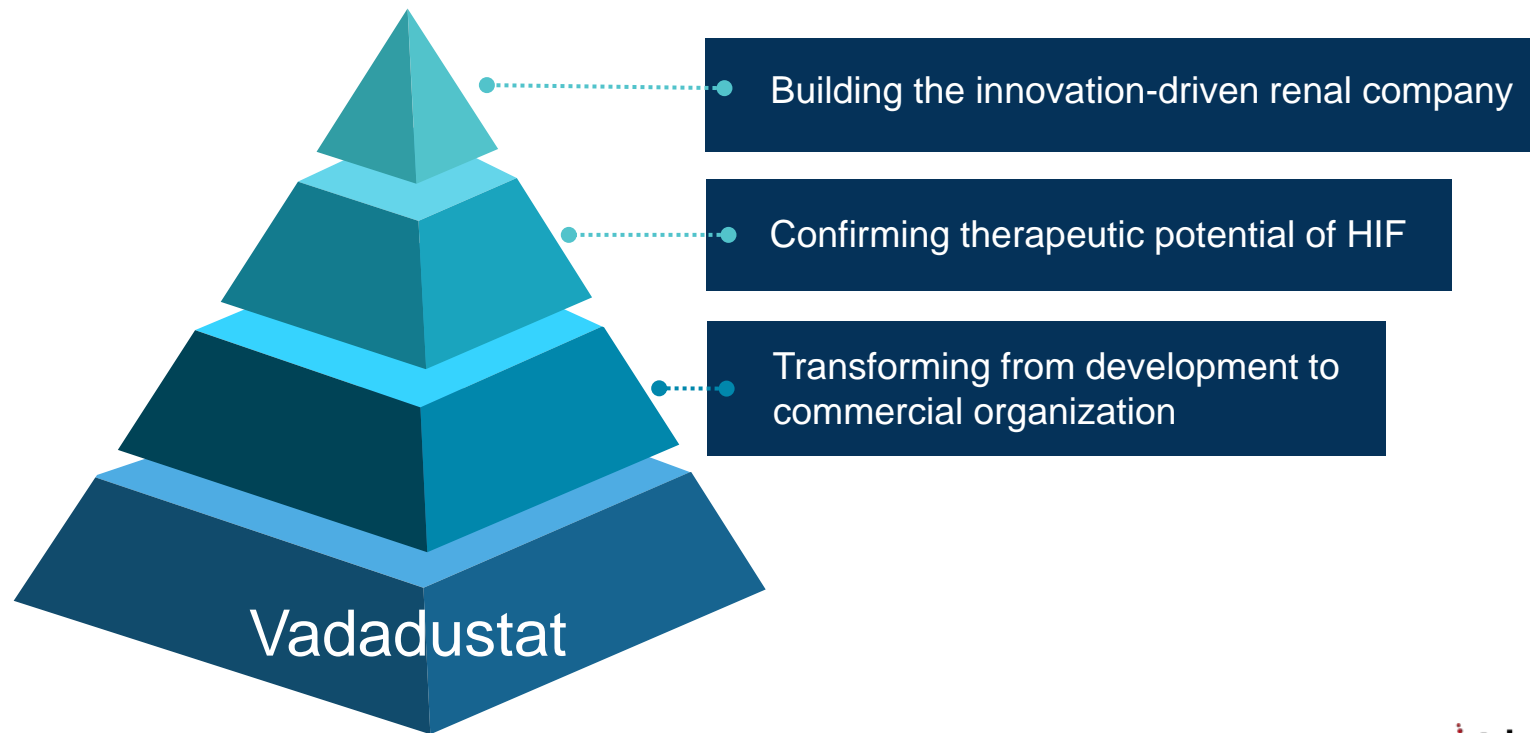
# Forward-Looking Statements

Statements in this presentation regarding Akebia's strategy, plans, prospects, expectations, beliefs, intentions or goals are forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including but not limited to statements regarding the expected period of time our cash resources and collaboration funding will fund our current operating plan; our strategy and our vision; becoming a commercial organization, our commercial readiness and the potential for rapid adoption and/or accelerated uptake of our product candidates, if approved, following launch; our readiness and ability to launch our product candidates, if approved; our potential to realize value following launch of our product candidates; our opportunities to create value; the potential of the HIF pathway; the rate and timing of enrollment, including full enrollment, of our clinical trials; the target enrollments of our clinical trials; the assessments and evaluations we expect from our clinical programs; the timing, availability and presentation of clinical trial data and results; the potential to grow our pipeline and our HIF portfolio, including by leveraging our core capabilities; the potential to accelerate the shift to an all oral treatment paradigm; the potential to build the HIF portfolio of choice; our upcoming milestones and the targeted timing thereof; the execution of our global Phase 3 program for vadadustat; the targeted timing of an IND submission of AKB-5169; replacing the former FO<sub>2</sub>RWARD and the former TRILO<sub>2</sub>GY with new study designs; the designs of our clinical trials; potential regarding Latin America; the timing of initiation of our clinical trials; and the potential of FO<sub>2</sub>RWARD and TRILO<sub>2</sub>GY to generate data to inform switching. The terms "assessing," "accelerate," "build," "confirm," "design," "driven," "estimate," "expect," "expand," "evaluating," "growth," "improve," "leverage," "milestone," "opportunity," "potential," "promise," "readiness," "seek," "strategy," "target," "transform," "upcoming," "vision" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Each forward-looking statement is subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statement, including the rate of enrollment in clinical studies of vadadustat; the