



**Allena**  
PHARMACEUTICALS

# Company Presentation

December 2019



# Allena Pharmaceuticals, Inc.

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This presentation also contains estimates and other statistical data made by independent parties and us relating to market size and growth and other data about our industry. This data involves a number of assumptions and limitations, and you are cautioned not to give undue weight to such estimates. In addition, projections, assumptions and estimates of our future performance and the future performance of the markets in which we operate are necessarily subject to a high degree of uncertainty and risk.

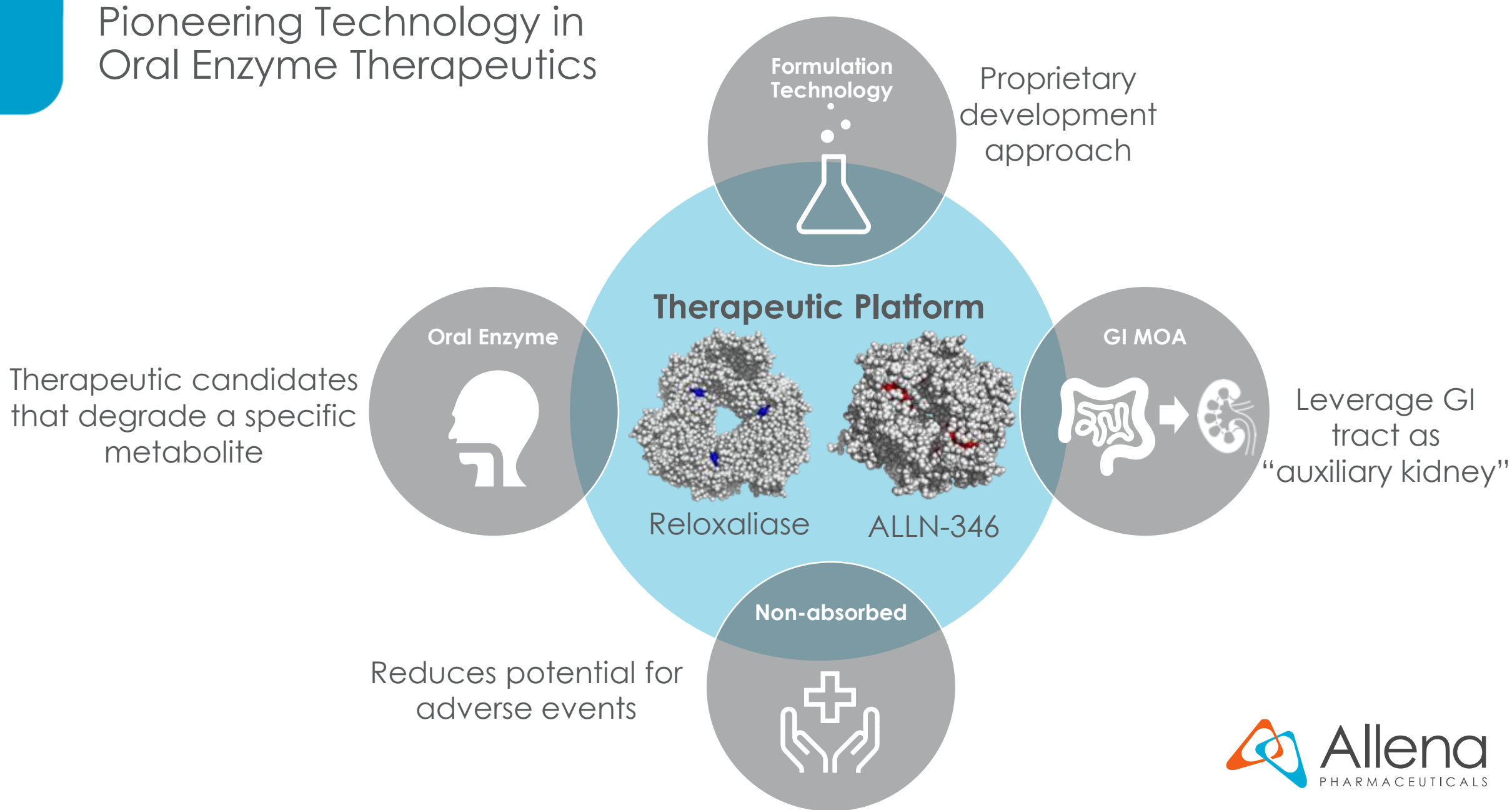
# Our Purpose



*Making a Difference for Patients with  
Rare Metabolic and Kidney Disorders*



# Pioneering Technology in Oral Enzyme Therapeutics



# Positive Topline Results from URIROX-1 and Study 206 Reinforce First-in-Class Potential for EH



## *Achieved Primary Endpoint:*

- ✓ **Highly statistically significant treatment difference (p=0.004), and a 23% reduction in 24-hour UOx from baseline on reloxaliase**
- ✓ **Consistent with Phase 2 studies**
- ✓ **Sustained over four weeks of treatment**
- ✓ **Safe and well-tolerated**

*High UOx and kidney stone burden in enrolled patients: greater than expected event rate*

## **Study 206**

- ✓ **2 patients with CKD Stage 3: reduction in UOx of 29% and 42%, and POx of 42% and 16%**
- ✓ **6 patients with CKD Stage 5: reduction in POx ranged from 19% to 68%**



## *URIROX-2 Positioned for Success*

- Same UOx primary endpoint
- URIROX-2 sized for long-term confirmatory endpoint (overpowered for UOx)
- Adaptive design
- Plan to engage with FDA to potentially streamline program

Plan to engage with regulatory agencies to explore potential registrational path

# Reloxaliase: Therapeutic Candidate with Blockbuster Potential

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- ▶ High Unmet Need in Enteric Hyperoxaluria (EH)
- ▶ Novel Non-absorbed Oral Biologic
- ▶ Successful Completion of URIROX-1, First Pivotal Phase 3 Study
  - Statistically significant and clinically meaningful reduction in UOx
  - Well received by KOLs and treating clinicians
- ▶ FDA Alignment on Accelerated Approval Strategy
  - URIROX-2, Pivotal Phase 3 study ongoing
  - Insights from URIROX-1 could potentially streamline URIROX program
  - Program milestones under review pending FDA engagement and capital requirements
- ▶ Consistent Results across Phase 3 and Phase 2 Studies
- ▶ Potential First FDA-Approved Treatment in EH
- ▶ Worldwide Marketing Rights

# First-in-Class Oral Enzyme Therapeutic Pipeline

Product	Indication	Discovery	Preclinical	Phase 1	Phase 2	Phase 3	Next Milestone	Commercial Rights
Reloxaliase	Enteric Hyperoxaluria						1Q20: FDA engagement to potentially streamline program	Worldwide
	Enteric Hyperoxaluria with Advanced CKD						1Q20: FDA engagement on potential registrational path	Worldwide
ALLN-346	Hyperuricemia with CKD						4Q19: IND filing	Worldwide

# Enteric Hyperoxaluria – Disease Overview

## Gastrointestinal Tract

Dietary Oxalate

Oxalate

Inflammation,  
CKD and ESRD

Kidney Stones

## Enteric Hyperoxaluria (EH)

Enteric: Pertaining to the intestinal tract

Hyper: High or excess

Oxal: Oxalate

Uria: In the urine

Definition: Excess absorption of oxalate in the GI tract due to gastric bypass surgery, inflammatory bowel disease, short bowel syndrome, celiac disease and chronic pancreatitis

Consequence: Kidney stones and calcium oxalate crystal deposits in the kidneys which can lead to inflammation, CKD and ESRD

Therapeutic Strategy:  $\geq 20\%$  reduction in urine oxalate (UOx) could result in a 25-50% lower incidence of kidney stone recurrence, and may increase renal survival<sup>1</sup>

<sup>1</sup>Borghini N Eng J Med. 2002; Taylor and Curhan, Kidney Int. 2008; Curhan GC et al., J Am Soc Nephrol., 28 2017; Clin J Am Soc Nephrol. 2016 Jan 7; 11(1): 119-126.



