



NASDAQ: UNCY

# Novel Treatments for Kidney Diseases

Company Presentation

February 2022

# 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, future revenues, projected costs, prospects, business strategy, and plans and objectives of management for future operations, including our plans to submit for regulatory filings. In some cases, you can identify forward-looking statements by terminology such as “believe,” “will,” “may,” “might,” “estimate,” “continue,” “anticipate,” “intend,” “target,” “project,” “model,” “should,” “would,” “plan,” “expect,” “predict,” “could,” “seek,” “goal,” “potential,” 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, and 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 forecasted in these statements. Any differences could be caused by a number of factors including but not limited to: our expectations regarding the timing, costs, conduct, and outcome of our clinical trials, including statements regarding the timing of the initiation and availability of data from such trials; the timing and likelihood of regulatory filings and approvals for our product candidates; whether regulatory authorities determine that additional trials or data are necessary in order to obtain approval; 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; our expectations regarding the potential market size and the size of the patient populations for our product candidates, if approved for commercial use, and the potential market opportunities for commercializing our product candidates; 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 maintain and establish relationships with third parties, such as contract research organizations, suppliers, and distributors; our ability to maintain and establish 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; our expectations related to the use of our available cash; our ability to develop, acquire, and advance product candidates into, and successfully complete, clinical trials; the initiation, timing, progress, and results of future preclinical studies and developments and projections relating to our competitors and our industry.

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.

## **Addressing important patient needs and large markets within kidney disease**

- Hyperphosphatemia patients live with extreme treatment burden
- No medicines approved for acute kidney injury (AKI)

## **Product candidates utilizing proven mechanisms of action**

- Renazorb: Phosphate binder for the treatment of hyperphosphatemia in patients with chronic kidney disease (CKD);
- UNI-494: novel pro-drug of nicorandil for the treatment of AKI and CKD with potentially improved dosing and improved side effects

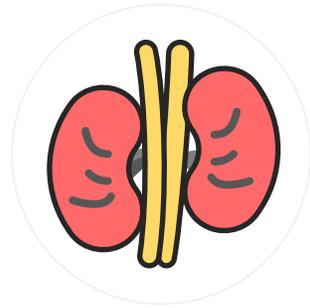
## **Significantly De-risked Regulatory Pathway for Renazorb**

- Type C meeting with the FDA in December 2021 provides clear guidance to file NDA
- Pursuing a 505(b)(2) regulatory pathway for U.S. approval
- Single required healthy volunteer clinical study to be started shortly with the FDA alignment

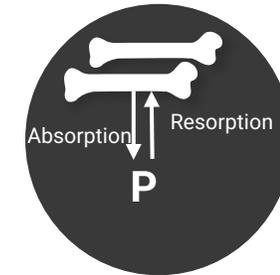
**Cash runway to file Renazorb NDA and to initiate clinical trials for UNI-494 until early 2023**

# Chronic Kidney Disease (CKD) and Hyperphosphatemia: Current Treatments

## Chronic Kidney Disease (CKD)



## Hyperphosphatemia

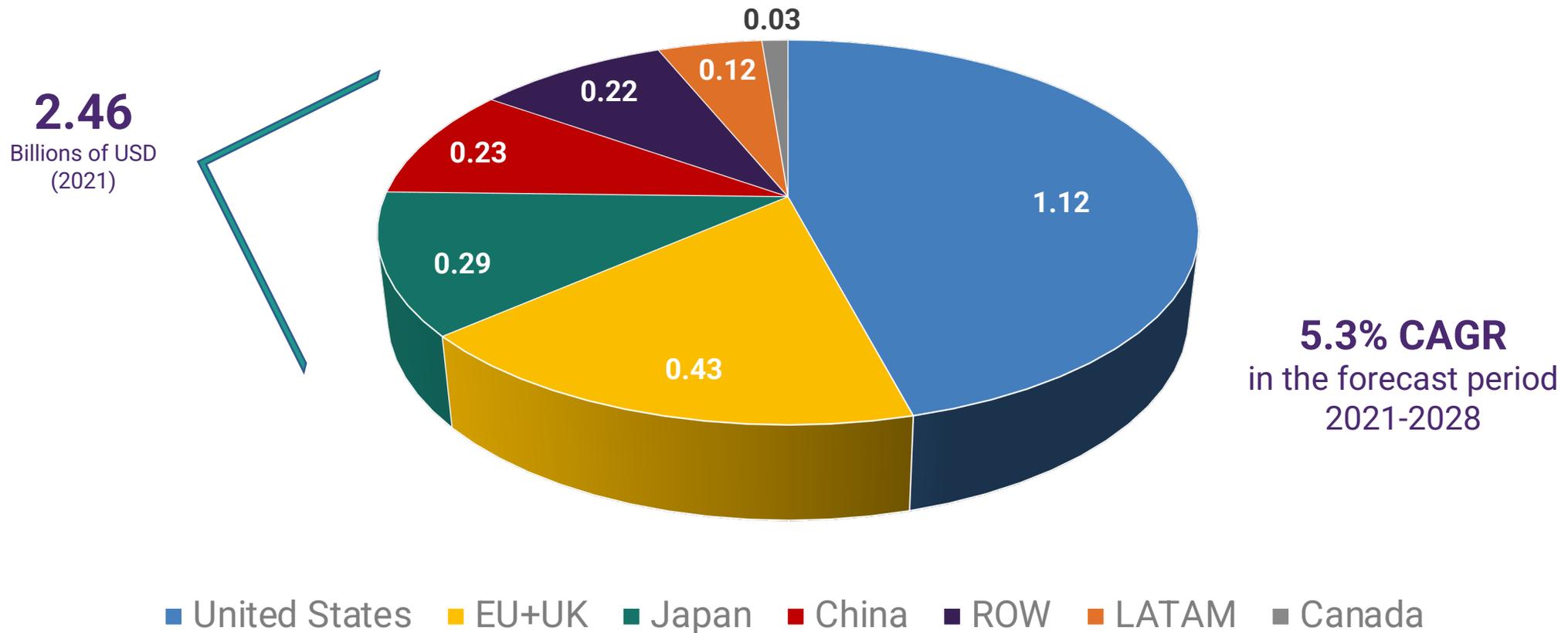


- Gradual loss of kidney function that can worsen over time leading to lasting damage
- CKD stages range from 1 to 5
- Stage 5 is End Stage Renal Disease (ESRD)
- **In CKD, hyperphosphatemia is caused by a chronic dysregulation of phosphates as a result of progressive kidney damage**

- Electrolyte disorder in which untreated elevated phosphate levels in the blood lead to cardiovascular complications and vascular calcification
- Occurs in at least **80% of patients with Stage 5 CKD on dialysis\*** (>500,000 patients in the US)

# Worldwide Hyperphosphatemia Market Opportunity

Unicycive owns worldwide rights to Renazorb



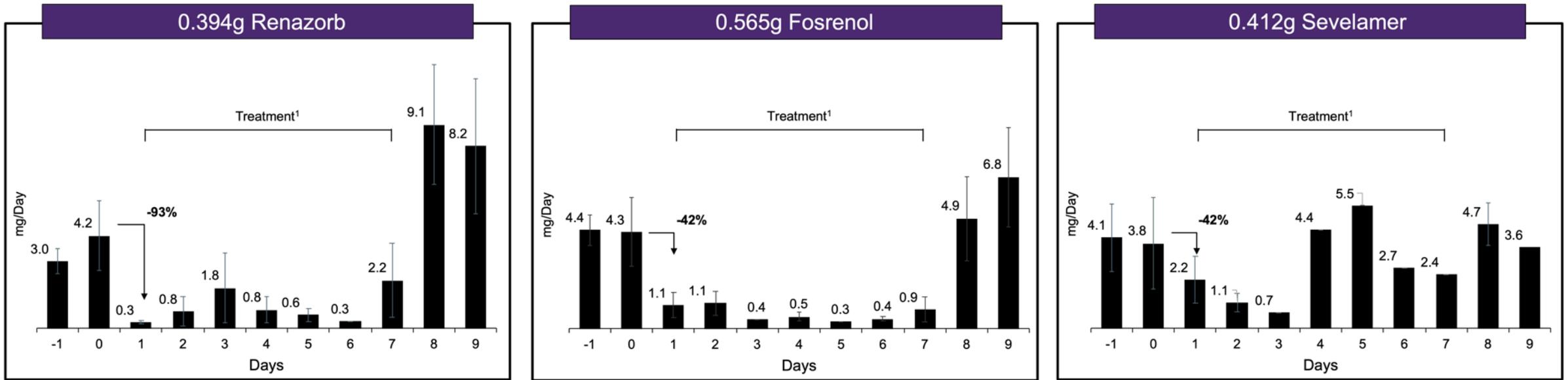
# Renazorb Pharmaceutical Properties

- ✓ Renazorb (lanthanum dioxycarbonate nanoparticles) binds to phosphate and forms an insoluble lanthanum phosphate complex, which is then excreted via the feces
- ✓ Results in reduction of serum phosphate levels
- ✓ Proprietary nano-particle technology
  - **Smaller tablets**
  - **Convenient formulation that is swallowed with water –not chewed**
- ✓ Reduced pill burden = potential for improved patient adherence