risk that clinical trials may not be successful; the risk that existing preclinical and clinical data may not be predictive of the results of ongoing or later clinical trials; manufacturing risks; the quality and manner of the data that will result from clinical studies of vadadustat; the actual funding required to develop and commercialize Akebia's product candidates and operate the company, and the actual expenses associated therewith; the actual costs incurred in the clinical studies of vadadustat and the availability of financing to cover such costs; the risk that clinical studies need to be discontinued for any reason, including for safety, tolerability, enrollment, manufacturing or economic reasons; early termination of any of Akebia's collaborations; Akebia's and its collaborators' ability to satisfy their obligations under Akebia's collaboration agreements; the timing and content of decisions made by regulatory authorities; the timing of any additional studies initiated for vadadustat; the actual time it takes to initiate and complete research and clinical studies; the success of competitors in developing product candidates for diseases for which Akebia is currently developing its product candidates; the scope, timing, and outcome of any ongoing legal proceedings; changes in the economic and financial conditions of the businesses of Akebia and its partners; and Akebia's ability to obtain, maintain and enforce patent and other intellectual property protection for vadadustat and its other product candidates. Other risks and uncertainties include those identified under the heading "Risk Factors" in Akebia's Annual Report on Form 10-K for the year ended December 31, 2017, filed with the SEC March 12, 2018, and other filings that Akebia may make with the SEC in the future. These forward-looking statements (except as otherwise noted) speak only as of the date of this presentation, and Akebia does not undertake, and specifically disclaims, any obligation to update any forward-looking statements contained in this presentation. Vadadustat is an investigational drug and has not yet been approved by the U.S. Food and Drug Administration (FDA) or any regulatory authority.

# Vision

Build the Innovation-Driven, Renal Company,  
while Confirming the Therapeutic Value of the  
Hypoxia Inducible Factor (HIF) Pathway