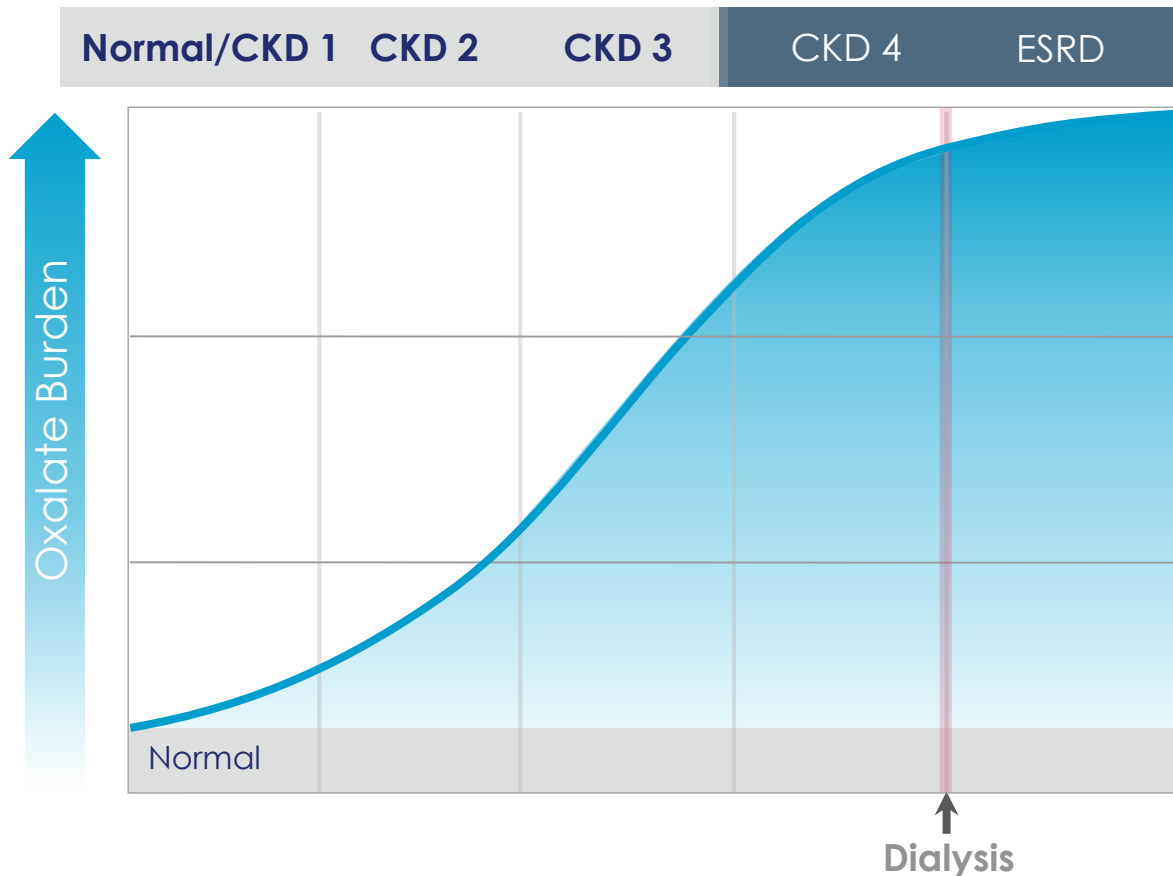
# Unmet Need: Reduce Risk of Oxalate Damage to the Kidney



Study Population:  
Enteric Hyperoxaluria

## Study 206

Enteric Hyperoxaluria with  
CKD and Hyperoxalemia



### Enteric Hyperoxaluria

- Most recognized manifestation is kidney stone disease
- May progress to CKD and nephropathy due to high plasma and/or urine oxalate
- Renal replacement therapy required in > 50% of EH patients with oxalate nephropathy; most remained dialysis dependent with ~30% mortality rate
- By reducing oxalate levels, potential to slow CKD progression, enable kidney transplant and protect new kidney post-transplant

Source: 1. Lumlertgul et al, *Kidney Int Rep* 2018



# Current Treatment Approach is Suboptimal

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## Diet & Behavioral Modification

- ▶ High Fluid Intake to Increase Urine Output
- ▶ Restrictions to Reduce Oxalate Intake  
(*Oxalate rich foods are part of a healthy diet*)
- ▶ Decrease Sodium Intake

## Targeted Therapeutics

- ▶ Thiazide Diuretics (for Hypercalciuria)
- ▶ Potassium Citrate (for Hypocitraturia)

## ESRD

- ▶ Kidney Transplantation
- ▶ Dialysis

## Surgery

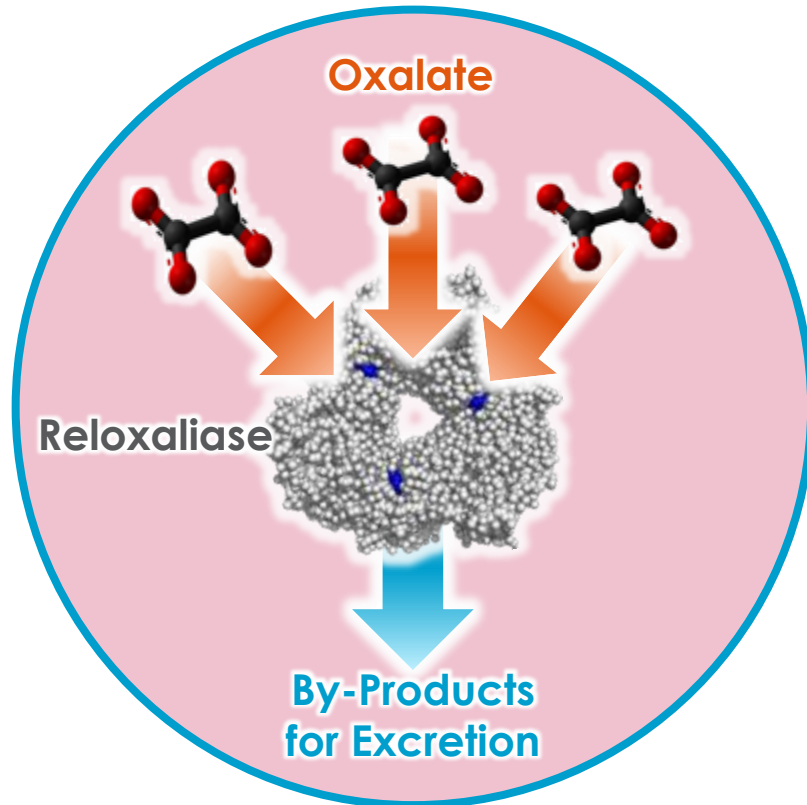
- ▶ Kidney Stone Removal
  - Ureteroscopy
  - Shockwave lithotripsy
  - Percutaneous nephrolithotomy

There are no FDA approved pharmacological therapies to treat any form of hyperoxaluria