# Renazorb Demonstrates Equivalent or Better Decrease in Urine Phosphate Excretion vs. Fosrenol and Sevelamer

Mean Urine Phosphate ( $\pm$ SE) Excretion per Day – In Vivo Preclinical Study



<sup>1</sup> Urine tests that reflect treatment of medication

# Phase 1 Clinical Trial: Renazorb was Well-Tolerated with Efficacy Similar to Existing Phosphate Binders



## **Study Design:**

Open label, dose ranging study (evaluated 4 doses : 1500, 3000, 4500 and 6000 mg/day ), in N=32 healthy volunteers



## **Primary endpoint: Phosphorus binding capacity**

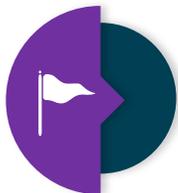
Renazorb showed statistically significant phosphate reduction with:

- ✓ 3000 mg/day ( $-92.8 \pm 22.9$  mg/L;  $p = 0.0004$ )
- ✓ 4500 mg/day ( $-111.4 \pm 22.8$  mg/L;  $p < 0.0001$ )
- ✓ 6000 mg/day ( $-103.8 \pm 22.9$  mg/L;  $p = 0.0001$ )



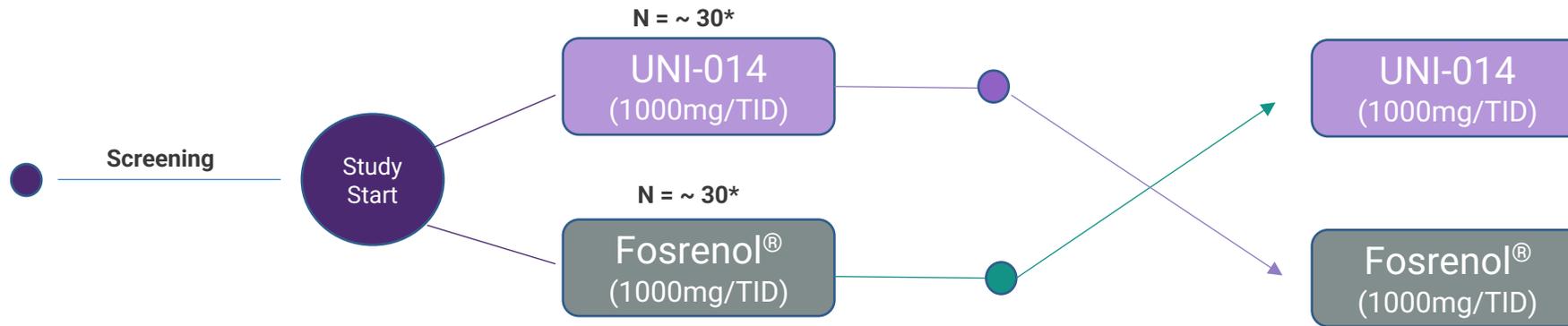
## **Secondary endpoint: Drug Safety**

All treatment-related adverse events (AEs) were mild in severity. No severe or life-threatening AEs were reported



***Results showed Renazorb is well tolerated with efficacy similar to that of available phosphate binders with 9 pills per day (Renvela) or 6 pills per day (Fosrenol)***

# Renazorb Bioequivalence Study

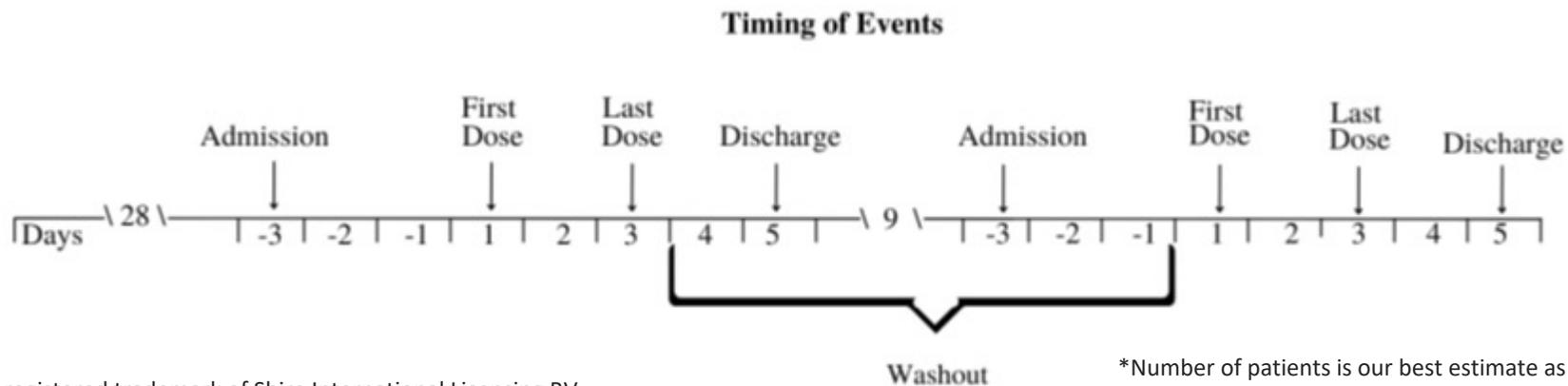


## Primary objective:

To demonstrate pharmacodynamic (PD) equivalence of orally administered UNI-014 1000 mg TID to orally administered Fosrenol 1000 mg TID in healthy subjects

## Secondary objective:

To compare the safety and tolerability of UNI-014 versus Fosrenol in healthy subjects



# The Ideal Phosphate Binder

*“Ideally, we would have phosphate binders with high phosphate-binding capacity (translating into low pill burden and good patient adherence), few adverse effects, no safety concerns, negligible interactions with other drugs, and all of this at a low cost ...we still do not have such a phosphate binder.”<sup>1</sup>*

**Juergen Floege, MD**  
Kidney Disease Improving Global Outcomes (KDIGO)  
CKD-MBD Guidelines, Executive Committee Member

