



UNICYCIVE

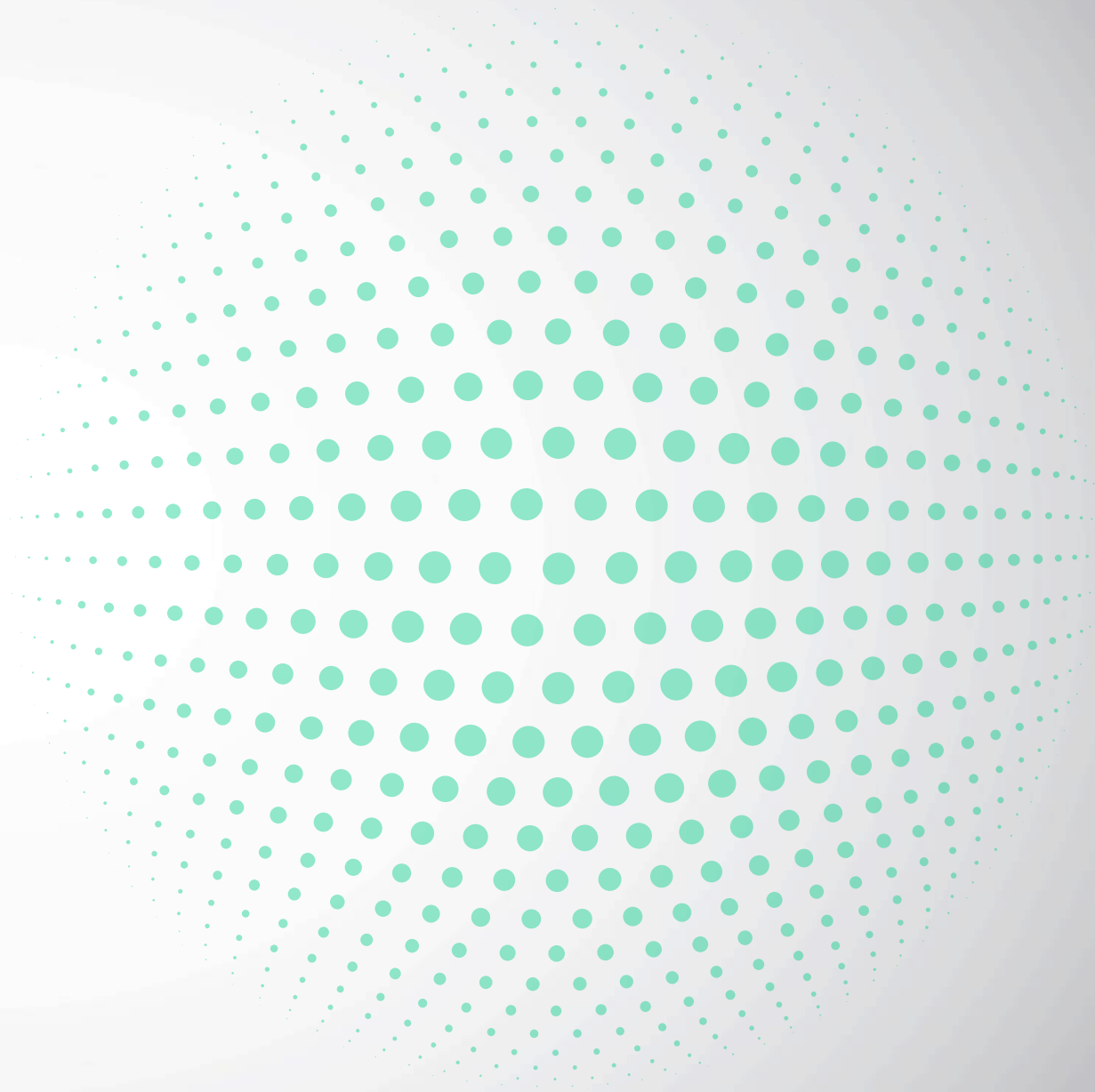
THERAPEUTICS INC.

NASDAQ: UNCY

Novel Treatments for Kidney Disease

Company Presentation

March 2023



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.



Investment Highlights

Beginning by addressing unmet patient needs and large markets within kidney disease

- Hyperphosphatemic Chronic Kidney Disease (CKD) patients live with extreme treatment burden
- Acute Kidney Injury (AKI) patients live without any approved medication

Unique product candidates with proven mechanisms of action

- RENAZORB™(lanthanum dioxycarbonate) is an investigational phosphate binder candidate for the treatment of hyperphosphatemia in patients with CKD on dialysis
- UNI-494 is a novel mitochondrial-targeted treatment for AKI and CKD entering first-in-human Phase 1 trial in 2023

Our first product RENAZORB is already blazing a positive pathway

- Multiple meetings with FDA provide clear guidance to file NDA under expedited 505(b)(2) pathway with single bioequivalence study
- Positive bioequivalence study completed in healthy volunteers
- On track to file NDA in mid-2023

Strong balance sheet to support Renazorb filing, launch and commercialization

- Up to \$130 million in long-term funding from top healthcare focused institutional investors with exercise of warrants based on achievement of defined milestones



RENAZORB™ for the Treatment of Hyperphosphatemia in Chronic Kidney Disease (CKD) Patients on Dialysis

RENAZORB (lanthanum dioxycarbonate) is an unapproved investigational new drug being developed under FDA's 505(b)(2) regulatory pathway. If approved, Renazorb will share the same product label and prescribing information as the reference-listed drug (RLD) Fosrenol (lanthanum carbonate) with the exception that Renazorb tablets are smaller in size and swallowed whole with water and not chewed