# Vadadustat Is the Foundation of Our Vision



# Execution and Transformation



## Retained Significant Value While Securing Significant Program Financing

- Otsuka U.S.
- Otsuka E.U.
- Mitsubishi Tanabe
- Vifor Pharma



## Commercial Readiness and Launch Acceleration

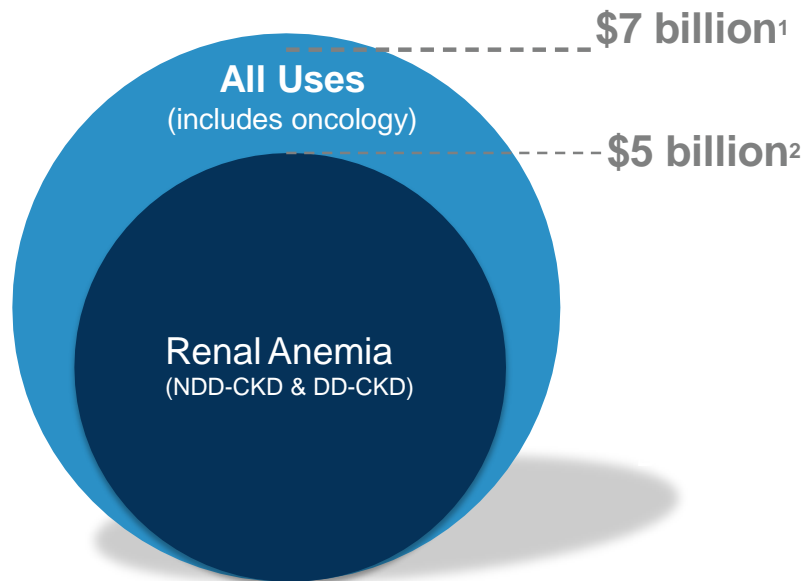
- Otsuka U.S.
- Vifor Pharma
- Strong intellectual property portfolio



## HIF Pipeline Development

- Johnson & Johnson AKB-5169 and library of well-characterized compounds

# Global ESA Market Remains Large



Strong CKD prevalence increase  
observed in Stages 3-5<sup>3</sup>

Greater ESA volume driven by  
hyporesponders<sup>4</sup>

Low treatment rate in non-dialysis<sup>5</sup>

<sup>1</sup> 2016 WW sales of ESA; EvaluatePharma® (December 2017)

<sup>2</sup> 2016 ESA sales in G7 countries in dialysis and non-dialysis; Decision Resources Group® Chronic Kidney Disease – Disease Landscape & Forecast 2016

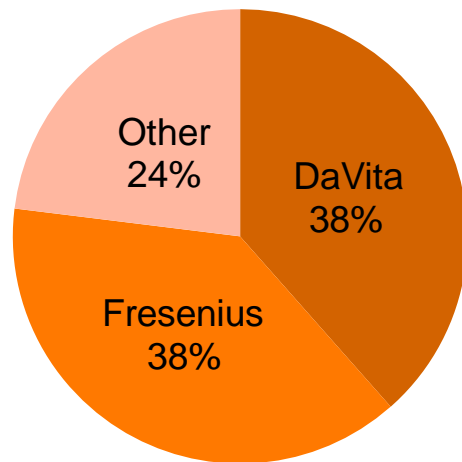
<sup>3</sup> United States Renal Data Systems, 2017 USRDS Annual Report, Vol. 1 – CKD in the United States, Figure 1.1

<sup>4</sup> Lou et al, Spectrum and Burden of Erythropoiesis-Stimulating Agent Hyporesponsiveness Among Contemporary Hemodialysis Patients, *Am J Kidney Dis.* 2016;68(5):763-771

<sup>5</sup> Company estimates and Decision Resources Group® ChartTrends Renal Anemia in CKD-ND US 2014

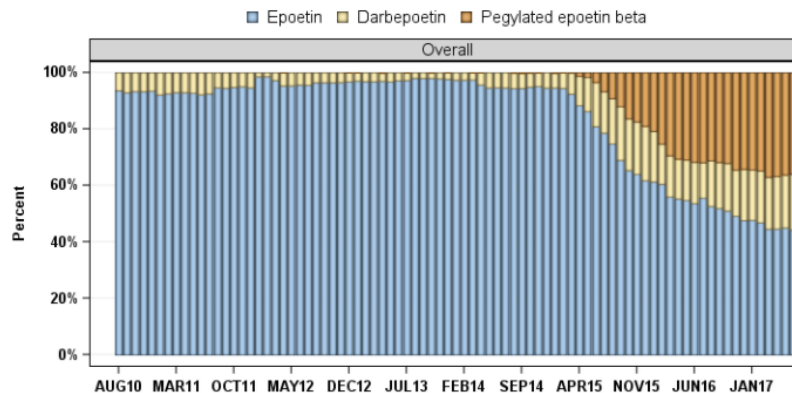
# Potential for Rapid Adoption Driven by Access to Large Dialysis Organizations and Their Influence on Treatment Protocols