High Phosphate-Binding Capacity

Low Pill Burden

Few Adverse Effects

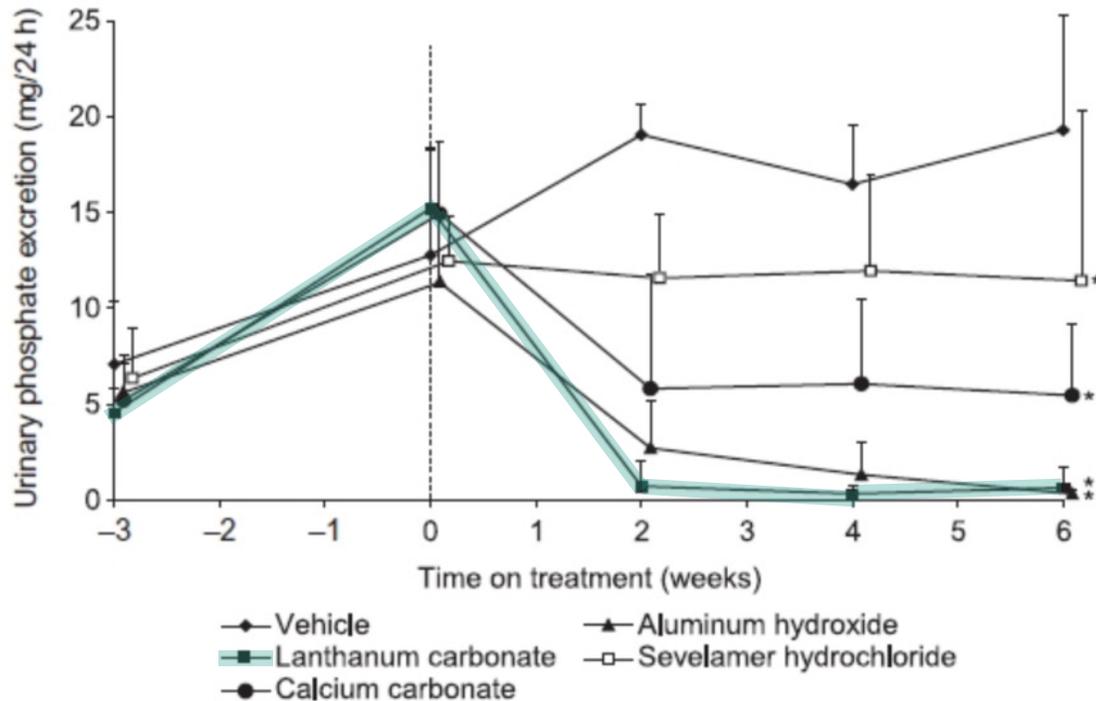
No Safety Concerns

Negligible Interactions With Other Drugs

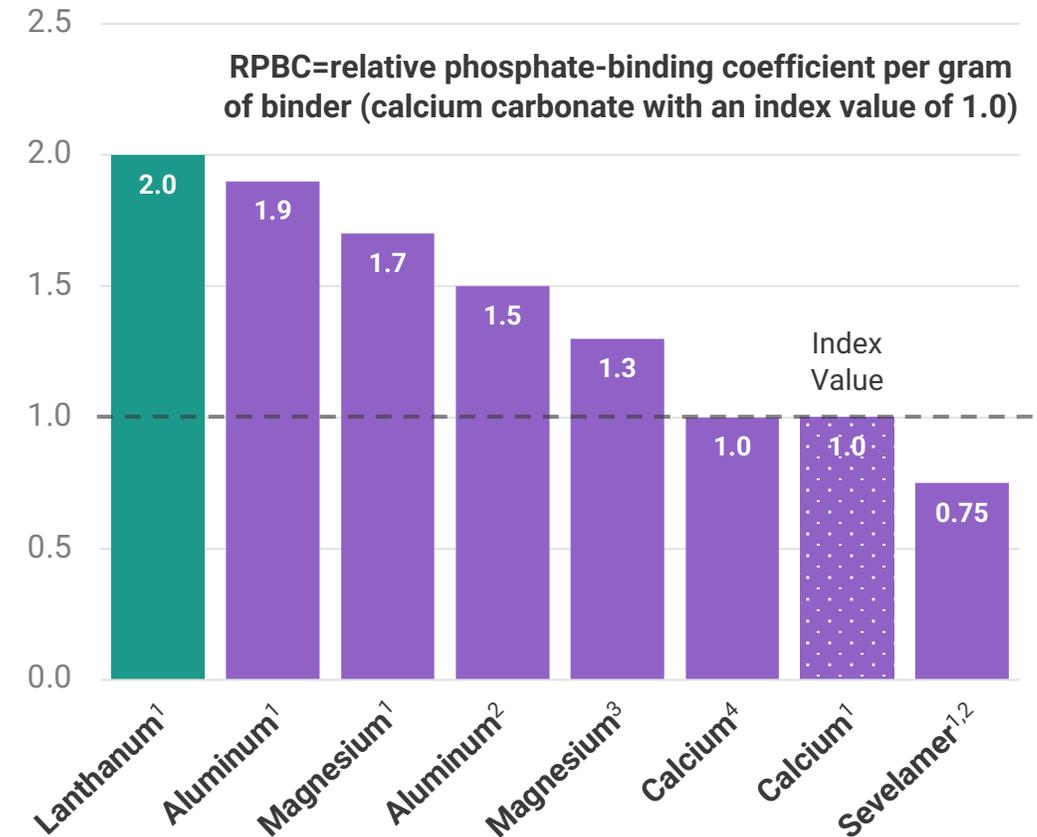
Low Cost

**Good Patient Adherence**

# Relative Phosphate Binding Ability of Hyperphosphatemia Treatment Options



Renal failure rat model (5/6 nephrectomy). All binders dosed at 1,000 mg/kg/day. *Renal Failure*, 33(2): 217-224, (2011)



<sup>1</sup> carbonate, <sup>2</sup> hydroxide, <sup>3</sup> hydrate, <sup>4</sup> acetate  
*Seminars in Dialysis*—Vol 24, No 1 (January–February) 2011 pp. 41–49

# Renazorb: Potential “Best-in-Class” Profile

Era	Drug	High Binding Capacity <sup>1</sup>	Safety <sup>2,3</sup>	Low Pill Burden <sup>4</sup>	Non-Chewable
1980's	Aluminum	+	-	+	+
1990's	Calcium	-	-	-	+
2000's	Sevelamer	-	+	-	+
2000's	Fosrenol	+	+	+	-
2010's	Velphoro	+	+	+	-
2010's	Auryxia	+	-	-	+
<b>2020's</b>	<b>Renazorb<sup>5</sup></b>	<b>+</b>	<b>+</b>	<b>+</b>	<b>+</b>

<sup>1</sup> *Renal Failure*, 33(2): 217–224, (2011); Seminars in Dialysis—Vol 24, No 1 (January–February) 2011 pp. 41–49

<sup>2</sup> KDIGO CKD-MBD Guideline Recommendations, 2009/2017, [kdigo.org](http://kdigo.org)

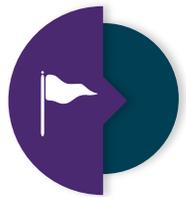
<sup>3</sup> Product package insert

<sup>4</sup> [dailymed.nlm.nih.gov](http://dailymed.nlm.nih.gov)

<sup>5</sup> Unicycive Therapeutics data on file

# Adverse Event Profile of Phosphate Binders

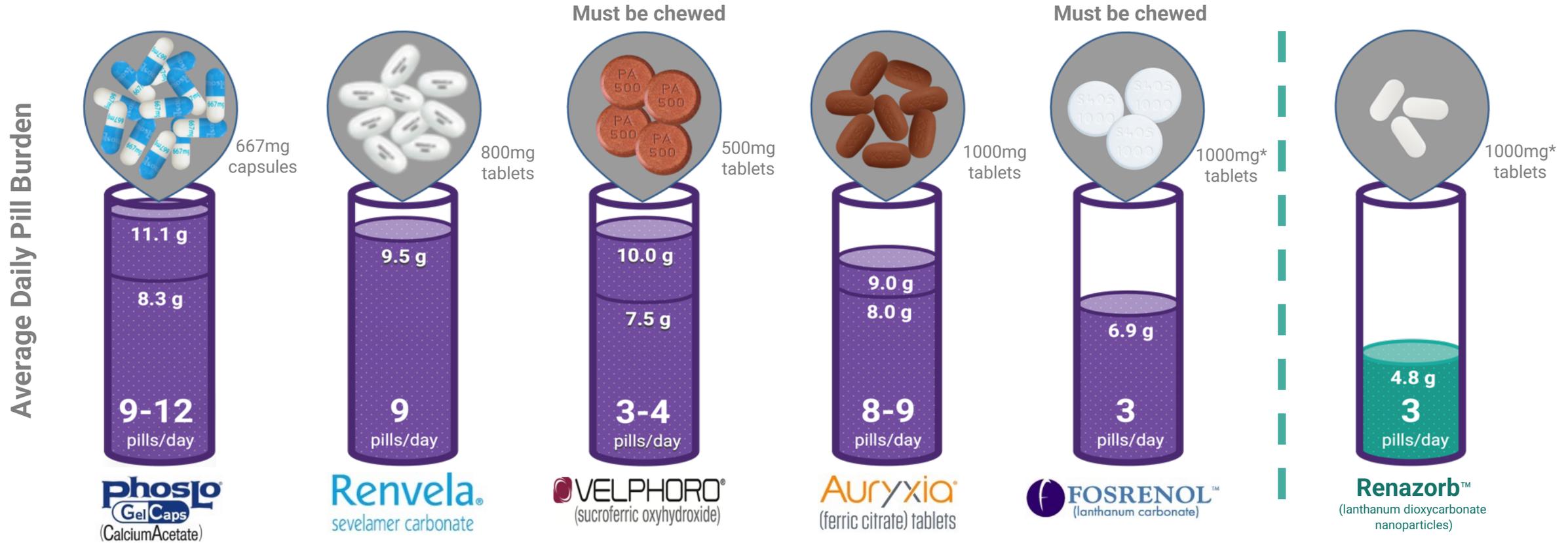
Auryxia	Renagel	Renvela	Velphoro	Fosrenol
<ul style="list-style-type: none"> <li>• Diarrhea (21%)</li> <li>• Discolored feces (19%)</li> <li>• Nausea (11%)</li> <li>• Constipation (8%)</li> <li>• Vomiting (7%)</li> <li>• Cough (6%)</li> </ul>	<ul style="list-style-type: none"> <li>• Vomiting (12%)</li> <li>• Diarrhea (16%)</li> <li>• Dyspepsia (11%)</li> </ul>	<ul style="list-style-type: none"> <li>• Vomiting (22%)</li> <li>• Nausea (20%)</li> <li>• Diarrhea (19%)</li> <li>• Dyspepsia (16%)</li> <li>• Abdominal pain (9%)</li> </ul>	<ul style="list-style-type: none"> <li>• Diarrhea (24%)</li> <li>• Discolored Feces (16%)</li> <li>• Nausea (10%)</li> </ul>	<ul style="list-style-type: none"> <li>• Nausea (11%)</li> <li>• Vomiting (9%)</li> <li>• Abdominal pain (5%)</li> </ul>