The Unmet Need in Hyperphosphatemia

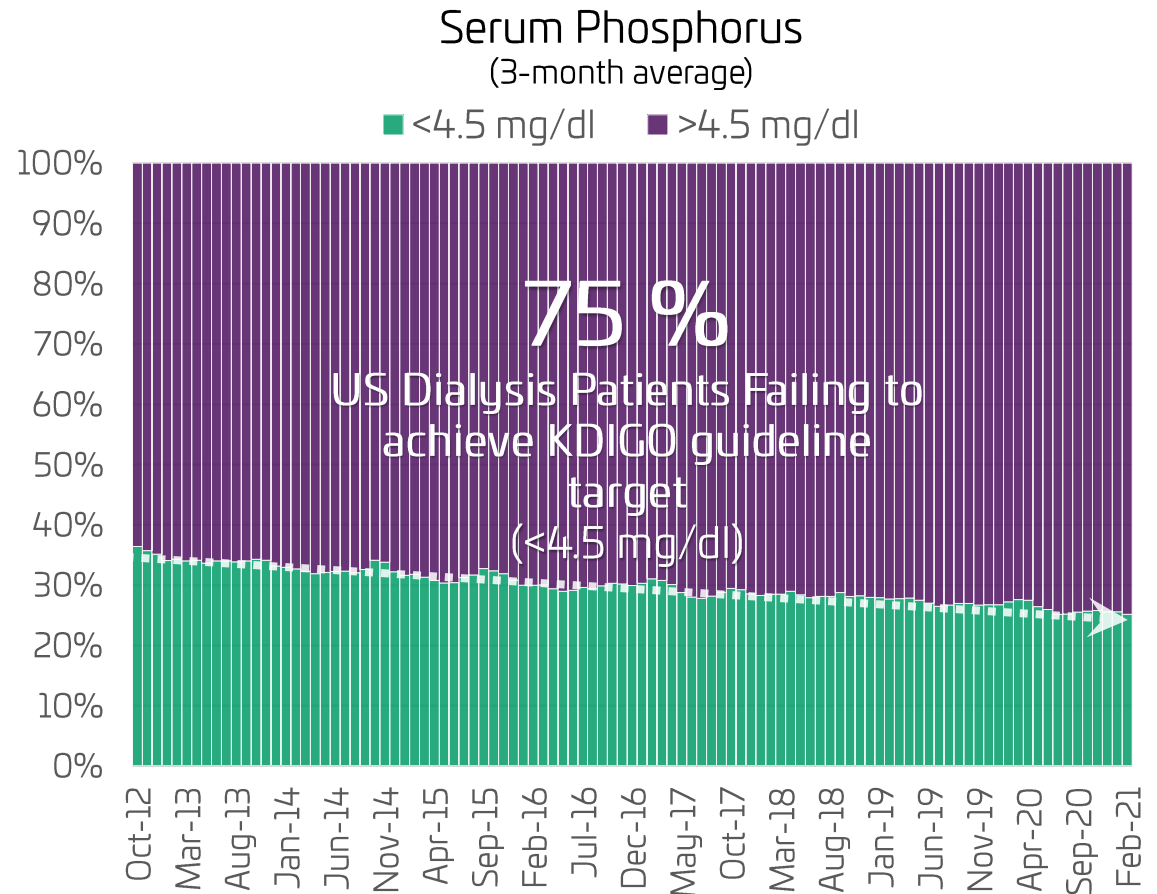


Hyperphosphatemia is prevalent and remains uncontrolled¹

- Occurs in at least 80% of patients with Stage 5 CKD on dialysis (>500,000 patients in the US)
- Despite the availability of 6 FDA-approved phosphate binders, hyperphosphatemia remains uncontrolled in an estimated 75% of US dialysis patients.¹

Dialysis patient daily pill burden is onerous²

- The daily pill burden of maintenance dialysis patients is among the highest across various chronic disease states including HIV/AIDS, diabetes mellitus, and congestive heart failure.²
- 19 pills per day (median)
- 62% of patients are non-adherent (self-reported)



¹US-DOPPS (Dialysis Outcomes and Practice Patterns Study), May 2021; <http://www.dopps.org/DPM>

²Chiu YW, et al. Clin J Am Soc Nephrol. 2009

RENAZORB Product Profile



Overview

- RENAZORB™ (lanthanum dioxycarbonate) is an unapproved IND being developed under FDA's 505(b)(2) regulatory pathway for the treatment of hyperphosphatemia
- If approved, RENAZORB will share the same product label and prescribing information as the reference-listed drug Fosrenol (lanthanum carbonate), however, RENAZORB tablets have the advantage of being (1) smaller in size and (2) are swallowed whole with water and not chewed

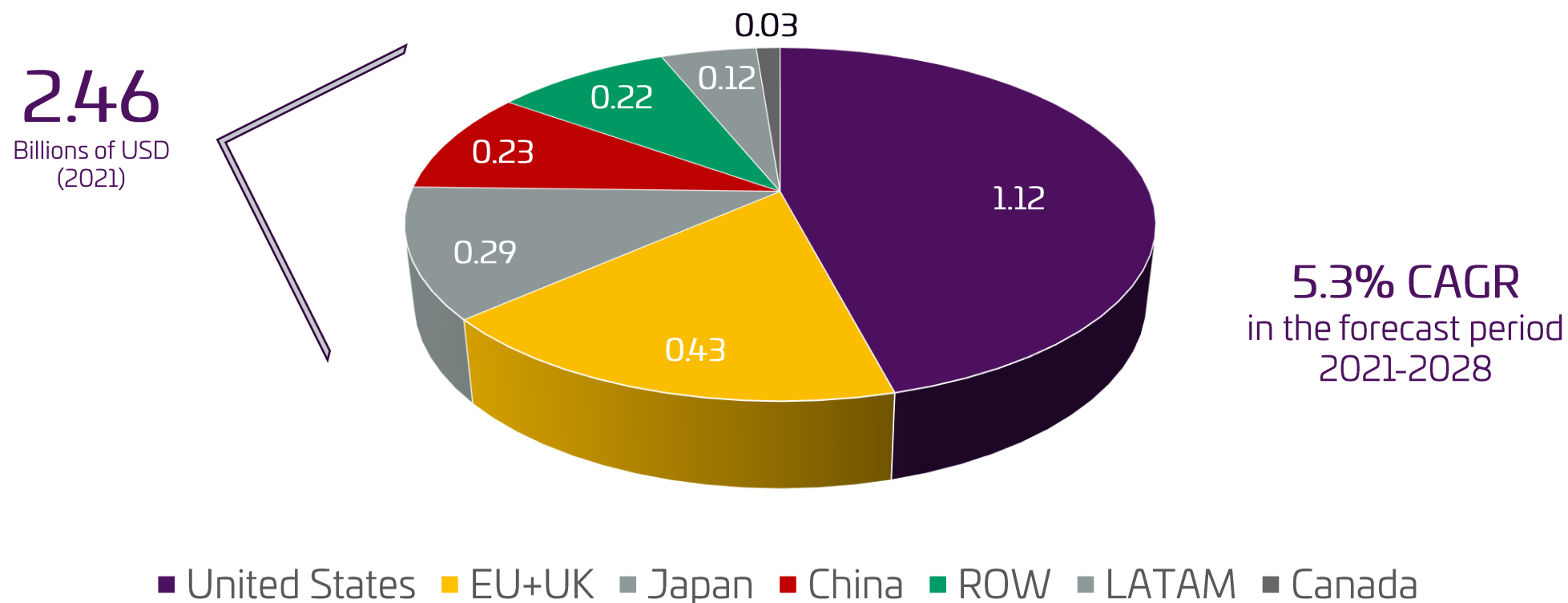
Proprietary Nanoparticle Technology

- UNICYCIVE has harnessed the phosphate binding potency of lanthanum to reduce the number and size of pills that patients must take to control hyperphosphatemia
 - Enhanced surface area
 - Lower molecular weight
 - Immediate release tablets
- Enables smaller pills
- Pills are swallowed (not chewed)

Strong Global Intellectual Property

- The U.S. 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

Global Hyperphosphatemia Market Opportunity



UNICYCIVE owns worldwide rights to Renazorb

Single Pivotal Bioequivalence (BE) Study to Satisfy FDA Requirement for 505(b)(2) NDA Filing



Primary Objective

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

Secondary Objective

To compare the safety and tolerability of RENAZORB versus Fosrenol in healthy subjects

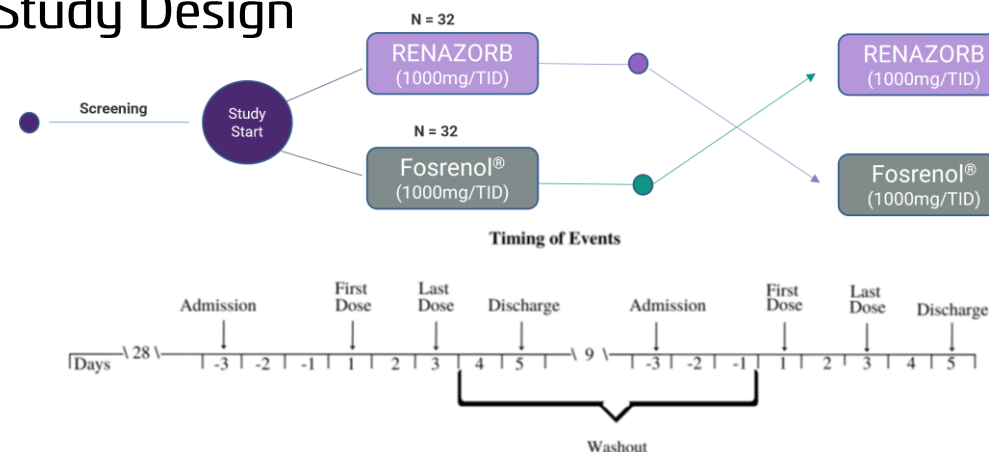
Primary Endpoint

Least squares (LS) mean change in urinary phosphate excretion (in mg/day) from baseline¹ to the evaluation period²