**US Dialysis Market (2016)<sup>1,2</sup>**



Mircera uptake illustrates opportunity for rapid adoption following protocol update<sup>3</sup>

**ESA use, by type**  
National sample



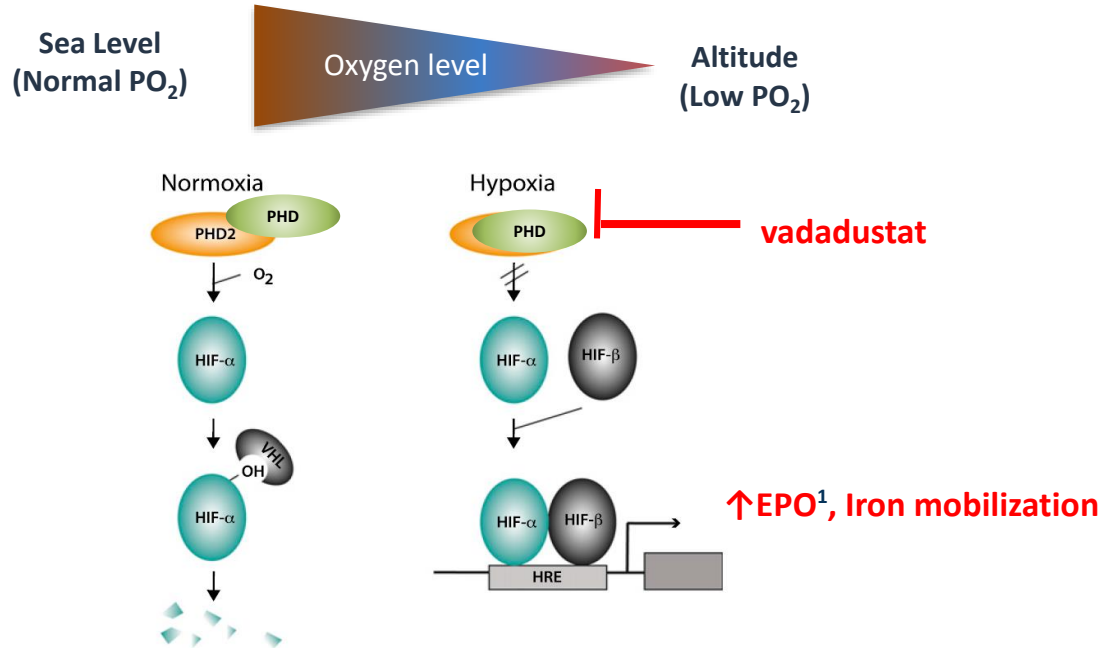
Values for each month reflect prescription among ESA-treated patients  
Facility sample transitioned from DOPPS 4 to 5 in Jan-Apr 2012 (see "Study Sample and Methods").  
Facility sample transitioned from DOPPS 5 to 6 in Mar-Jul 2015 (see "Study Sample and Methods").  
Source: US-DOPPS Practice Monitor, August 2017; <http://www.dopps.org/DPM>

<sup>1</sup> Fresenius and DaVita reported dialysis patients in the US according to 2016 Annual Reports

<sup>2</sup> USRDS 2017 Annual Data Report; ESRD Prevalence in the US

<sup>3</sup> DOPPS Practice Monitor (March 2018); Roche Investor update of license agreement with Galenica for commercialization of Mircera on May 2015