**Renazorb reference drug has fewer Adverse Events compared to other agents**

Source: Information for each Phosphate Binder taken from respective Package Inserts

# Relative Pill Burden from Phosphate Binders



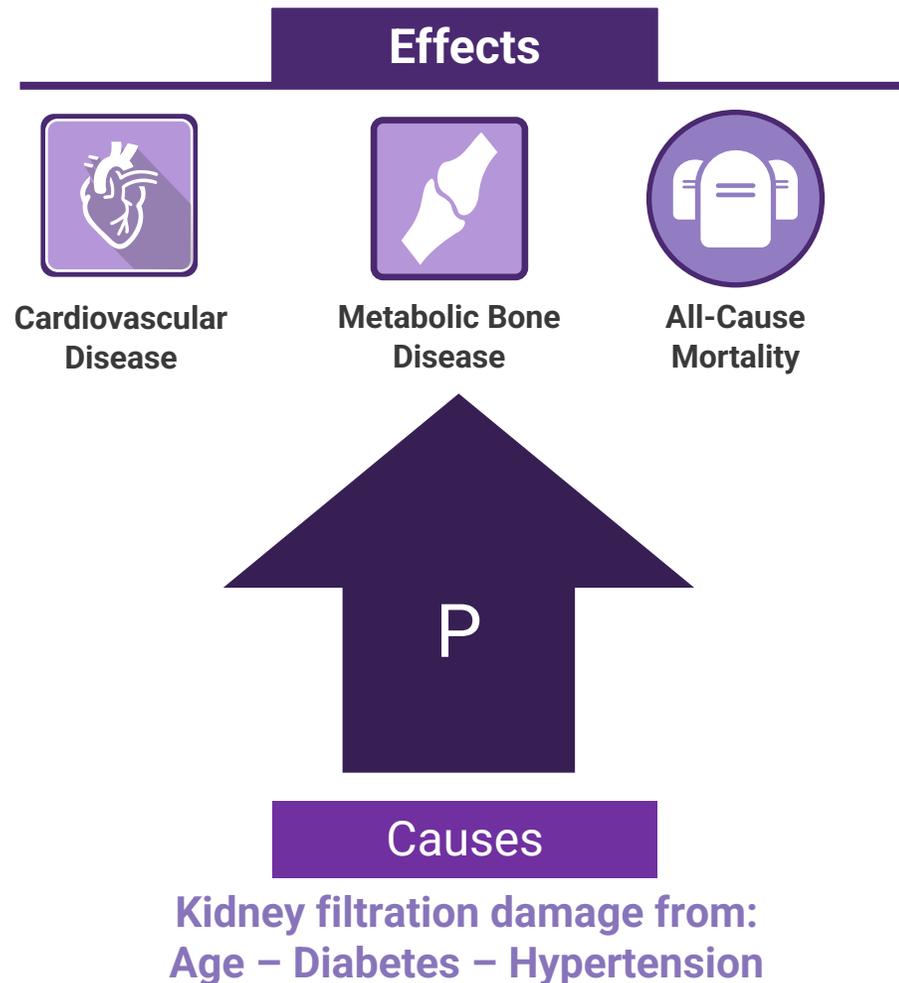
**Renazorb has the potential to significantly lower pill burden for patients**

Source: Average daily dose and product weights from [dailymed.nlm.nih.gov](http://dailymed.nlm.nih.gov) (product images proportionally sized)

Phoslo® is a registered trademark of Fresenius Medical Care, Renvela® is a registered trademark of Sanofi, Velphoro® is a registered trademark of Vifor Fresenius, Auryxia® is a registered trademark of Akebia Therapeutics. Fosrenol™ is a trademark of Takeda Pharmaceutical Company Limited