# Reloxaliase: First-in-class Therapeutic Candidate for EH

## Mechanism of Action

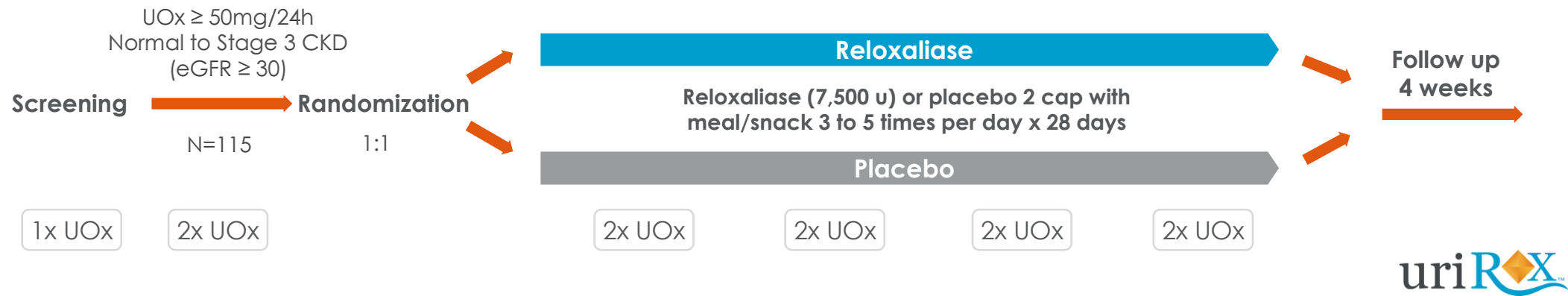
Oxalate Degradation in the Gastrointestinal Tract



## Target Product Characteristics

- ▶ Crystalline Oxalate-Specific Enzyme
- ▶ Oral Capsule Formulation
- ▶ Taken with Food
- ▶ Non-Absorbed/Non-Systemic
- ▶ Room Temperature Stability

# URIROX-1: Evaluate the Safety and Efficacy of Reloxaliase in Patients with Enteric Hyperoxaluria



## Primary Endpoint:

- Percent change from baseline in 24h UOx excretion during Weeks 1 to 4

## Key Secondary Endpoint:

- Proportion of subjects with a  $\geq$  20% reduction from baseline in 24h UOx excretion during Weeks 1 to 4

## Pre-specified, Stratified Analysis

- Subset analysis of the primary and lead secondary endpoint in subjects with a history of bariatric surgery

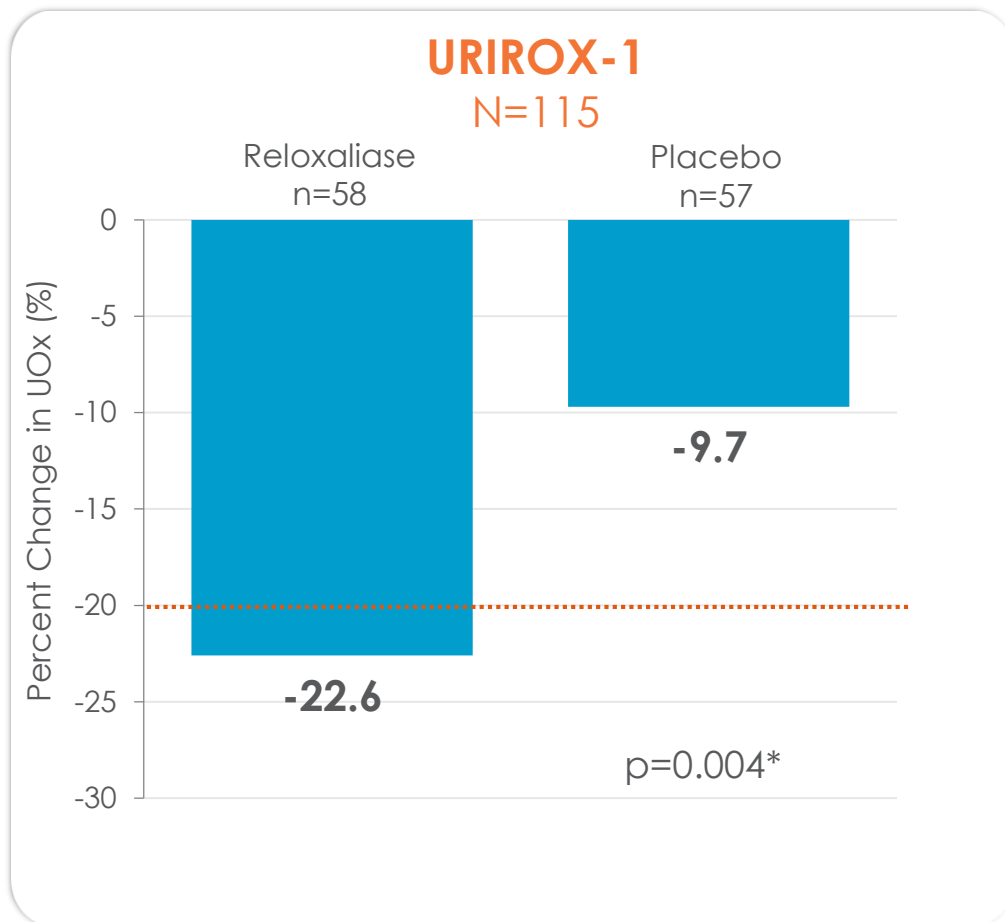
# URIROX-1: Patient Demographics and Baseline Characteristics

Category / Statistic	Reloxaliase (N=58)	Placebo (N=57)
Age (years) – Mean (SD)	58.7 (10.09)	58.6 (10.18)
Gender, n (%) Female	28 (48.3)	27 (47.4)
Enteric condition, n (%)		
Bariatric surgery [Roux-en-Y gastric bypass]	40 (69.0) [27 (46.6)]	38 (66.7) [27 (47.4)]
Inflammatory bowel disease	10 (17.2)	10 (17.5)
Short bowel syndrome	3 (5.2)	8 (14.0)
Pancreatic insufficiency	3 (5.2)	0
Other	2 (3.4)	1 (1.8)
Baseline UOx (mg/24h) – Mean (SD)	87.3 (28.87)	91.1 (41.64)
Baseline UOx ≥ 90 mg/24h, n (%)	22 (37.9)	23 (40.4)
Number of kidney stone episodes in past 5 years- Mean (SD)	8.8 (27.49)	14.2 (43.23)
eGFR (mL/min/1.73m <sup>2</sup> ) - Mean (SD)	76.4 (22.71)	80.5 (24.60)
CKD Stage 3, n (%)	16 (27.6)	14 (24.6)

## High Burden of Disease

- ▶ Baseline UOx of 89.2 mg/day
- ▶ Average 11 stone events in last 5 years
- ▶ 16.5% reported KS events during study<sup>1</sup>
- ▶ 26% CKD Stage 3

# URIROX-1 Primary Endpoint: Statistically Significant Reduction of UOx



- ▶ Achieved primary endpoint
- ▶ Highly statistically significant response versus placebo (P=0.004)
- ▶ 22.6% reduction in UOx from baseline (LS mean)
- ▶ -14.3% LS mean treatment difference