Secondary Endpoint

To compare the safety and tolerability of RENAZORB versus Fosrenol in healthy subjects

Study Design



FDA Alignment Gained

- Acceptability of 505(b)(2) pathway for registration
- Pharmacodynamic vs pharmacokinetic endpoint
- FDA BE study guidance for lanthanum carbonate
- Agreement on study design, dose and endpoints

¹Baseline is defined as the approximately 48-hour urine collection period starting on Day 2 and ending on Day 1

²Evaluation period is defined as the approximately 72-hour urine collection period starting on Day 1 and ending on Day 4

In Pivotal Bioequivalence (BE) Study, RENAZORB Met All Endpoints



- ✓ Primary Endpoint Met
- ✓ Secondary Endpoint Met
- ✓ Pharmacodynamic bioequivalence established
- ✓ Enables 505(b)(2) NDA Filing (mid 2023)

Safety Results

- Treatment emergent adverse events were comparable between the Renazorb and Fosrenol groups
- No subjects in the study experienced a serious adverse event (requiring hospitalization or study withdrawal)
- There were no deaths in the study

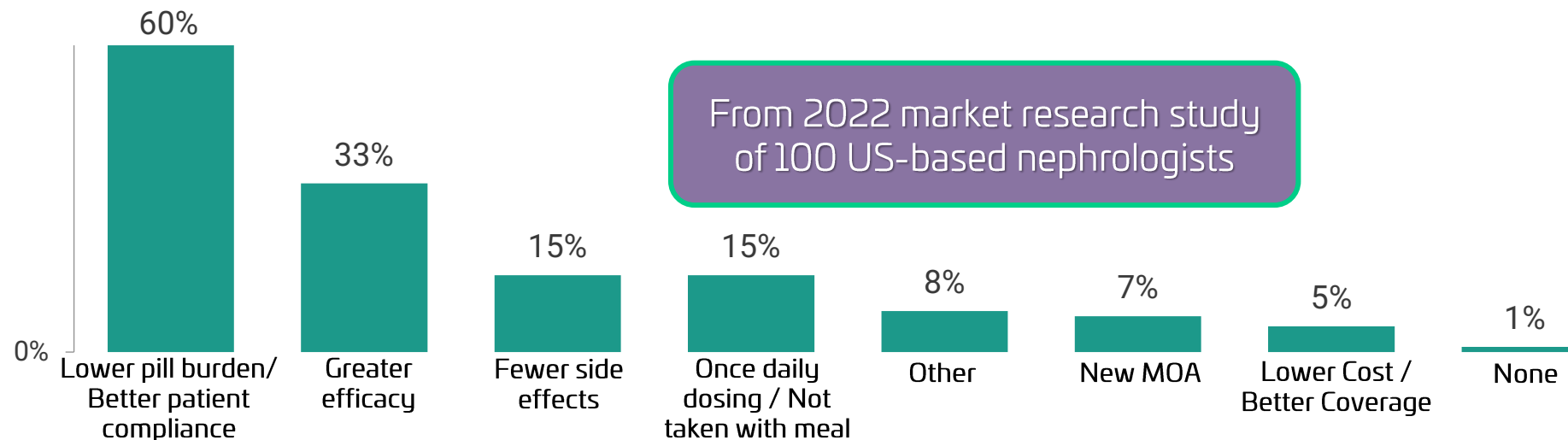
Current Treatments are Inadequate —High Pill Burden is the Chief Culprit



Juergen Floege, MD, Nephrologist
Executive Committee Member,
KDIGO CKD-MBD Guidelines
June 2020

*“Ideally, we would have phosphate binders with high phosphate-binding capacity (translating into low pill burden and good patient adherence)...**we still do not have such a phosphate binder.**”¹*

Greatest Unmet Need in Treatment of Hyperphosphatemia with Phosphate Binders (Unaided)



Question: *What is the greatest unmet need in the treatment of hyperphosphatemia with phosphate binders?*

Primary Market Research: Renazorb Conjoint Study, March 2022

¹Phosphate binders in chronic kidney disease: an updated narrative review of recent data, J Nephrol. 2020 Jun;33(3):497-508

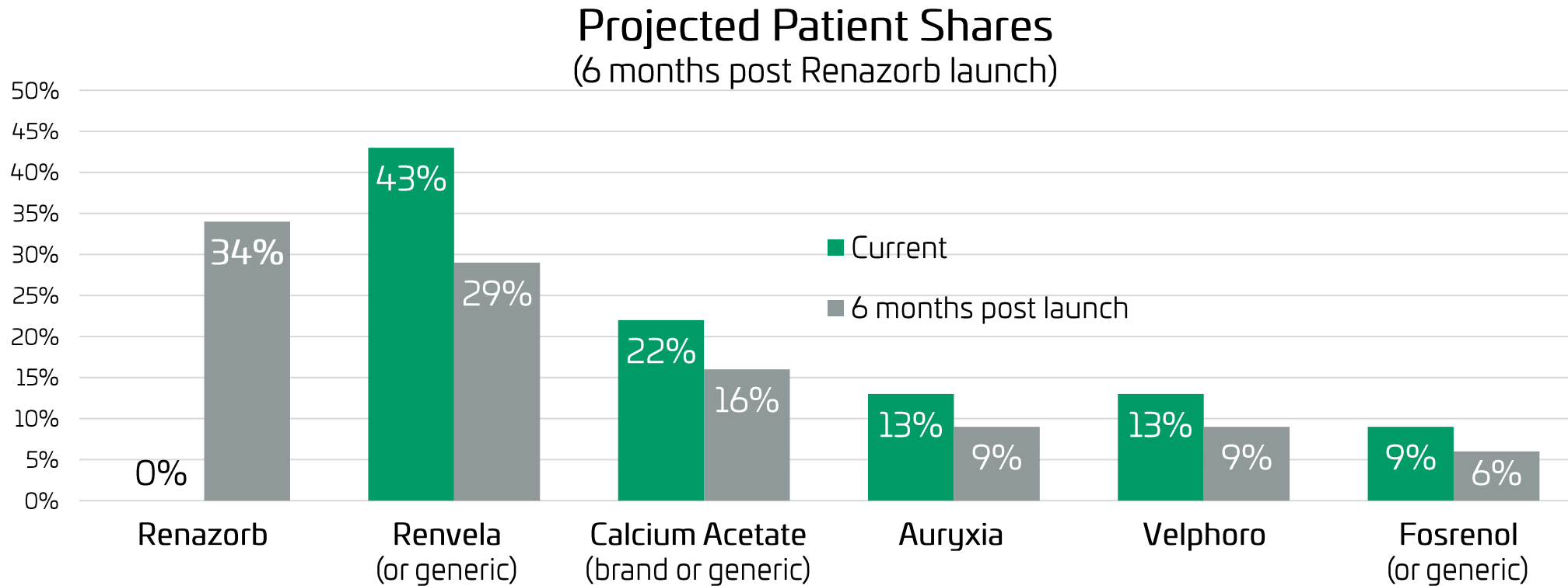
RENAZORB May Reduce Daily Pill Burden by 2 to 4-Fold Compared to Available Phosphate Binders