\*elemental lanthanum

# Hyperphosphatemia Risk Factors & Treatments



Current treatments focus on controlling the level of phosphate in the body

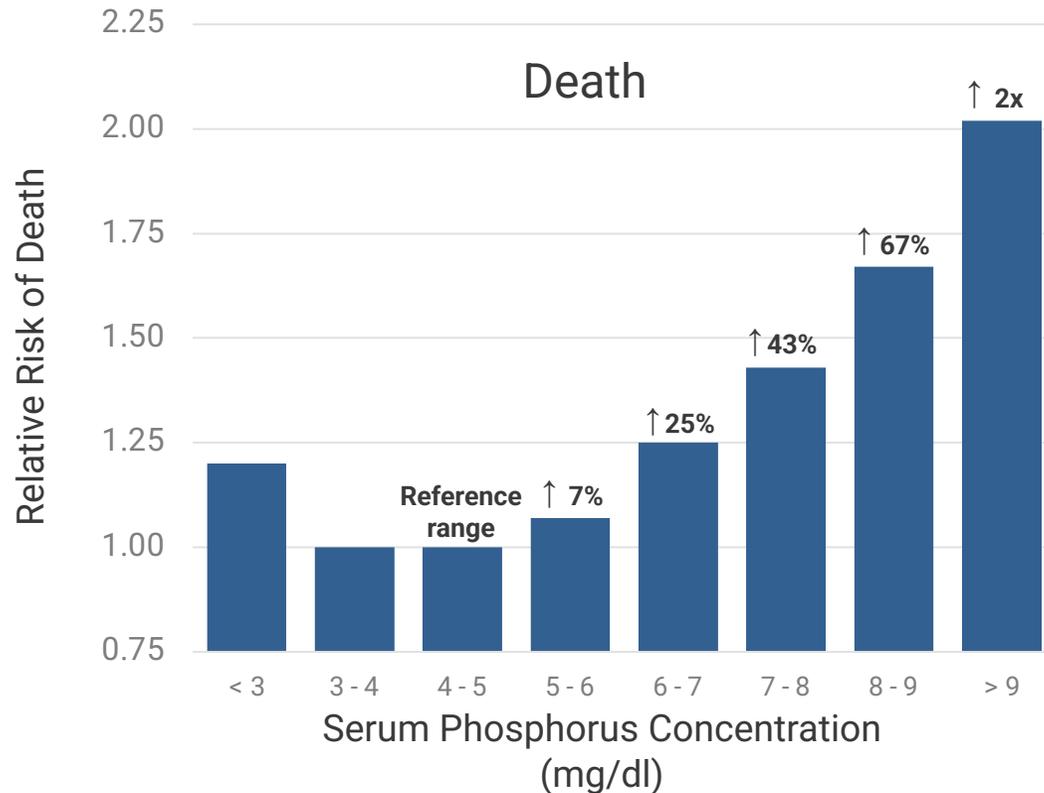


- Diet restrictions
- Dialysis
- **\*Phosphate binders**

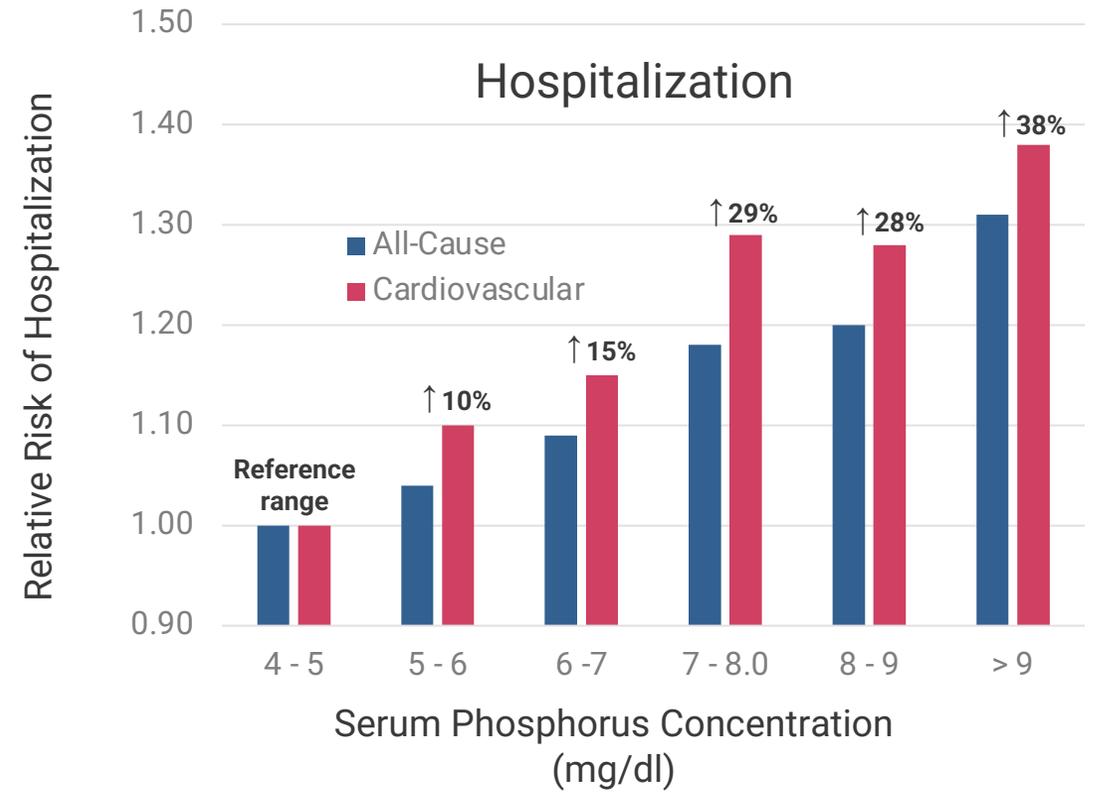
**Non-Calcium Phosphate Binders - Most Common Treatment in non-dialysis CKD patients**

- **Non-compliance** an issue with current products due to concurrent treatment comorbidities and chewable formulations causing ***pill burden***
- Current products require patients to take multiple and/or large pills with an average of **9 pills a day**

# Hyperphosphatemia is Strongly Associated with Increased Mortality and Hospitalization



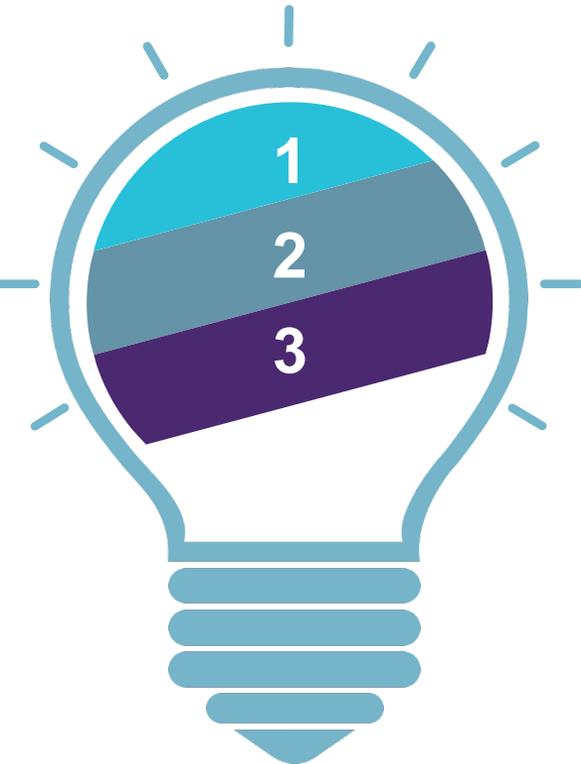
**Uncontrolled phosphorus confers a 7% - 102% increase in relative risk of mortality**



**Uncontrolled phosphorus confers a 10% - 38% increase in relative risk of hospitalization due to cardiovascular causes**

Mineral Metabolism, Mortality, and Morbidity in Maintenance Hemodialysis  
 Geoffrey A. Block, Preston S. Klassen, J. Michael Lazarus, Norma Ofsthun, Edmund G. Lowrie and Glenn M. Chertow  
 JASN August 2004, 15 (8) 2208-2218; DOI: <https://doi.org/10.1097/01.ASN.0000133041.27682.A2>

# Renazorb Global Intellectual Property



Renazorb is protected by a family of U.S. patents and a related family of patents outside the U.S.



Both the U.S. patent family and the foreign patent family were filed in 2011, and the U.S. coverage has statutory expiry in 2031



Corresponding patents granted in Canada, Europe, Japan, China, Australia, and other countries also have statutory expiration dates in 2031

# Renazorb Strategy and Key Milestones

## **FDA Regulatory Strategy** - based on Type C interaction and written response from FDA (Q4, 2021)

- 505(b)(2) regulatory pathway for the potential U.S. approval of Renazorb
- Leverage pre-clinical and clinical data from existing lanthanum-based product (Fosrenol)

## **Strategy involves the following studies for potential approval of Renazorb:**

- Bioequivalence study in healthy volunteers comparing urinary phosphorus changes between Renazorb and Fosrenol
- 6-month oral toxicity study in mice
- Standard information on manufacturability and commercial supply readiness of product

## **Commercial strategy underway to leverage large market opportunity**

- Product positioning, market access, and market shaping activities ongoing to optimize value proposition
- Pursuing dual commercial model pathways to address highly-concentrated nephrology market opportunity
  - Outsourced contract sales organization
  - Partnership with pharma company already selling into the nephrology call point



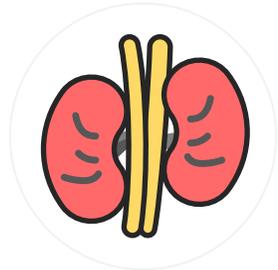
UNI-494 for Acute Kidney Injury

# UNI-494: Development Strategy



- 1 UNI-494 is a novel pro-drug of a marketed agent, nicorandil, with improved properties and long patent life
- 2 Nicorandil has compelling published scientific data which supports development of UNI-494 for Acute Kidney Disease (AKI) and Chronic Kidney Disease (CKD)
- 3 Pursuing AKI as initial indication with CKD as a follow-on program

# Acute Kidney Injury (AKI) and Current Treatment



## Acute Kidney Injury (AKI) Background

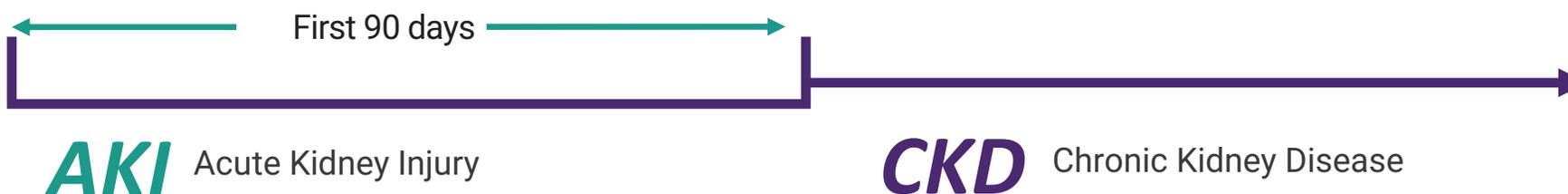
- A loose collection of syndromes characterized by a sudden decrease in estimated glomerular filtration rate (eGFR)
- Persistent AKI is characterized by the continued decreased in urine output or increases in serum creatinine (as defined by KDIGO) beyond 48 hour from AKI onset up to day 7
- AKI and CKD can form a continuum whereby initial kidney injury can lead to persistent renal injury, eventually leading to CKD

## There are no approved medicines to treat AKI

- In most cases the damage to the kidney is irreversible, and the patient needs to have a renal transplant or be on dialysis for life
- Treatment options include:

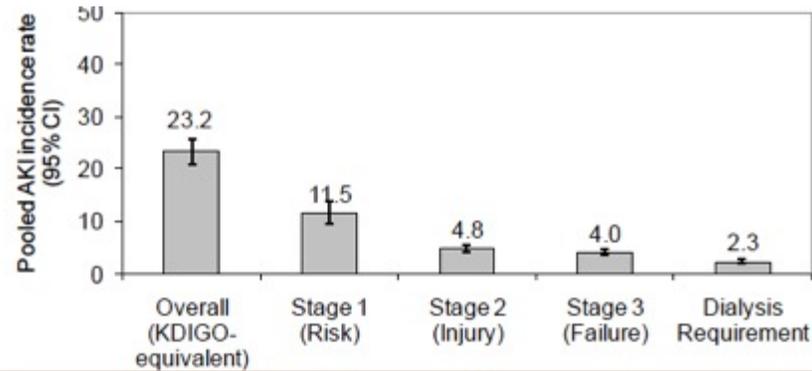


- Renal replacement therapy
- Renal transplant
- Radical surgery and dialysis

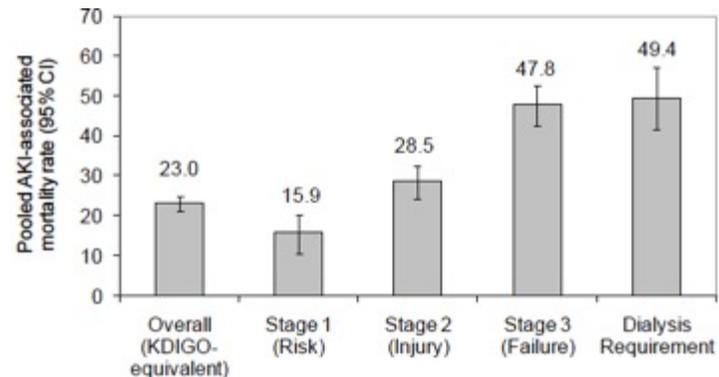


# AKI Incidence & Mortality

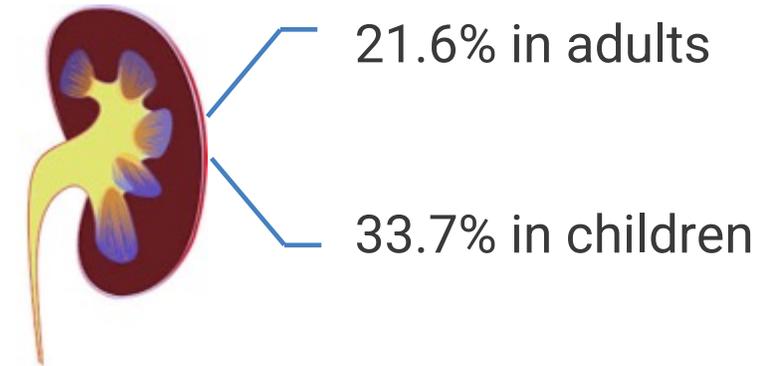
**1 in 5 adults and 1 in 3 children worldwide experience AKI during a hospital episode of care**



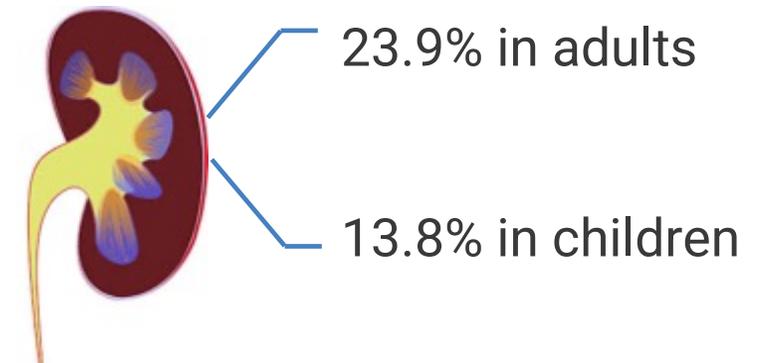
No. studies	154	112	108	108	189
No. patients	3,585,911	3,303,992	3,281,715	3,281,715	29,400,495



## AKI-Associated Incidence Rates



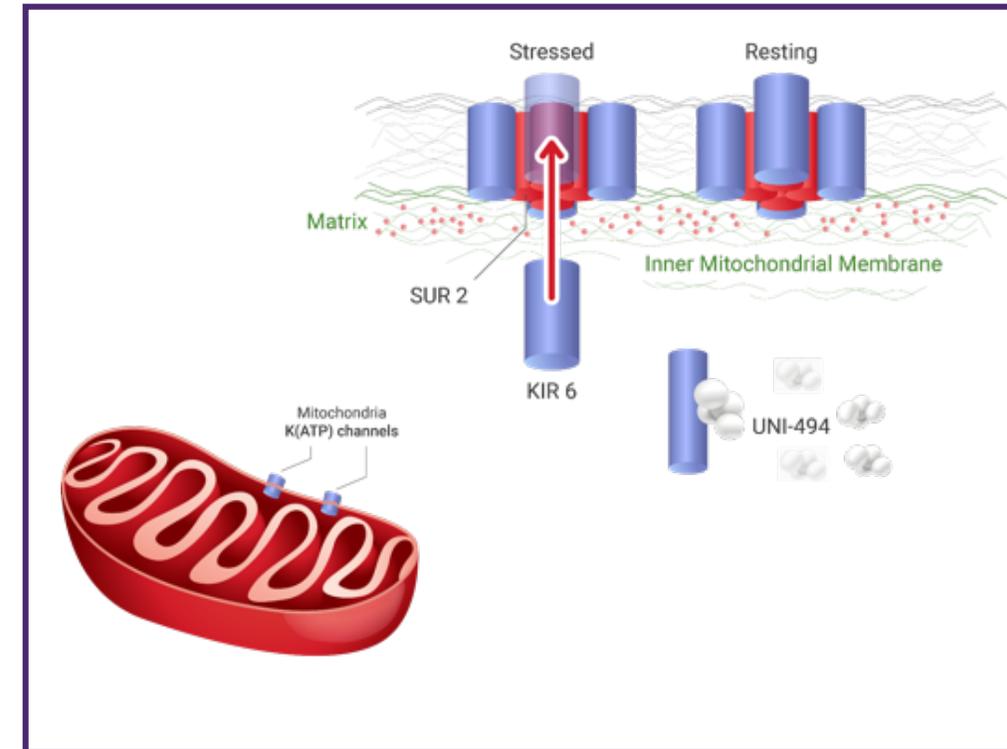
## AKI-Associated Mortality Rates



Among the 154 studies (n=3,585,911) that adopted a KDIGO-equivalent AKI definition

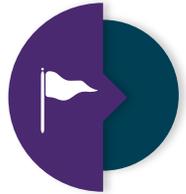
# Nicorandil Mechanism of Action: Application Beyond Angina

- Indicated for treatment of angina
- Approved ex-U.S. for ~40 years
- Dual mechanism in angina – NO donor and ATP-sensitive K<sup>+</sup> channel (KATP) agonist
- Widely published evidence that nicorandil exhibits broad mitochondrial protection
- Primary mechanism likely to be via opening of mitochondrial KATP channel
  - Damage and stress opens the mitochondrial permeability transition pore (MPTP)
  - MPTP opening requires closing of a specific K<sup>+</sup>-ATP channel on the mitochondrial membrane
  - Nicorandil binds to and prevents closing of this channel
  - Results in blockade of exogenous stress-induced production of Radical Oxygen Species (ROS) and cellular damage