\*Percent change from Baseline in 24-hour UOx excretion during Weeks 1 to 4

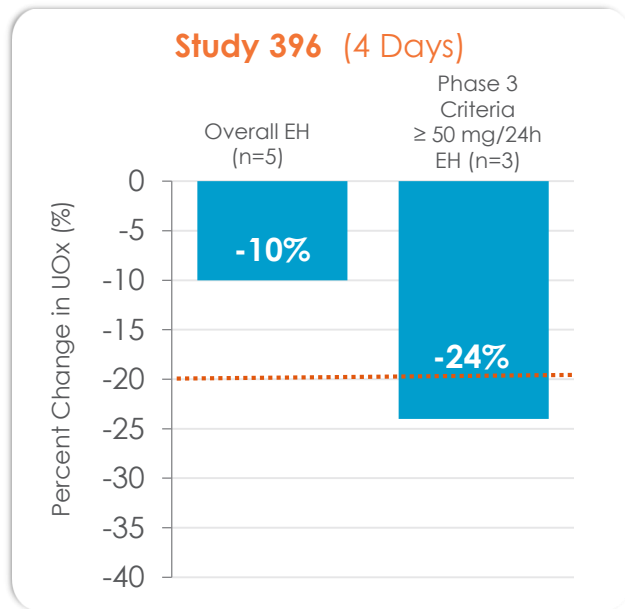
# URIROX-1: Summary of Efficacy

	Overall Population		Pre-Specified Sub-Population Analysis	
	Reloxaliase (N=58)	Placebo (N=57)	Bariatric Reloxaliase (N=40)	Bariatric Placebo (N=38)
<b>PRIMARY ENDPOINT: Percent change in 24h UOx from Baseline during Weeks 1-4</b>				
Comparison in percent change from baseline <sup>a</sup>				
LS mean relative ratio (95% CI) <sup>b</sup>	-14.329 (-22.81, -4.92)		-16.190 (-26.68, -4.20)	
P-value	<b>0.004</b>		<b>0.010</b>	
<b>SECONDARY ENDPOINT: Proportion with ≥20% Reduction in 24h UOx from Baseline during Weeks 1-4</b>				
n/N (%)	28/58 (48.3)	18/57 (31.6)	20/40 (50.0)	11/38 (28.9)
Comparison between treatments <sup>c</sup>				
Odds ratio (95% CI)	2.141 (0.97, 4.74)		2.891 (1.07, 7.82)	
P-value	<b>0.061</b>		<b>0.036</b>	

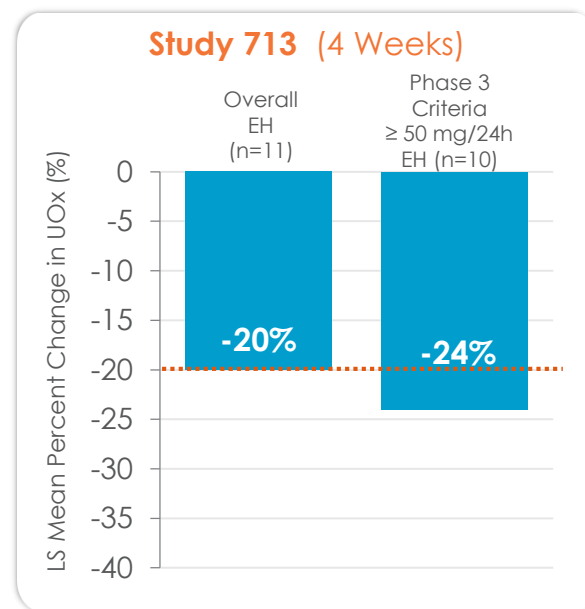
CI, confidence interval; LS, least squares; MMRM, mixed model repeated measures; N, number of subjects dosed; SE, standard error  
<sup>a</sup>Baseline is defined as the average of the UOx values derived from the two baseline 24-hour urine collections prior to randomization.  
<sup>b</sup>LS means, CIs, and p-values are based on an MMRM model.  
<sup>c</sup>Odds ratio, confidence interval, and p-value are from a stratified logistic regression model.

# Consistent Reloxaliase Treatment Effect Across Phase 2 and Phase 3 Studies

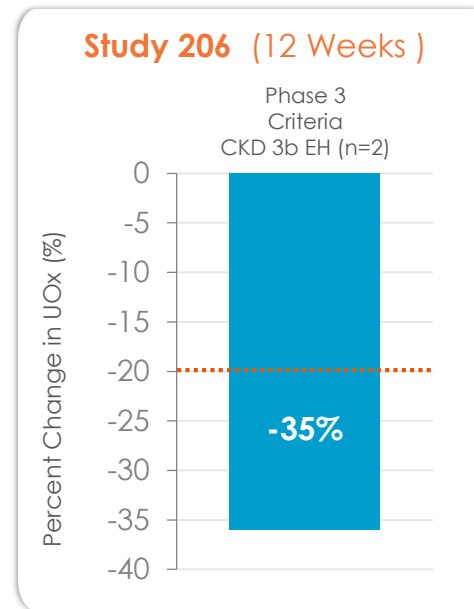
- ▶ Consistent reduction in UOx of  $\geq 20\%$  from baseline in reloxaliase treated patients
- ▶ Highly significant response in pivotal trial compared to placebo (P=0.004)
- ▶ Well tolerated