Source: Average daily dose: dailymed.nlm.nih.gov, Pill volumes and weights: Data on file, Unicyclic Therapeutics, Product images are proportionally sized

Renvela® is a registered trademark of Sanofi, Calphron® is a registered trademark of NEPHRO-TECH, INC., Auryxia® is a registered trademark of Akebia Therapeutics. Fosrenol™ is a trademark of Takeda Pharmaceutical Company Limited, Velphoro® is a registered trademark of Vifor Fresenius

If approved, RENAZORB profile is projected to command a high preference share of patients



Base: n=100 Nephrologists, Question: *Assuming Binder X (Renazorb) were 6 months post-launch with cost and coverage similar to Velphoro and Auryxia, how, if at all, would your prescribing change among your patients who are receiving a phosphate binder?*

Source: Renazorb Conjoint Market Research Study, Reason Research, March 2022

Commercial Strategy



Commercial planning underway to leverage large market opportunity

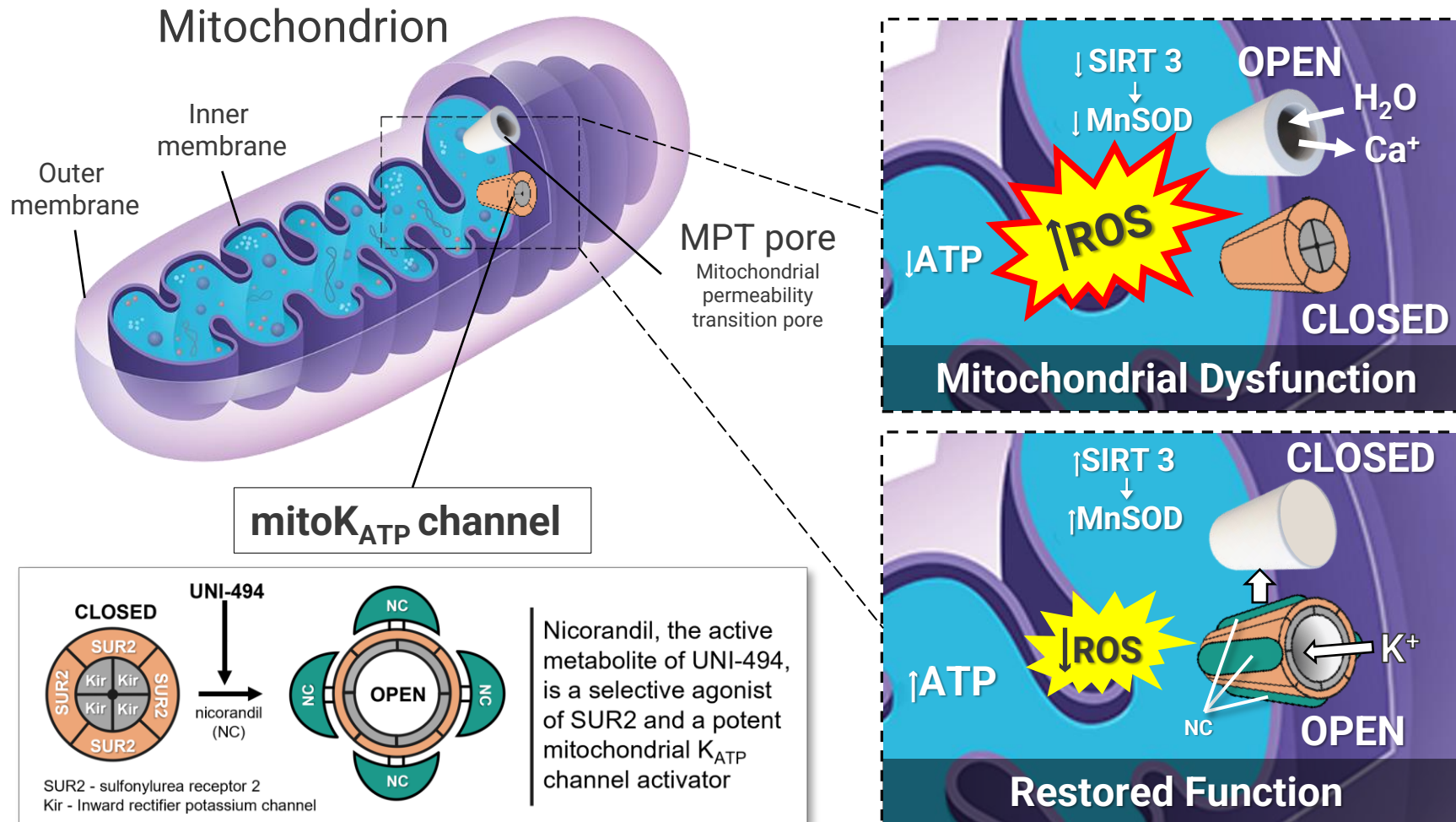
- Product positioning, market access, and market shaping activities ongoing to establish best-in-class value proposition
- Key Opinion Leader (KOL) engagement activities ongoing
- Concentrated universe of phosphate binder prescribers allows for cost-efficient targeting with relatively small commercial footprint
- Pursuing parallel commercial model options
 - Build-out innovative, efficient commercial launch capability leveraging internal and outsourced resources
 - Partner with established biopharma company already selling into the nephrology call point
 - License and/or distribution deal(s) with Dialysis Organization(s)
- Capitalize on CMS plan to expand patient access to phosphate binders in 2025
 - At least two years of separate payment (Transitional Drug Add-On Payment Adjustment – TDAPA) for new drugs at 100% of average selling price (ASP)