**Proposed primary mechanism of action of UNI-494**

# Nicorandil: Clinical Evidence for Renoprotection



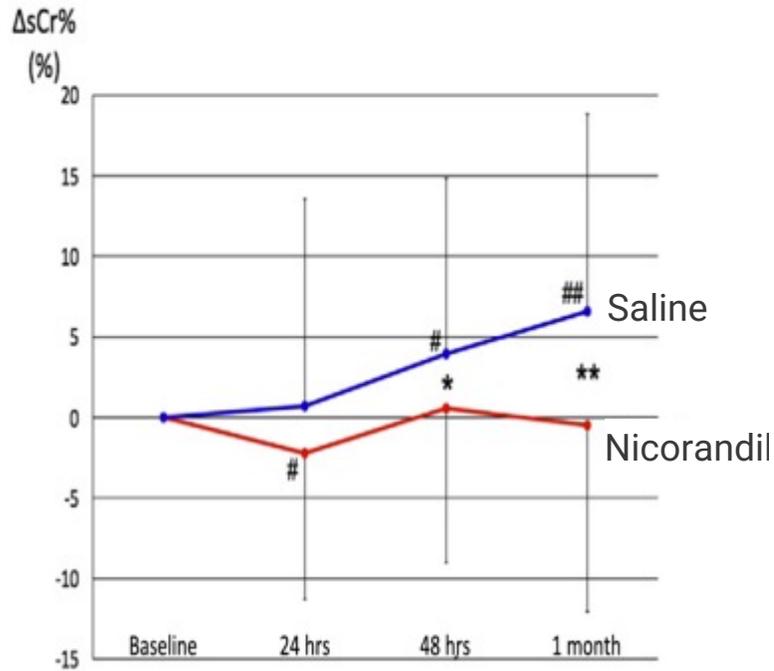
*Nicorandil is associated with improved clinical outcomes in several randomized clinical trials in patients with kidney disease*

Clinical Setting	Outcome	Reference
<b>Acute Kidney Injury</b>		
Patients with poor kidney function scheduled for PCI (n=213) randomized to saline or nicorandil	<ul style="list-style-type: none"> <li>Significant reduction in contrast-induced nephropathy (2.0% vs 10.7%)</li> <li>Reduction in contrast-induced increase in sCr and cystatin C</li> <li>Reduction in contrast-induced decline in eGFR</li> </ul>	<b>Nawa et al., 2015</b>
At-risk patients scheduled for PCI (n=128) randomized to placebo or nicorandil	<ul style="list-style-type: none"> <li>Significant reduction in contrast-induced nephropathy (<u>4.7% vs 21.9%</u>)</li> <li>Significant reduction in contrast-induced decline in eGFR</li> </ul>	<b>Iranirad et al., 2017</b>

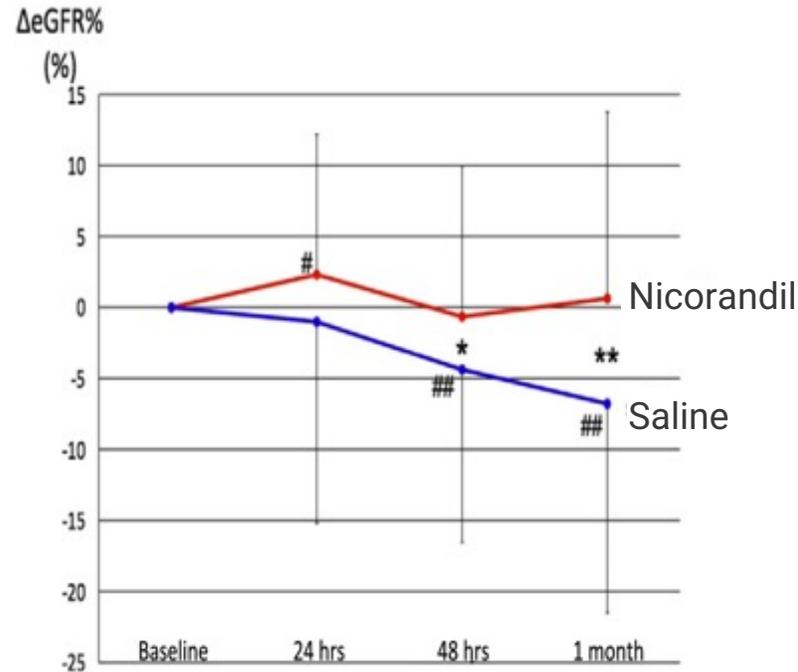
Clinical Setting	Outcome	Reference
<b>Chronic Kidney Disease</b>		
Proteinuric patients (n=108) randomized to placebo or nicorandil for 6 months	<ul style="list-style-type: none"> <li>Significant (44%) reduction in proteinuria</li> <li>Significant reduction in urinary endothelin-1 excretion</li> </ul>	<b>Lee &amp; Chang, 2009</b>
Hemodialysis patients (n=129) who underwent PCI and were randomized to chronic placebo or nicorandil	<ul style="list-style-type: none"> <li>Significant improvement in 3-year all-cause survival (79% vs 61%)</li> <li>Significant improvement in 3-year cardiac death-free survival (87% vs 71%)</li> </ul>	<b>Nishimura et al., 2009</b>

# Nicorandil efficacy starts within 24 hours and continues for weeks

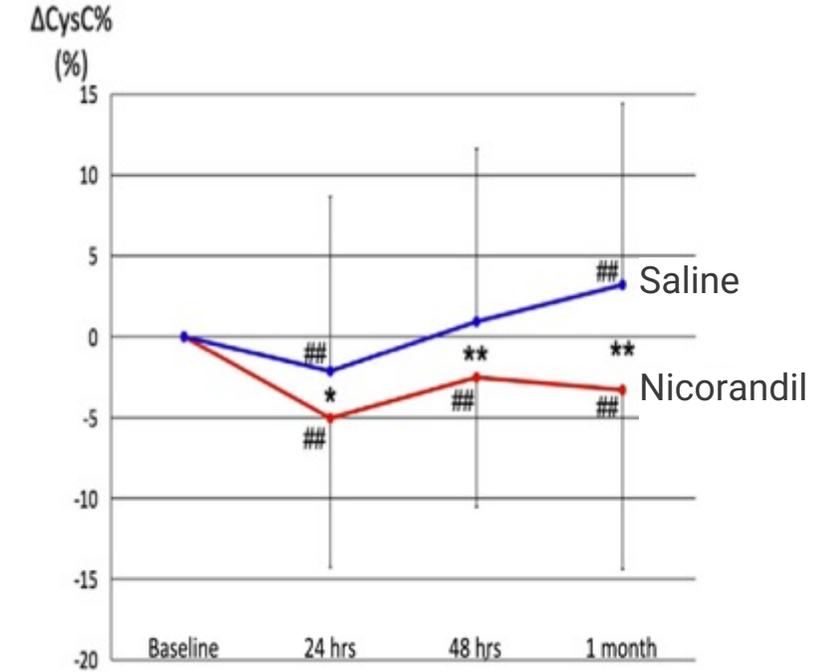
## Serum creatinine



## Estimated GFR



## Cystatin C



**Nicorandil is Effective in Reducing Contrast-Induced Nephrology (CIN) Incidence: 2% in Patients Treated with Nicorandil versus 10.7% with Placebo/Saline**

# UNI-494: Potential to Improve Nicorandil

- Nicorandil is well-tolerated overall
  - Most common Adverse Events (AEs) are related to vasodilation (headache, flushing, dizziness)
  - Effective in numerous animal models of kidney disease without affecting blood pressure
- Two historic challenges with development of nicorandil in kidney disease
  - 1) Nicorandil has a short half-life (~1 hour), necessitating BID (2 times/day) dosing or greater
  - 2) Associated with gastro-intestinal (GI) tolerability and rare GI ulcerations and perforations