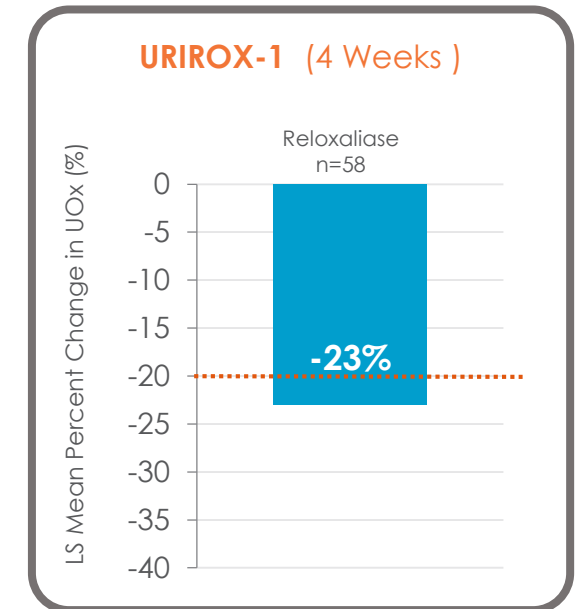
■ UOx Presented at ASN 2014



Presented at ASN 2017



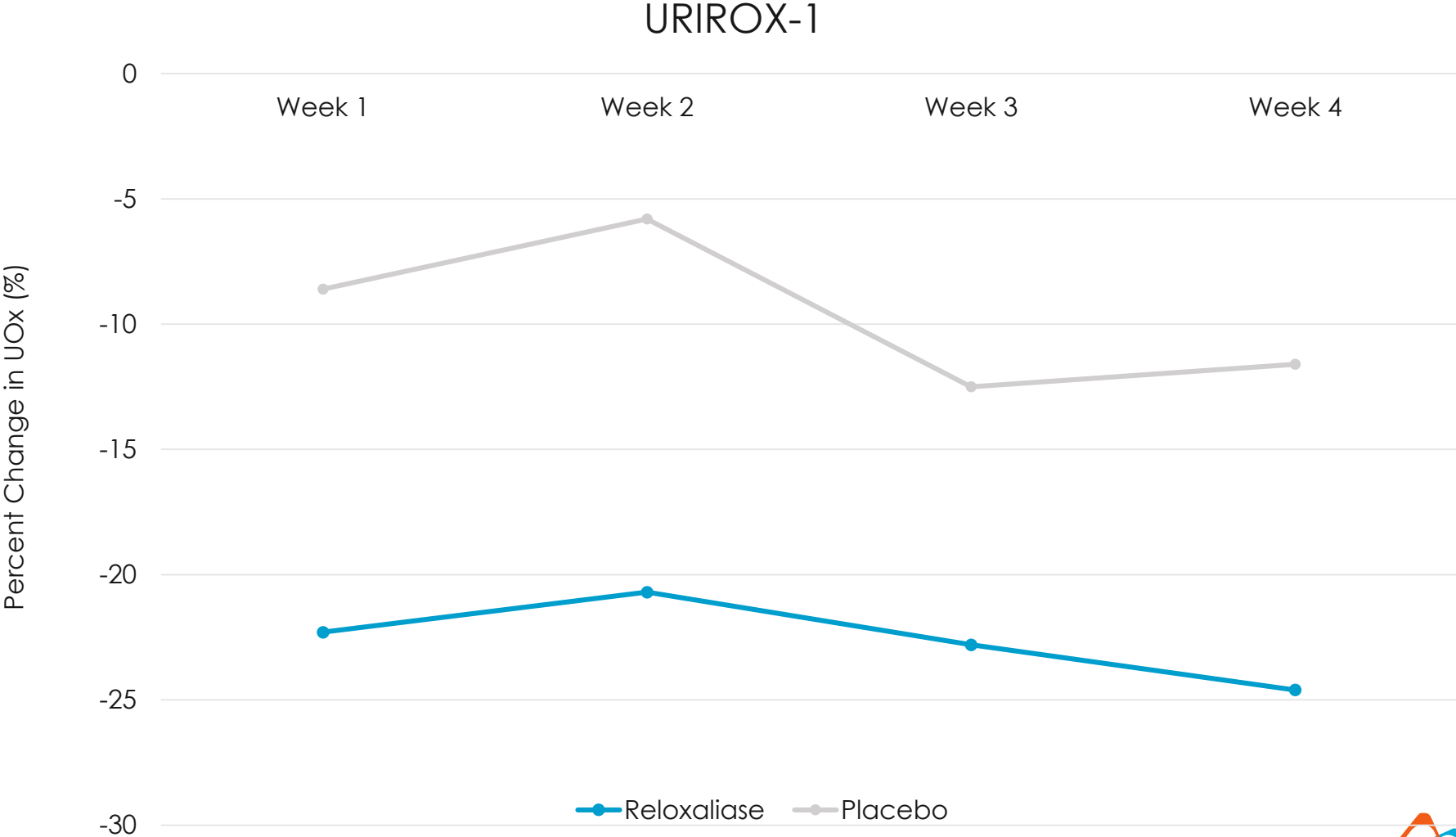
Presented at OHF 2019



Presented at ASN 2019



# Reloxaliase Demonstrates Sustained Reductions in UOx Across Weeks 1-4



# Reloxaliase Generally Well-Tolerated in Clinical Trials to Date

	Study 396	Study 649		Study 713		URIROX-1	
	All (n=16)	Reloxaliase (n=30)	Placebo (n=24)	Reloxaliase (n=32)	Placebo (n=35)	Reloxaliase (n=58)	Placebo (n=57)
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
<b>TEAE<sup>1</sup></b>	9 (56.3%)	13 (43.3%)	6 (25.0%)	16 (50%)	22 (62.9%)	40 (69.0%)	30 (52.6%)
<b>Severe TEAE</b>	0	0	0	0	0	1 (1.7) <sup>4</sup>	0
<b>Related TEAE</b>	2 (12.5%)	5 (16.7%)	2 (8.3%)	3 (9.4%)	8 (22.9%)	17 (29.3%)	11 (19.3%)
<b>Serious AE (SAE)</b>	0	1 (3.3%) <sup>2</sup>	0	0	0	1 (1.7%) <sup>4</sup>	0
<b>Related SAEs</b>	0	0	0	0	0	0	0
<b>AEs Leading to Study Drug Withdrawal</b>	0	1 (3.3%) <sup>2</sup>	0	0	2 (5.7%) <sup>3</sup>	0	1 (1.8%)
<b>AEs Leading to Death</b>	0	0	0	0	0	0	0

1. TEAE = Treatment emergent adverse events are defined as AEs with onset at the time of or following the first dose of treatment with study drug through 7 days after their last dose of study medication, or AEs starting before the start of treatment but increasing in severity or relationship at the time of or following the start of treatment through 7 days after their last dose of study medication.
2. One subject reported congestive heart failure of moderate severity, considered not related to study drug, but secondary to a recent cardioversion for atrial fibrillation. This resulted in hospitalization and withdrawal from the study; same subject in both rows.
3. Two placebo treated subjects withdrew from study drug, one after nearly 4 weeks of treatment due to nausea, considered not related, and another due to hives/dermatitis with onset 3 days after starting placebo, considered possibly related.
4. Unrelated to reloxaliase

# Phase 3 Program Design for Accelerated Approval Strategy

uriROX

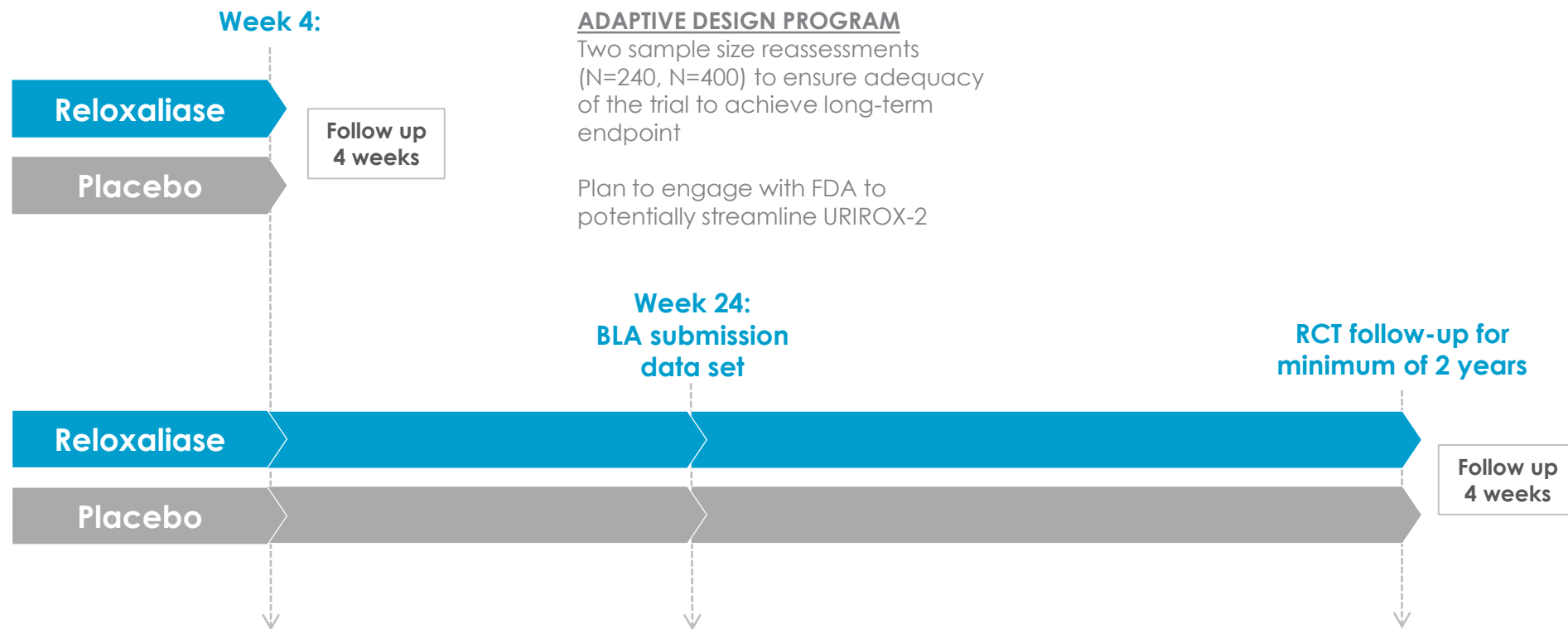
N=115 (1:1)

UOx  $\geq$  50mg/24h, Normal to Stage 3 CKD (eGFR  $\geq$  30)