UNI-494: Mitochondrial-Targeted Therapy for Kidney Disease

UNI-494 Restores Mitochondrial Function

Mechanism of Action



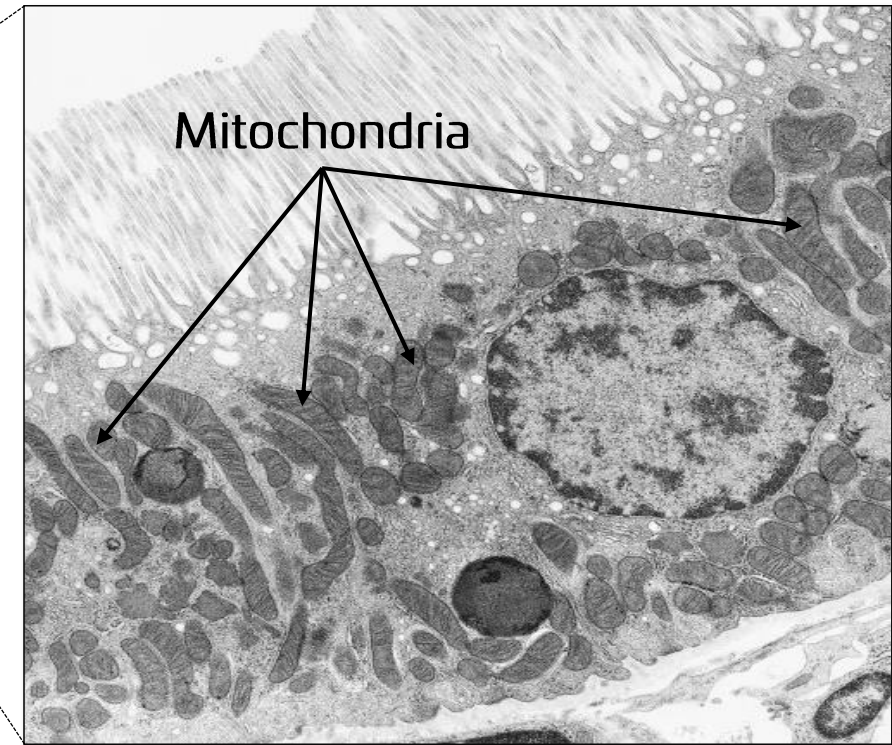
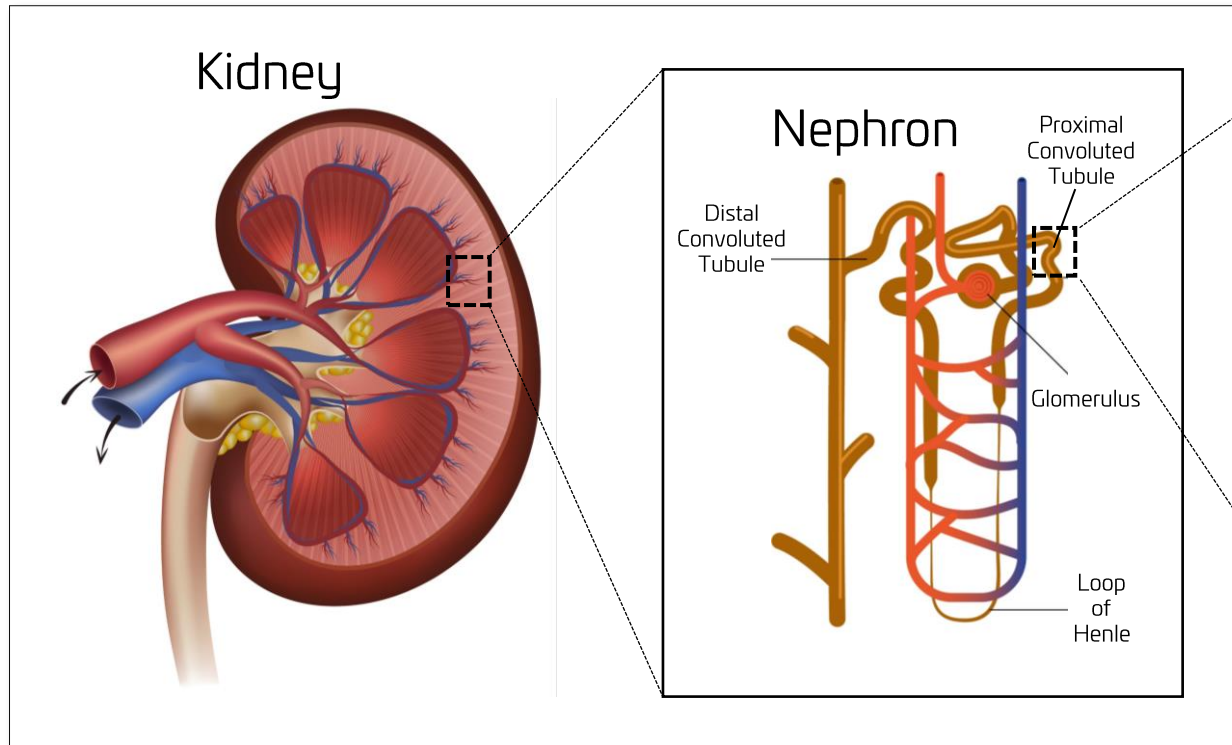
- A hallmark feature of mitochondrial dysfunction is chronic opening of MPT pores and overproduction of reactive oxygen species (ROS)
- Chronic opening of MPT pores leads to water and solute influx, swelling, injury and cell death
- UNI-494 is an ATP-sensitive K⁺ channel (K_{ATP}) activator
- Binds to SUR2 subunit of K_{ATP} channel that in turn leads to closing of MPT pores
- Down-regulates production of ROS

Due to its High Energy Demands, the Kidney is a Prime Target for Mitochondrial Injury



"The kidney constitutes 1% of body weight but utilizes 10% of total body oxygen consumption."¹

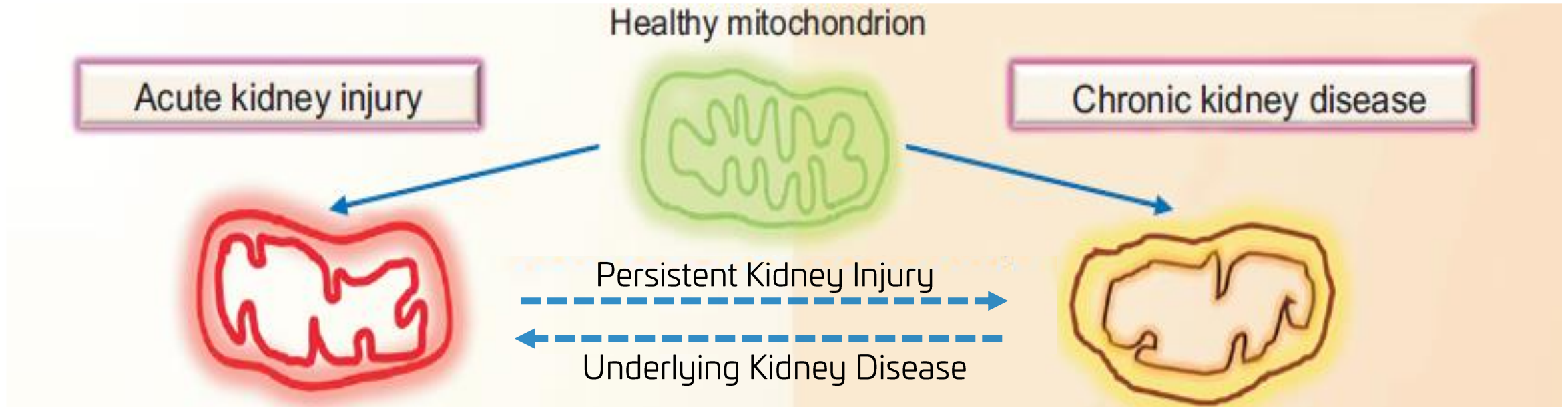
"The proximal tubule is the primary target of injury and progression of kidney disease."¹



Transmission Electron Micrograph of Proximal Tubule
Brenner and Rector's The Kidney, 8th ed.

¹Am J Physiol Renal Physiol. 2016 Jul 1; 311(1): F145-F161

“Acute-On-Chronic” Kidney Disease



Acute and Chronic kidney injury are **bidirectional** processes

- Acute kidney injury (AKI) leads to chronic kidney disease (CKD)
- Underlying CKD predisposes patients to AKI

CKD and ESRD Burden of Disease



Chronic Kidney Disease (CKD)¹

- More than 1 in 7, that is 15% of US adults or 37 million people, are estimated to have CKD
- Nearly 1 in 3 US adults with diabetes or hypertension have CKD
- As many as 9 in 10 adults with CKD do not know they have CKD
- Mortality is more than twice as high in CKD patients compared to non-CKD
- Medicare spending for CKD in 2020
= **\$70 Billion**

End Stage Renal Disease (ESRD)²

- 786,000 US patients living with ESRD
- Over 550,000 on dialysis
- ESRD patients waitlisted for kidney transplant wait over 49 months for a transplant
- ~20% yearly mortality for dialysis patients
- Medicare spending for ESRD in 2020
= **\$49.3 Billion**

[1] Centers for Disease Control and Prevention. *Chronic Kidney Disease in the United States, 2021*.