## UNI-494 novel pro-drug

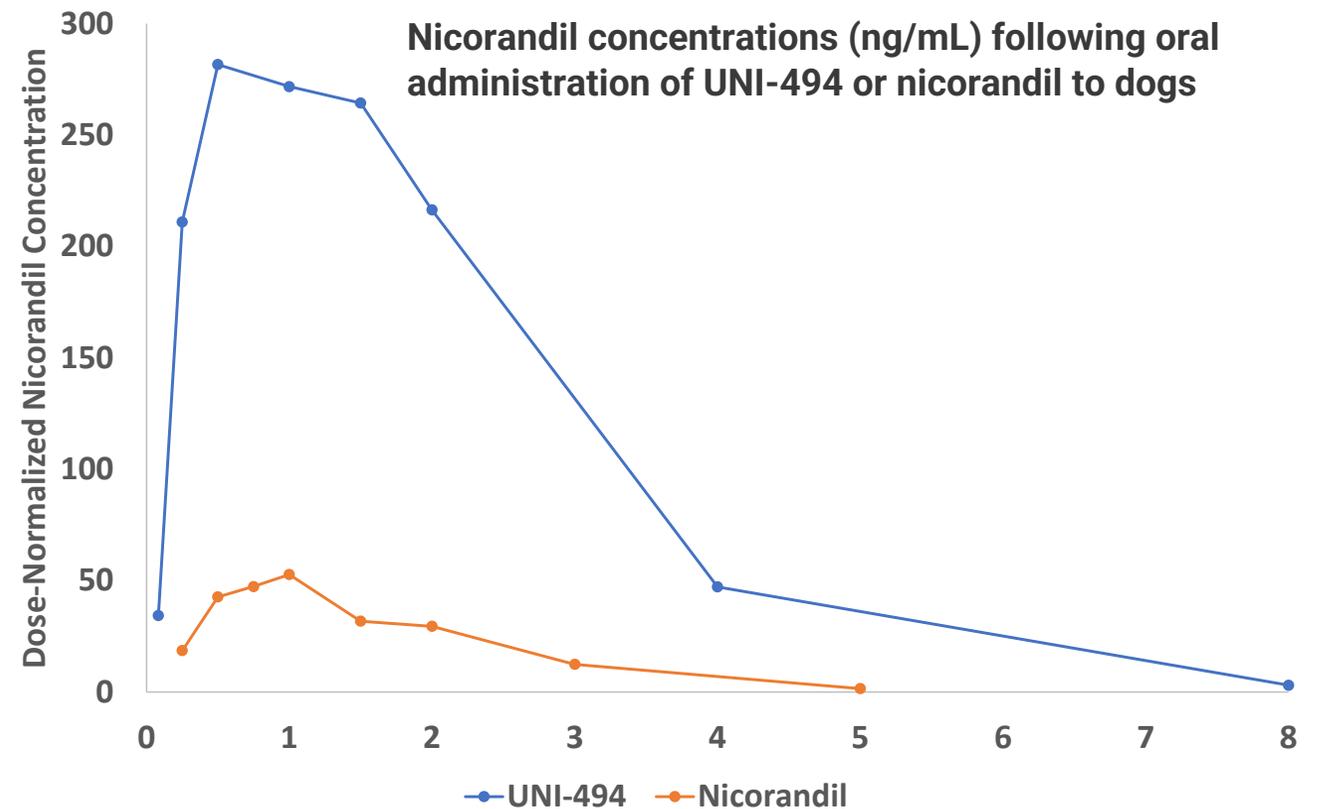
- Utilizes a known, safe, chemical linker to create pro-drug
- Pro-drug addresses gut safety concerns present with nicorandil
- Slow release of active drug in plasma from pro-drug may reduce need for TID/BID dosing
- Linker metabolizes safely

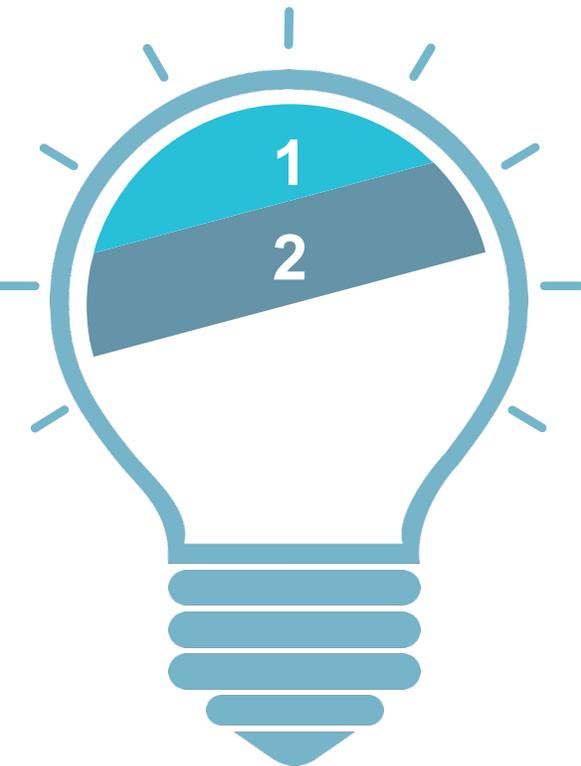


***UNI-494 aiming to improve dosing and reduce the side-effects of nicorandil***

# UNI-494 Animal Studies Increased Drug Exposure 4X vs Nicorandil

- PK data normalized by dose of nicorandil and compared to historical data
- Dosing of UNI-494 resulted in a **4X** greater exposure (\*AUC) of nicorandil than dosing nicorandil alone





UNI-494 is protected by a broad issued patent covering method of manufacture:

- Patent granted in the U.S. with expiry 2032
- Patent pending in Europe, Japan and China
- Exclusively licensed to Unicycive



We are also pursuing additional IP coverage for UNI-494 in the U.S. and globally:

- Current U.S. provisional application, if granted, would expire 2040
- Additional international patent applications planned from this patent family

# UNI-494 FDA Strategy and Key Milestones

## FDA Regulatory Strategy:

- Confirm pro-drug has acceptable tolerability in animal studies at desired doses
- Identify pro-drug dose(s) for initial human study, Demonstrate conversion of UNI-494 to nicorandil in humans
- Seek FDA clearance to initiate Phase 1 study (IND approval)

## Unique attributes for regulatory approval of UNI-494:

- Leverage pre-clinical and clinical data from nicorandil outside United States with comparability package
- Design of more homogenous AKI patient population including patients with CIN where nicorandil has been shown to be efficacious

## Milestones

- ✓ Completed chemical synthesis for animal studies - 3Q, 2021
- ✓ Initiated animal safety studies - 3Q, 2021
- Complete preclinical studies – 1H, 2022
- File IND – mid-2022
- Initiate Phase 1 clinical trial – 2H, 2022

## Management



**Shalabh Gupta, MD**  
Chief Executive Officer

UBS, Genentech



**John Townsend, CPA**  
Chief Financial Officer

Guardion Health Sciences,  
Cytori Therapeutics



**Doug Jermasek, MBA**  
EVP, Corporate Strategy

Genzyme-Sanofi, Akebia,  
Keryx, Pfizer, Abbott



**Pramod Gupta, PhD**  
EVP, Pharmaceutical &  
Business Operations

Spectrum, B&L, Abbott



**Keith Ward, PhD**  
Chief Development Advisor

Reata, B&L, GSK

## Board of Directors



**Brigitte Schiller, MD**  
CMO at Satellite  
Healthcare



**Sandeep "Steve" Laumas, MD**  
Goldman Sachs,  
North Sound Capital



**John Ryan, MD, PhD**  
Wyeth, Merck,  
Kadmon



**Shalabh Gupta, MD**  
UBS, Genentech

## Scientific Board



**Ravi Mehta, MD**  
Prof Emeritus of  
Medicine, UCSD



**Pablo Pergola, MD, PhD**  
Director, Clinical Advancement  
Center, PLLC, a wholly-owned  
subsidiary of Renal Associates



**Glenn Chertow, MD, MPH**  
Chief, Division of Nephrology at  
Stanford University School of  
Medicine



**Myles Wolf, MD**  
Charles Johnson, Prof  
of Medicine and Chief,  
Division of Nephrology  
at Duke University  
School of Medicine

## Renazorb

- ✓ FDA meeting
- ✓ Present clinical and preclinical data at NKF Conf
- Initiate BE study in healthy volunteers
- Complete 6-month mouse study
- Data readout from BE study
- Near-term NDA filing

## UNI-494

- ✓ Early animal PK studies completed
- ✓ Multi-kilo scale chemical supplies for animal safety studies completed
- ✓ Animal safety studies initiated
- Phase 1 human studies planning initiated (start 2H'2022)
- Global patent progress ongoing

## **Addressing important patient needs and large markets within kidney disease**

- Hyperphosphatemia patients live with extreme treatment burden
- No medicines approved for Acute Kidney Injury

## **Product candidates utilizing proven mechanisms of action**

- Renazorb: Phosphate binder for the treatment of hyperphosphatemia in patients with chronic kidney disease (CKD);
- UNI-494: novel pro-drug of nicorandil for the treatment of AKI and CKD with potentially improved dosing and improved side effects

## **Significantly De-risked Regulatory Pathway for Renazorb**

- Type C meeting with the FDA in December 2021 provides a clear guidance to file NDA
- Pursuing a 505(b)(2) regulatory pathway for U.S. approval
- Single required healthy volunteer clinical study to be started shortly with the FDA alignment

## **Cash runway to file Renazorb NDA and to initiate clinical trials for UNI-494 until early 2023**



Shalabh Gupta, MD  
CEO

Thank You