# Activation of HIF: Mechanism of Action Designed to Mimic Physiologic Effect of Altitude



<sup>1</sup>EPO = Erythropoietin

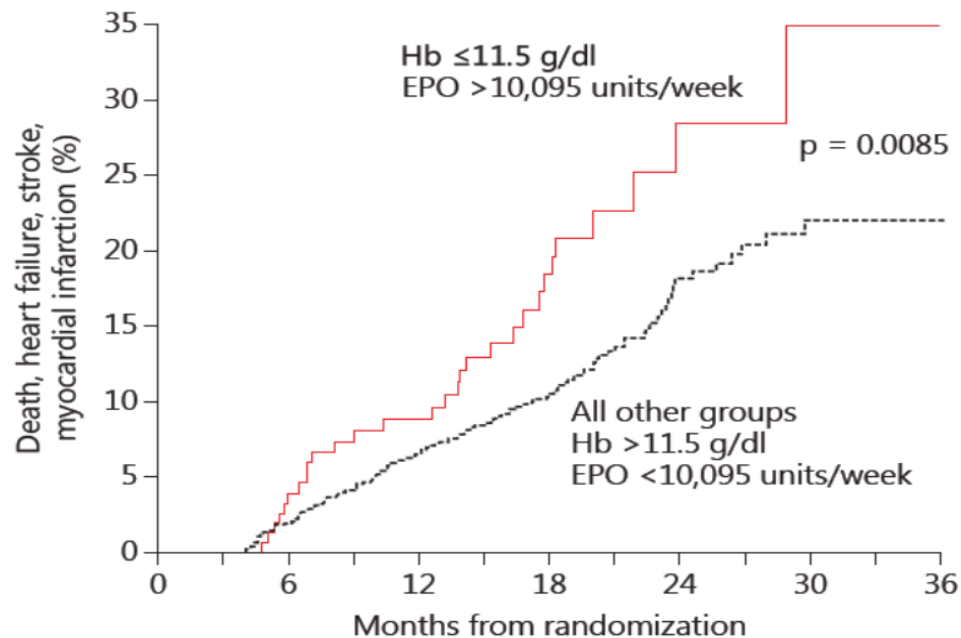
Adapted from Bighmam A. and Lee F. *Genes Dev* 2014;28:2189–2204



# High EPO Levels Associated with Increased Cardiovascular Risks

## Kaplan-Meier Survival Curves<sup>1</sup>

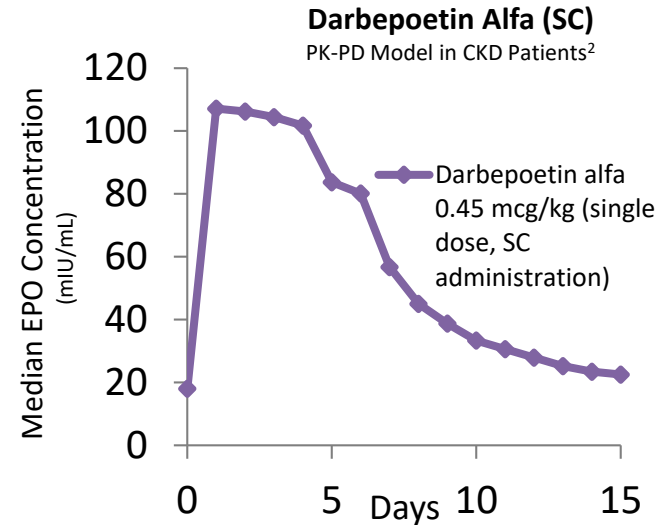
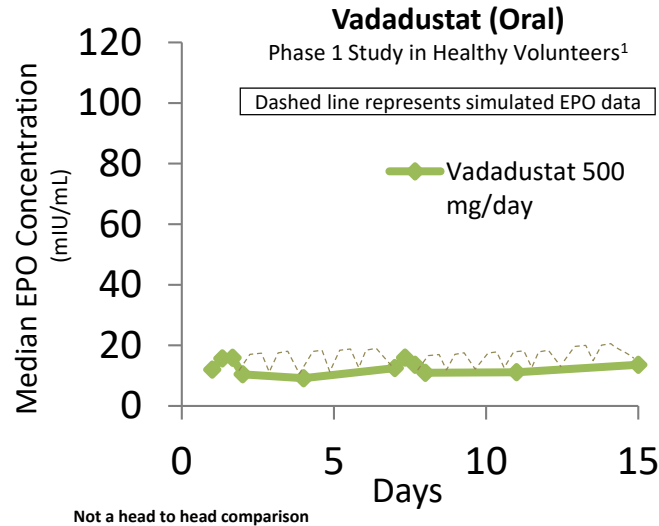
Death, Heart Failure, Stroke, Myocardial Infarction (%)



<sup>1</sup> McCullough P.A., et al. Am J Nephrol 2013;37:549-558 (DOI:10.1159/000351175);  
Permission granted by S. Karger AG, Basel.