[2] United States Renal Data System. 2020 USRDS Annual Data Report: Epidemiology of Kidney Disease in the United States

Acute Kidney Injury (AKI) and Current Treatment



Acute Kidney Injury (AKI) Background

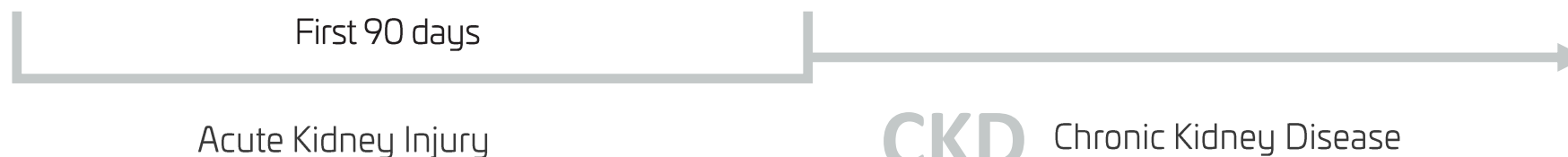
- Characterized by a sudden loss of kidney function
- Persistent AKI is characterized by the continued decreased in urine output or increases in serum creatinine (as defined by KDIGO) beyond 48 hour from AKI onset up to day 7
- AKI and CKD can form a continuum whereby initial kidney injury can lead to 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:



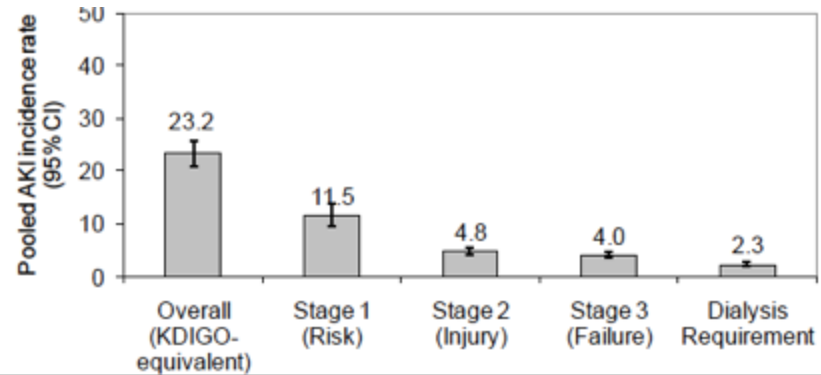
- Renal replacement therapy
- Renal transplant
- Radical surgery and dialysis



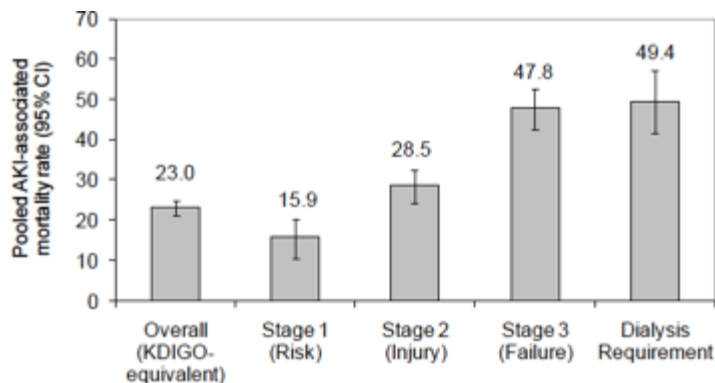
AKI Incidence & Mortality



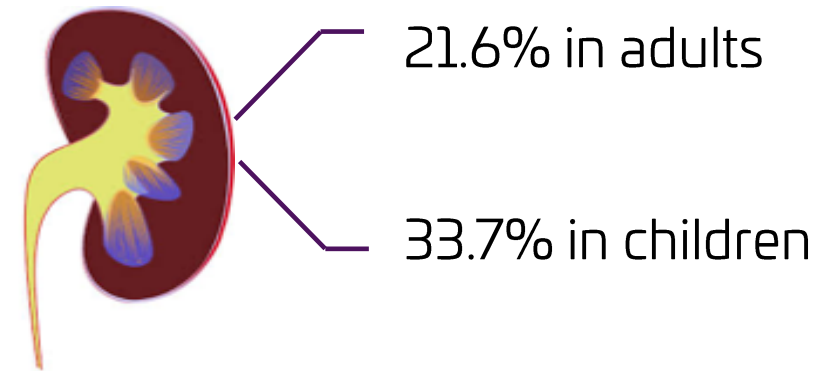
1 in 5 adults and 1 in 3 children worldwide experience AKI during a hospital episode of care



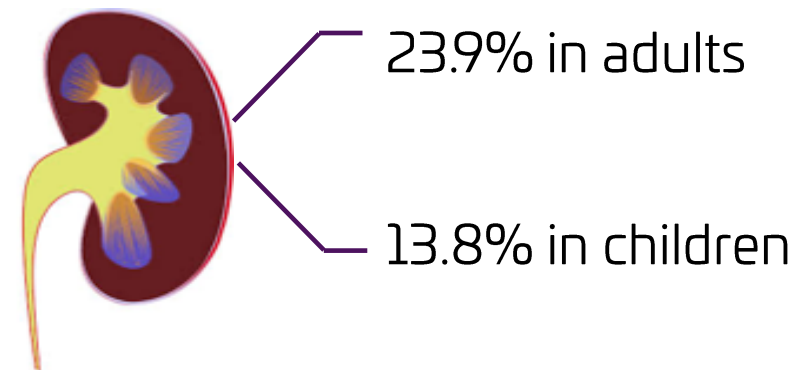
No. studies	154	112	108	108	189
No. patients	3,585,911	3,303,992	3,281,715	3,281,715	29,400,495



AKI-Associated Incidence Rates



AKI-Associated Mortality Rates



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

UNI-494 Active Metabolite (Nicorandil) Exhibits Renoprotection in Animal Models of Renal Disease



Model	Regimen	Outcome	Reference
STZ-induced diabetic nephropathy in eNOS ko mice	Therapeutic – treatment initiated 4 weeks after STZ induction 30 mg/kg/day for 8 weeks	No decrease in BP but significant reduction in proteinuria, glomerular injury, collagen deposition, and podocyte loss	Tanabe et al., 2012
5/6 th nephrectomy in rats	Therapeutic – treatment initiated at time of nephrectomy – 15 mg/kg for 12 weeks	No decrease in BP but significant reduction in proteinuria, sCr and BUN, glomerular injury, and tubulointerstitial injury	Shiraishi et al., 2014
Anti-Thy1 nephritis in rats	Prophylactic – treatment initiated 3 days before anti-Thy1 injury 10 and 30 mg/kg/day for 12 days	No decrease in BP but significant reduction in proteinuria, renal hypertrophy, collagen deposition, and TGF β expression	Sudo et al., 2009
Acute ischemia-reperfusion injury in rats	Therapeutic– treatment initiated 10 min prior to ischemic injury-10 mg/kg	Significant protection against I-R-induced injury including proteinuria and histological damage	Shimizu 2011
Dahl salt-sensitive hypertensive rats	Prophylactic – treatment initiated at time of switch to high salt diet	No decrease in BP but significant reduction in proteinuria, NAG excretion, and oxidative stress	Tashiro et al., 2015
Spontaneously hypertensive WHY rat	Therapeutic – treatment initiated at 11 weeks of age	No decrease in BP but significant reduction in proteinuria, kidney size, and tubular damage	Serizawa et al., 2013