Reloxaliase (7,500 u) or placebo 2 cap with meal/snack 3-5 x per day

uriROX-2

N $\approx$ 400 (1:1)



## ADAPTIVE DESIGN PROGRAM

Two sample size reassessments (N=240, N=400) to ensure adequacy of the trial to achieve long-term endpoint

Plan to engage with FDA to potentially streamline URIROX-2

### PRIMARY ENDPOINT

Percent change from baseline in 24h UOx excretion during Weeks 1 to 4

### SECONDARY ENDPOINT

Proportion of subjects with a  $\geq$  20% reduction from baseline in 24h UOx during Weeks 1-4

### SECONDARY ENDPOINT

Percent change from baseline in 24h UOx excretion during Weeks 16 to 24

### ADDITIONAL FILING DATA ELEMENTS

- Model of relationship between UOx and KS events, informed by data from the study
- Sufficient conditional power to meet long term primary endpoint

### POST-APPROVAL CONFIRMATORY ENDPOINTS

**Primary:** Kidney stone disease progression  
**Secondary:** Change in eGFR and ER visits / hospitalizations / procedures for management of kidney stones



# Positive URIROX-1 Results Highlight Potential for Accelerated Approval Submission and Provide Insights for URIROX-2 Success

## Accelerated Approval Submission

- URIROX-2 shares common UOx primary endpoint and key secondary endpoints with URIROX-1
- Sized for demonstrating long-term clinical benefit, URIROX-2 is overpowered to achieve UOx primary endpoint (n~400)
- Consistent and sustained reloxaliase treatment effect
- Continued attractive tolerability profile

## Post-Approval Confirmatory Endpoints

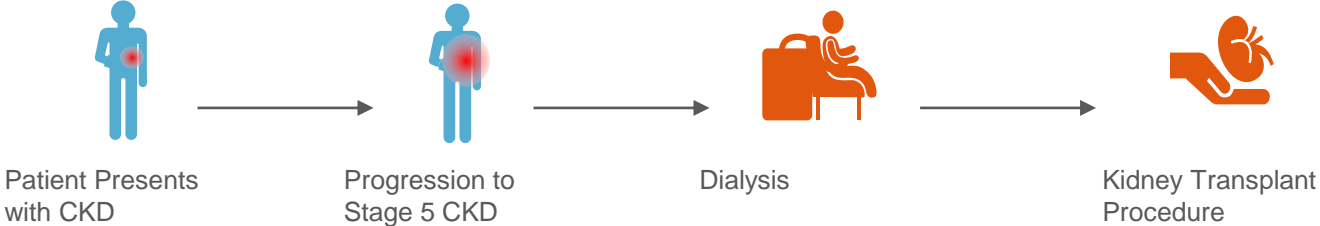
- UOx decrease in placebo group not expected to be sustained in longer URIROX-2 study due to less frequent urine collections and difficulty maintaining dietary changes for 2+ years
- Literature review of metabolic disease studies suggests that treatment response is retained or improved over time despite placebo effect<sup>1</sup> (e.g., hyperphosphatemia, diabetes)
- URIROX-2 kidney stone event rate modeled conservatively based on medical records and claims
  - URIROX-2 will also capture asymptomatic events via imaging
  - URIROX-1 data suggests higher rate of stone events

Plan to engage with the FDA in 1Q20 to discuss measures to potentially streamline URIROX-2



# Reloxaliase has Potential to Benefit EH Patients With Advanced CKD

*EH Patients with CKD can Progress to ESRD*



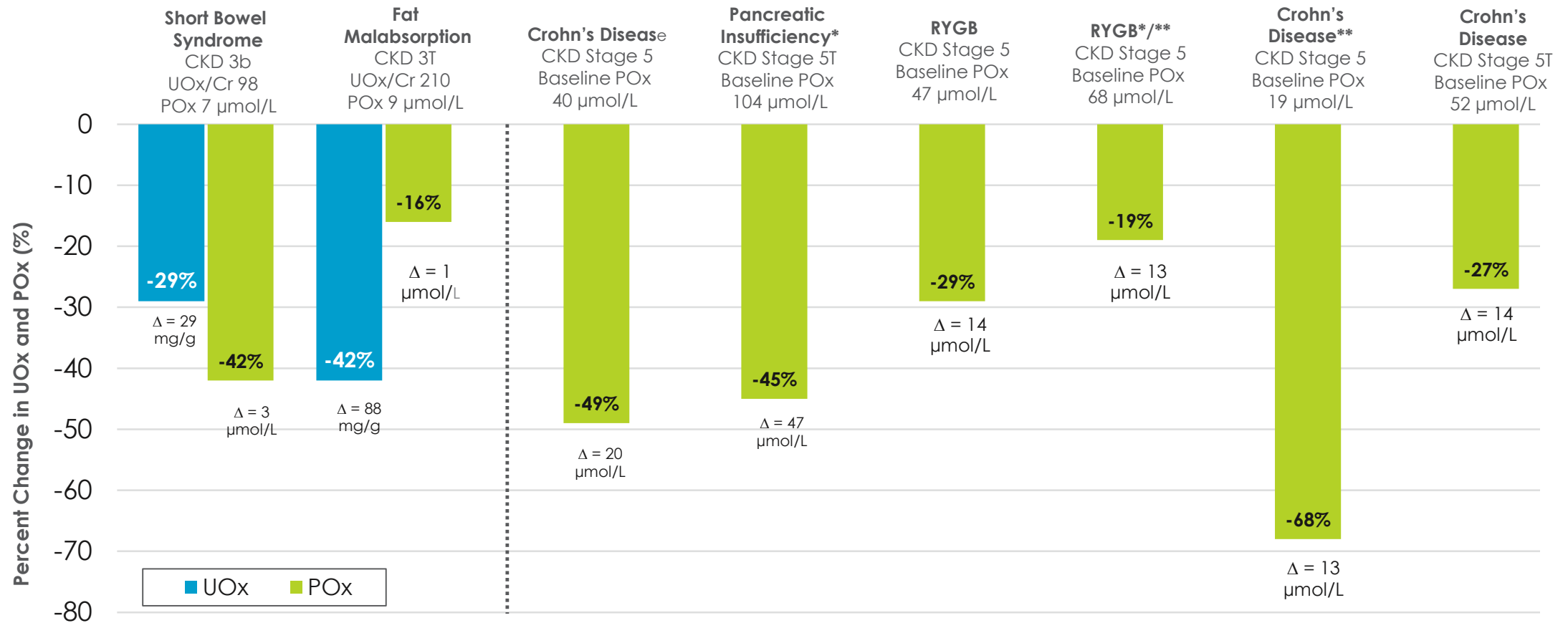
Opportunity		URIROX-2 <sup>†</sup> Population	Study 206 Population*
1	<b>Delay CKD Progression</b> Delay progression to more severe stages of CKD	✓	✓
2	<b>Increase Pre-Transplant Eligibility</b> Lower oxalate levels in EH patients seeking a transplant, allowing them to qualify for a transplant		✓
3	<b>Improve Post-Transplant Graft Success</b> Lower oxalate levels in the post-transplant population to decrease the chance of graft failure and/or renal function decline		✓



<sup>†</sup>URIROX-2 Long-Term efficacy endpoints include change in estimated glomerular filtration rate (eGFR) from Baseline

\*Potential clinical outcomes to be assessed in future studies

# Study 206: Reloxaliase Demonstrates Robust Reduction in Oxalate Burden in Eight EH Patients with Advanced CKD



Plan to engage with regulatory agencies in 1Q 2020 to explore potential registrational path