# Vadadustat Avoided Supra-Physiological EPO Levels

## EPO vs. Time by Study



<sup>1</sup> Akebia Therapeutics, Inc. Data on File (2010). Data from Phase 1 study in healthy volunteers with vadadustat once daily dosing. Pre-dose EPO concentrations were evaluated on Days 1, 4, 7, 11, 15 and 22. Post-dose data to assess acute rise in EPO following vadadustat dosing was only completed on Day 1 and Day 7 (8 and 16 hours post-dose). Dashed line represents estimated EPO levels based on post-dose data from Day 1 and Day 7.

<sup>2</sup> Doshi S et al. Journal of Clinical Pharmacology, 2010;50:755-90S. Original figure redrawn to depict darbepoetin alfa serum concentration (ng/mL/(mcg/kg)) converted to mIU/mL. Data from 6 clinical studies conducted with extensive PK sampling in CKD patients following subcutaneous (SC) administration of a single dose or first dose of a monthly dosing regimen ranging from 0.4-0.6mcg/kg, dose normalized to 0.45 mcg/kg.

# Randomized, Open-Label, Active-Controlled, Non-Inferiority Phase 3 Cardiovascular Outcomes Studies

Non-dialysis dependent (NDD)

N = 3700

PRO<sub>2</sub>TECT

CORRECTION

Not ESA Treated

Vadadustat vs  
Darbepoetin Alfa

PRO<sub>2</sub>TECT

CONVERSION

ESA Treated

Vadadustat vs  
Darbepoetin Alfa

Dialysis dependent (DD)

N = 3200

INN<sub>2</sub>VATE

CORRECTION  
CONVERSION

New-Onset Dialysis\*

Vadadustat vs  
Darbepoetin Alfa

INN<sub>2</sub>VATE

CONVERSION

ESA Treated

Vadadustat vs  
Darbepoetin Alfa

**Primary Efficacy Endpoint: Change in hemoglobin (Hb) from baseline**  
**Primary Safety Endpoint: Major Adverse Cardiovascular Events (MACE)**

Full Enrollment Targeted by End of 2018

\* ≤16 weeks of dialysis treatment, with or without prior ESA treatment

# Global Clinical Program Assessments

## **Demonstrate effect on Hgb & Iron**

- Assessing Hemoglobin in the target range over time
- RBC transfusions and I.V. iron requirements
- ESA rescue

## **Dosing and PK Profile**

- Dosing regimens (QD, TIW)
- Evaluating range of vadadustat doses

## **Characterize Safety Profile**

- MACE rate
- Thromboembolic events
- Heart failure
- Drug-drug interactions

## **Other Assessments**

- Number of hospitalizations
- Rate of CKD progression
- Biomarkers

# Additional Vadadustat Global Program Studies in Dialysis

## FO<sub>2</sub>RWARD

### Phase 2 Study with Global Commercial Focus

- New study replaces former FO<sub>2</sub>RWARD study
- Design includes broader dialysis population in addition to hyporesponders
- Includes larger sample size
- Includes once-daily and 3X-weekly dosing
- Designed to generate data to inform ESA-switching protocols
- Expected to initiate in Q2 2018
- Top-line results expected late 2018/early 2019

## TRILO<sub>2</sub>GY

### Three Times Weekly Phase 3 Study

- New study replaces former TRILO<sub>2</sub>GY study
- Design includes once-daily and 3X-weekly dosing and an ESA control
- Includes larger sample size
- Designed to generate data to inform switching from Epogen®, Aranesp® and Mircera®
- Expected to initiate in late 2018/early 2019
- Top-line results expected in early 2020