Nicorandil: Clinical Evidence for Renoprotection

Acute Kidney Injury



Clinical Setting	Outcome	Reference
Acute Kidney Injury		
Patients with poor kidney function scheduled for PCI (n=213) randomized to saline or nicorandil	<ul style="list-style-type: none"> Dose: 0.096 mg/mL cont. infusion; 4 hours before and 24 hours after PCI Significant reduction in contrast-induced nephropathy (2.0% vs 10.7%, $p < 0.02$) Reduction in contrast-induced increase in sCr and cystatin C Control arm showed significant decline in eGFR (-4.2% vs +2.1%; $p < 0.001$), @ 1 month 	Nawa et al., 2015
At-risk patients scheduled for PCI (n=128) randomized to placebo or nicorandil	<ul style="list-style-type: none"> Dose: 10 mg/day; 30 mins before to 3 days after PCI Significant reduction in contrast-induced nephropathy (4.7% vs 21.9%, $p < 0.008$) No change in eGFR from baseline, significant decline in eGFR in control arm) 	Iranirad et al., 2017

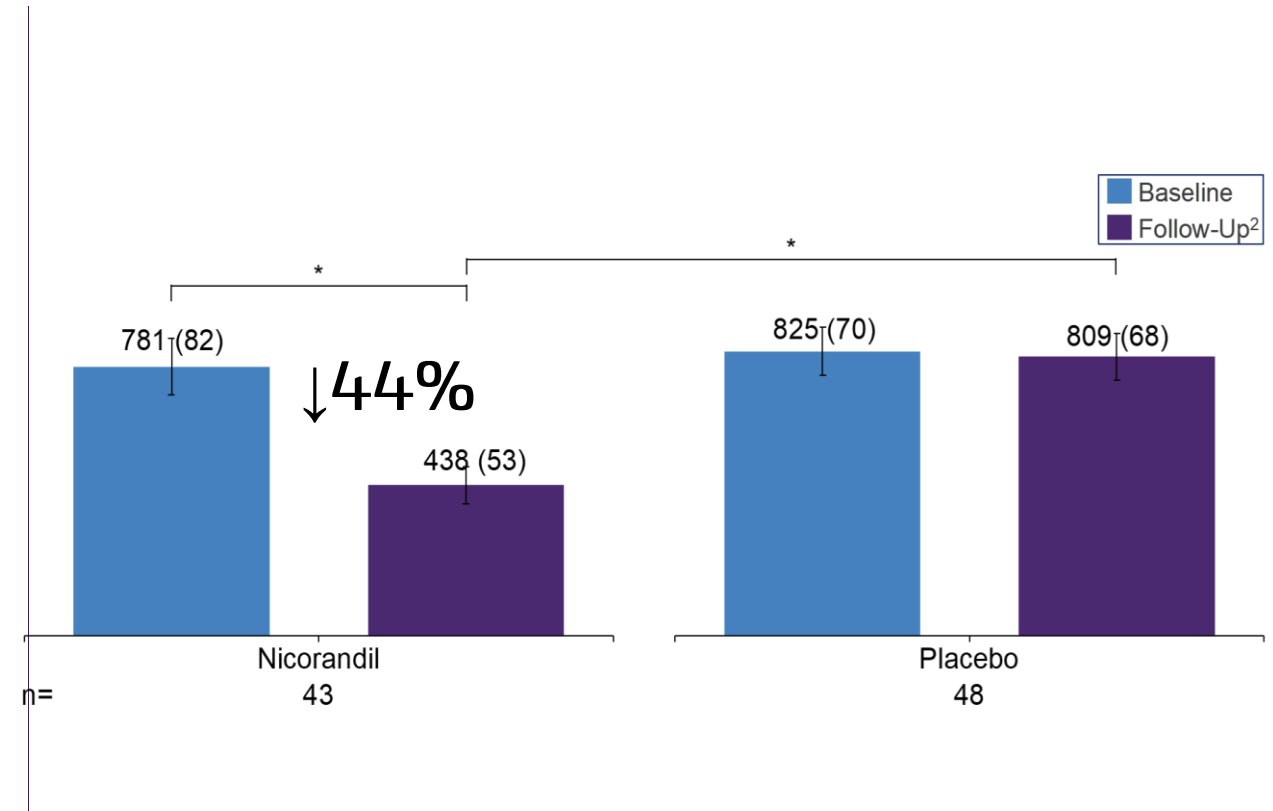
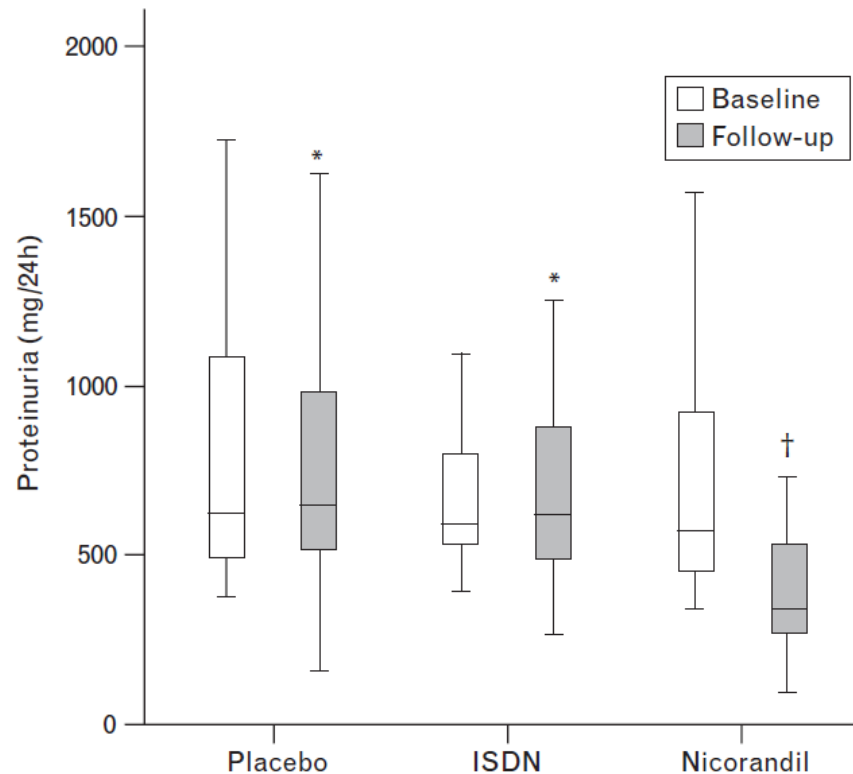
Nicorandil: Clinical Evidence for Renoprotection

Chronic Kidney Disease



Clinical Setting	Outcome	Reference
Chronic Kidney Disease		
Proteinuric patients (n=136) randomized to placebo, ISDN or nicorandil for 6 months	<ul style="list-style-type: none"> • Dose 15 mg/day for 6 months • Significant (44%) reduction in proteinuria ($p < 0.0001$); • Significant reduction in urinary endothelin-1 excretion 	Lee & Chang, 2009
Hemodialysis patients (n=129) who underwent PCI and were randomized to chronic placebo or nicorandil	<ul style="list-style-type: none"> • Dose 15 mg/day • Significant improvement in 3-year all-cause survival (79% vs 61%) ($p = 0.01$) • Significant improvement in 3-year cardiac death-free survival (87% vs 71%) ($p = 0.009$) 	Nishimura et al., 2009

Patients Treated with Nicorandil Had Significantly Lower Urine Protein Excretion¹ at Follow-Up² Compared to Baseline