Urinary Oxalate (UOx mg/d) was normalized to creatinine mg/g; UOx reduction was calculated as a mean change from baseline using UOx measurements over 12 weeks; UOx was not measured in subjects on dialysis or on subjects with eGFR ≤ 15 ml/min/1.73m<sup>2</sup>

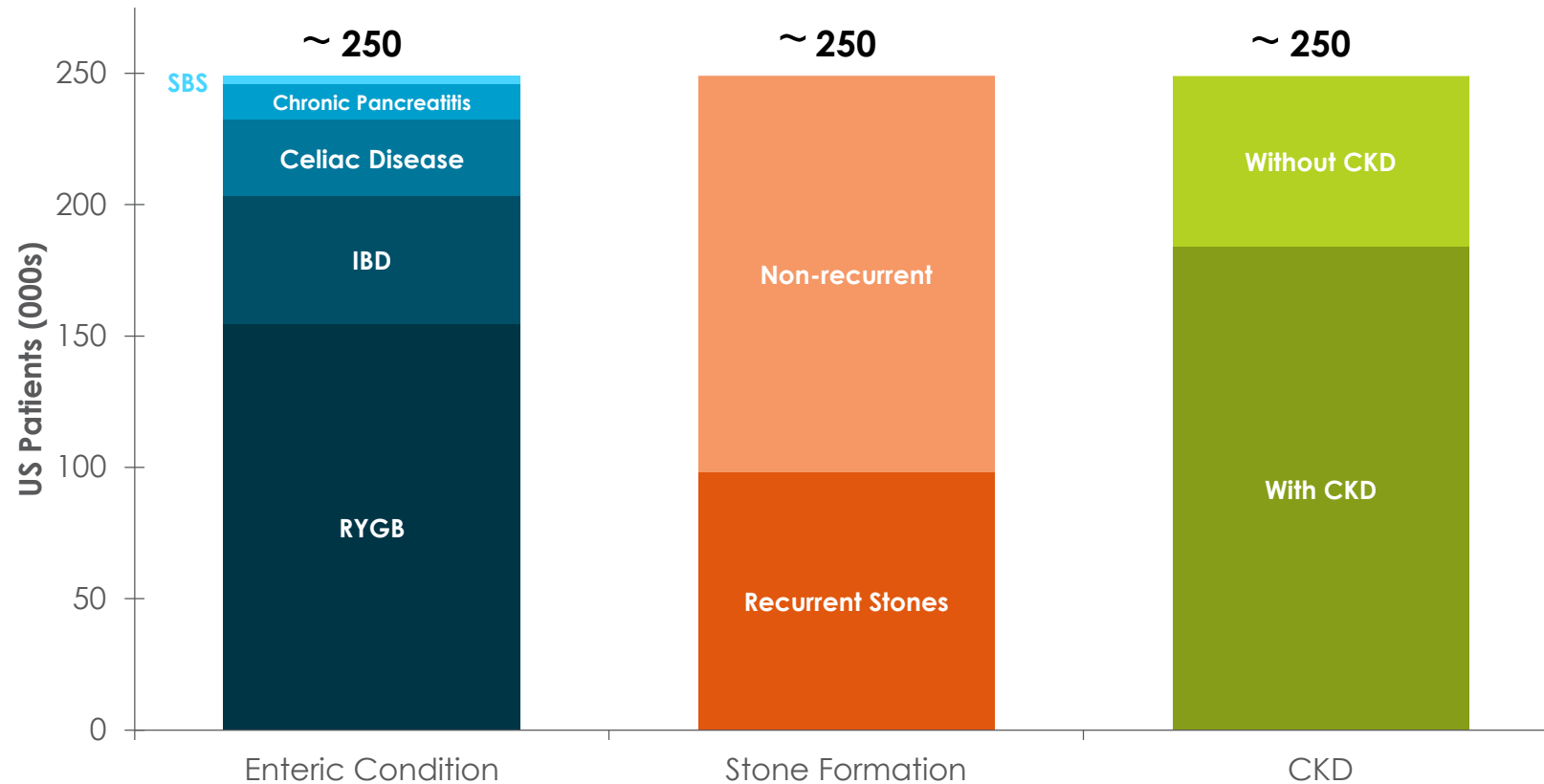
Plasma oxalate (POx µmol/L) reduction was calculated as a mean change from baseline using POx measurements over 12 weeks. \*Subject had only 1 POx sample during the study

\*\*Subject treatment ongoing



# Enteric Hyperoxaluria – Patient Segmentation

## US Enteric Hyperoxaluria Patients, 2019



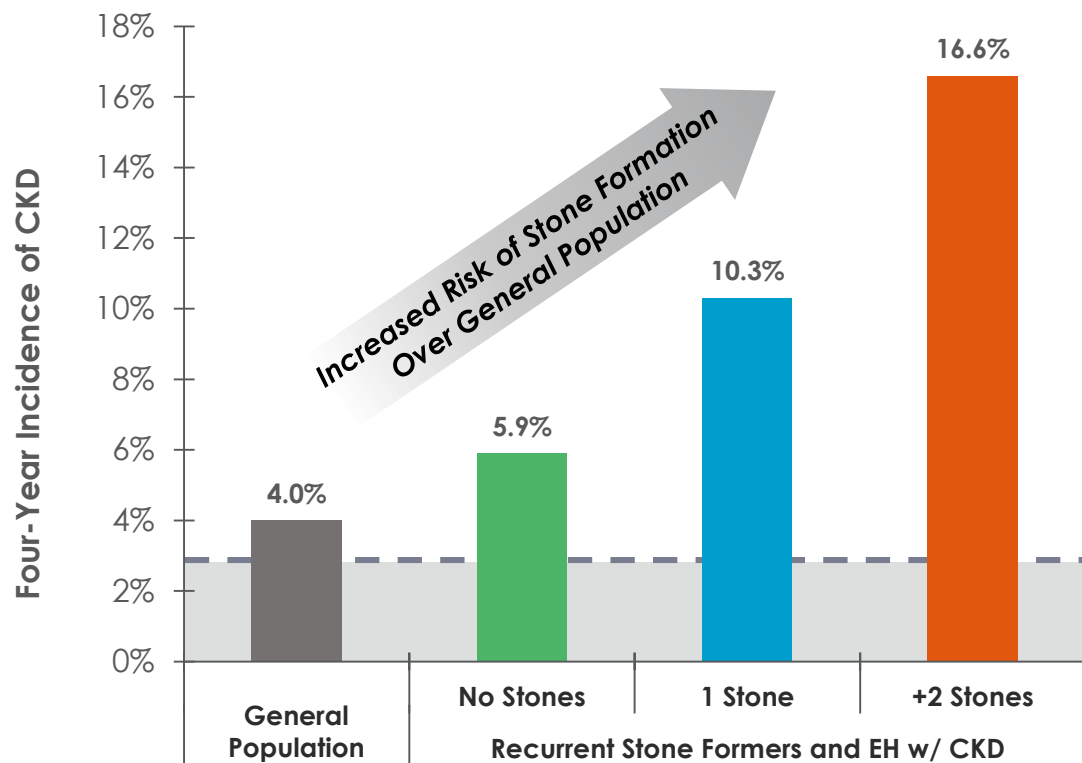
Source: Health Advances interviews and analysis, Health Advances EH Patient Markov Model.

# Enteric Hyperoxaluria – Increased Risk of CKD

- ▶ Patients with enteric disease are much more likely to develop CKD, particularly those with a history of kidney stones.