# Japan Phase 3 Program Is Underway

## Ongoing Studies

- NDD- and DD-CKD programs in Japan initiated
- Data read-out expected 2019
- Mitsubishi Tanabe Pharma Corp (MTPC) fully responsible for Phase 3 development program in Japan
- Akebia provided MTPC with option to access global Phase 3 vadadustat data for payments up to \$25M

# Collaborators' Commercial Infrastructure and Portfolio in Renal Support Launch of Vadadustat

## 50-50 Profit Split in U.S. (Otsuka)

- R&D cost sharing
- Access to Otsuka strong infrastructure (1,000 reps)

## Strong Capabilities in E.U. & Japan

- Strong renal portfolio fit for Mitsubishi (Japan) & Otsuka (E.U.)
- Strong market access and KOL relationships
- Established field force in key markets

## Potential to Realize Additional Value from International Markets

- Strong R&D and commercial presence in China (Otsuka)
- Commercial presence in all major markets
- Optionality for expansion or further partnering in LatAm



Mitsubishi Tanabe



Otsuka



# Vifor Pharma Provides Access to Significant Segment of the U.S. Dialysis Market with Potential for Accelerated Uptake Following Approval

## Applicable upon Inclusion in the Bundle

- HIF class in bundle as base case. If not, Akebia retains all rights
- Strategic relationship between Vifor-Fresenius
- Vadadustat is the only HIF that Vifor can supply to Fresenius for anemia due to CKD

## Potential for Rapid Commercial Uptake

- Optimal setting for pilot studies and protocol optimization
- Facilitate adoption in appropriate non-dialysis patients following approval

## Strong Economics

- Equity investment at a premium
- Milestone following approval
- Majority of profit on sales retained by Akebia and Otsuka





# What's Next? Grow Late Stage Pipeline and Expand HIF Portfolio

## Build Unique Position in Promising HIF Areas

- GI inflammation promising area for new HIF-based standard of care
- Opportunities to expand portfolio, similar to J&J transaction

## Leverage Core Capabilities

- Opportunities to expand renal pipeline as vadadustat Phase 3 program progresses
- Seek capability-enhancing opportunities

## The Innovative Renal Company Leveraging HIF Pathway

- Accelerate shift to improved all oral treatment paradigm
- Build HIF portfolio of choice as clinical and regulatory validation occurs

# Strong Foundations Are Established

Create strong value proposition



Secure significant program financing



Establish strategic partnerships for global launch



Access to significant segment of U.S. dialysis market



*Existing cash resources and cost-share funding from collaborators expected to fund current operating plan into Q1 2020*

# Upcoming Milestones

PRE-CLINICAL

PHASE 1

PHASE 2

PHASE 3

TARGETED TIMING

## ANEMIA IN CKD

### VADADUSTAT Program

#### NDD-CKD

PRO<sub>2</sub>TCT Correction

PRO<sub>2</sub>TCT Conversion

#### DD-CKD

INNO<sub>2</sub>VATE Correction/Conversion

INNO<sub>2</sub>VATE Conversion

FO<sub>2</sub>RWARD

TRILO<sub>2</sub>GY

Full enrollment: **2018**  
Top-line results: **2019\***

Top-line results: **Late 2018/Early 2019**

Top-line results: **Early 2020**

Japan NDD-CKD Correction/Conversion

Japan PD-CKD Correction/Conversion

Japan HD-CKD Correction

Japan HD-CKD Conversion

Read-out: **2019**

## INFLAMMATORY BOWEL DISEASE

AKB-5169

IND submission: **2018**

## VARIOUS POTENTIAL THERAPEUTIC TARGETS

HIF Portfolio

Research: **Ongoing**

\*Subject to the accrual of MACE events

Note: NDD-CKD denotes non-dialysis-dependent chronic kidney disease and DD-CKD denotes dialysis-dependent chronic kidney disease.





THANK YOU