1 Proteinuric (300– 3000 mg/day), valsartan-treated hypertensive patients with blood pressure less than 140/90 mmHg

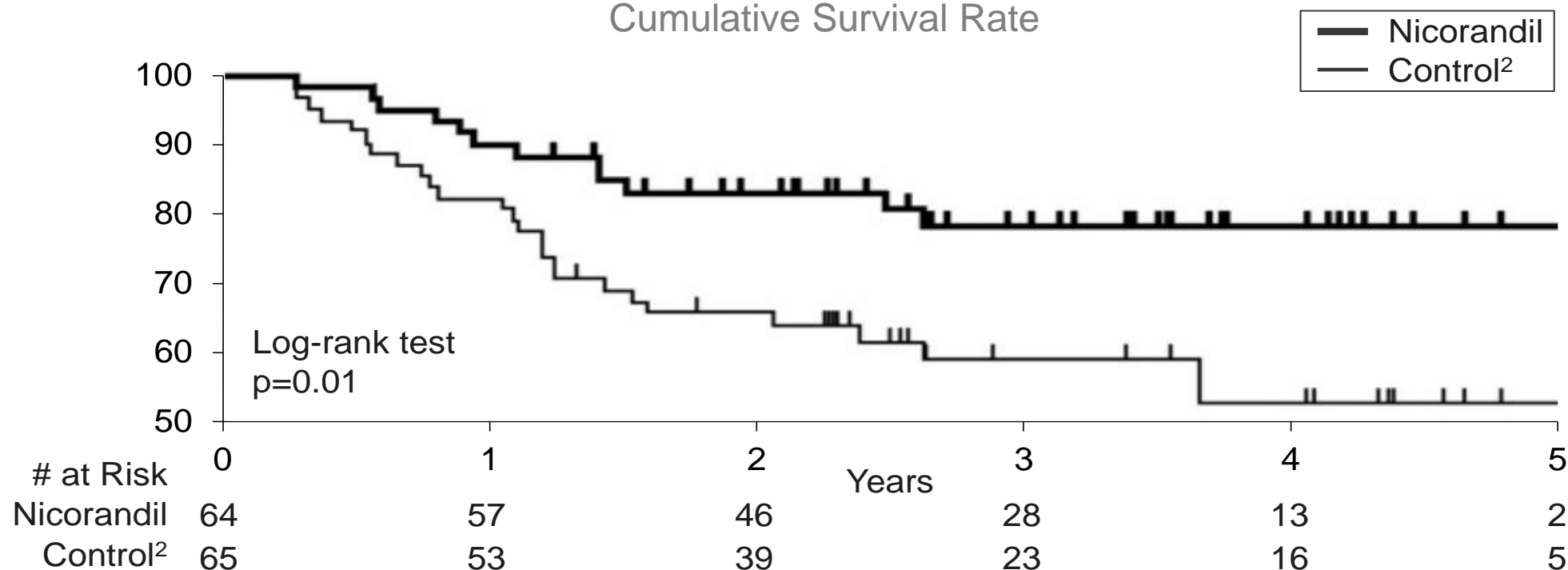
2 Post 6-month intervention therapy

SOURCE: Lee TM, et al. J of Hypertension.2008; Updated as of 3/3/22

Nicorandil Reduces the Risk of Death in Hemodialysis Patients Undergoing PCI Compared to Control



KM Graph for All-Cause Death¹ in Nicorandil (n=64) and Control² Groups (n=65)
Cumulative Survival Rate

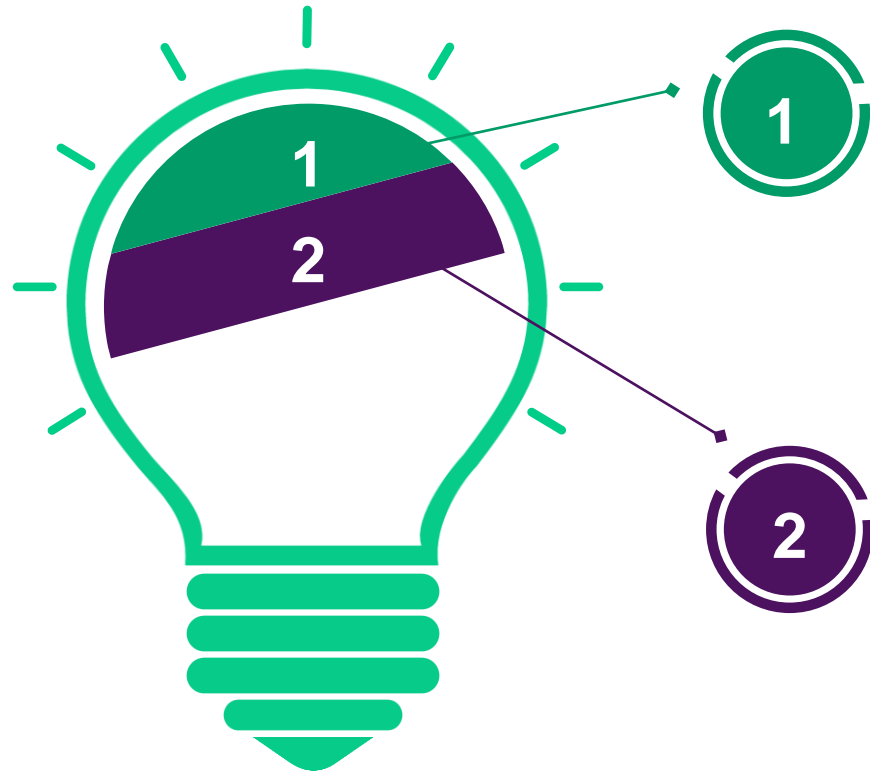


¹ In hemodialysis patients who had obtained complete coronary revascularization (absence of both restenosis and de novo coronary lesions) by means of 1 or more PCI procedures

² Lack of nicorandil

Nishimura M, et al. Am J Kidney Dis. 2009.; Updated as of 3/3/22

UNI-494 Global Intellectual Property



UNI-494 is protected by a broad issued patent

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

Additional patents filed for UNI-494 in the U.S. and globally

- If granted, would expire 2040
- International patent applications planned from this patent family
- Additional multiple patent applications being filed

UNI-494: Development Strategy



- 1 UNI-494 MOA which targets mitochondrial dysfunction has clinical potential in numerous disease states (renal, cardiac, hepatic, ophthalmic, neurologic)
- 2 MHRA (UK) clearance and Phase 1 trial started in the UK
- 3 FDA IND filing for Phase 2 POC study (trial expected in 2H 2023)
- 4 Explore partnering collaborations for non-renal indications

Unicycive Leadership



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



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

\$130 Million in Long-Term Financing



Having the financial backing of both existing and new investors from these high profile, healthcare focused funds provides strong validation of the best-in-class potential for Renazorb® and provides funding for its commercial launch, if approved.

Shalabh Gupta, M.D.,
CEO of Unicycive



Catalyst Rich 2023 and Beyond



RENAZORB

- ✓ FDA alignment on regulatory path
- ✓ Successful BE study in healthy volunteers
- ✓ License agreement in China
- ✓ License agreement in S Korea
- ❑ NDA filing in mid 2023
- ❑ Additional partnering/licensing
- ❑ Buildout of commercial infrastructure

UNI-494

- ✓ Animal safety studies completed
- ✓ Drug supplies for clinical studies manufactured
- ✓ MHRA approval to initiate first in human trial
- ✓ Phase 1 initiated (1Q'23)
- ❑ FDA IND filing for Phase 2 POC study

✓ Up to \$130 Million Funding to Support through Renazorb Approval and Commercialization

Investor Relations

T: (650) 900-5470

ir@unicycive.com