## Risk of Developing CKD

Four-Year Incidence of CKD, Truven Analysis



## Risk of Developing CKD by Enteric Indication

Four-Year Incidence of CKD, Truven Analysis

Enteric Indication	No Stones	1 Stone	+2 Stones
 <b>Crohn's Disease</b>	5.4%	11.3%	15.6%
 <b>Ulcerative Colitis</b>	5.4%	11.8%	15.6%
 <b>RYGB</b>	5.2%	8.7%	16.2%
 <b>Chronic Pancreatitis</b>	10.0%	17.5%	20.5%
 <b>Short Bowel*</b>	9.6%	16.6%	21.5%

\*Small bowel resection or gastrectomy with Roux-en Y.

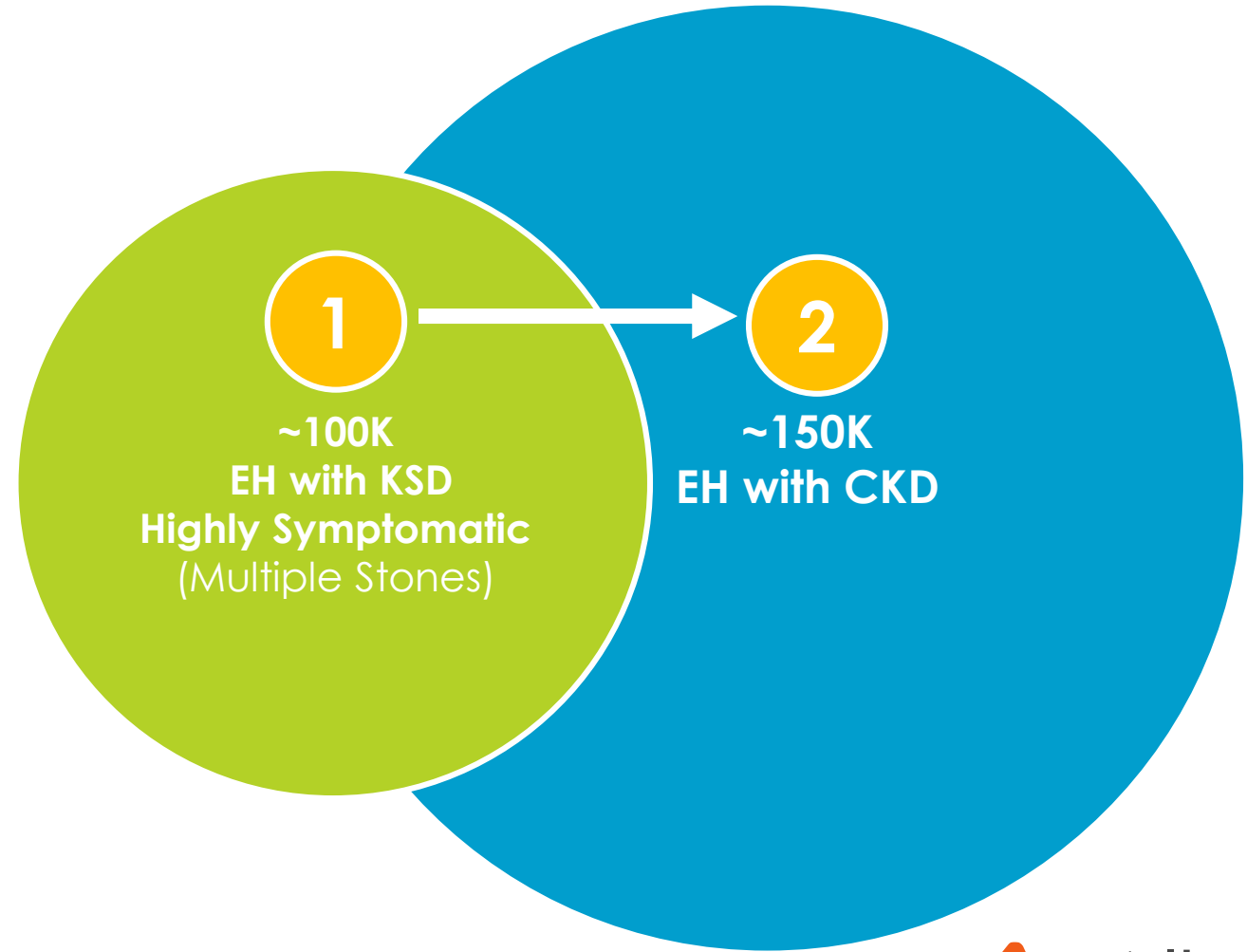
Source: Health Advances analysis, Allena Truven analysis, CDC CKD Surveillance Program, UpToDate.



# Unlocking Blockbuster Potential in Enteric Hyperoxaluria

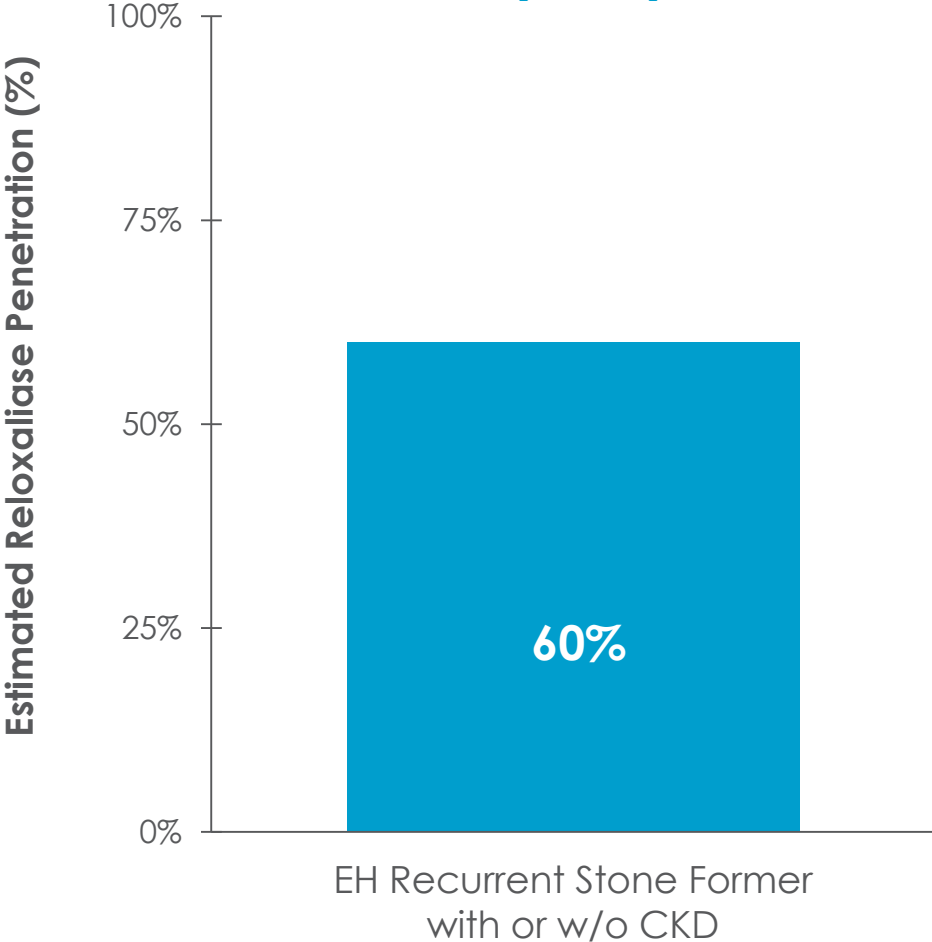
US Target Patient Population is ~250,000

- 1 Launch Focus
- 2 Clinical Outcomes Data to Drive Penetration



# Market Research Supports Early Launch Focus on Recurrent Stone Formers

## Estimated Reloxaliase Penetration in EH (N=18)



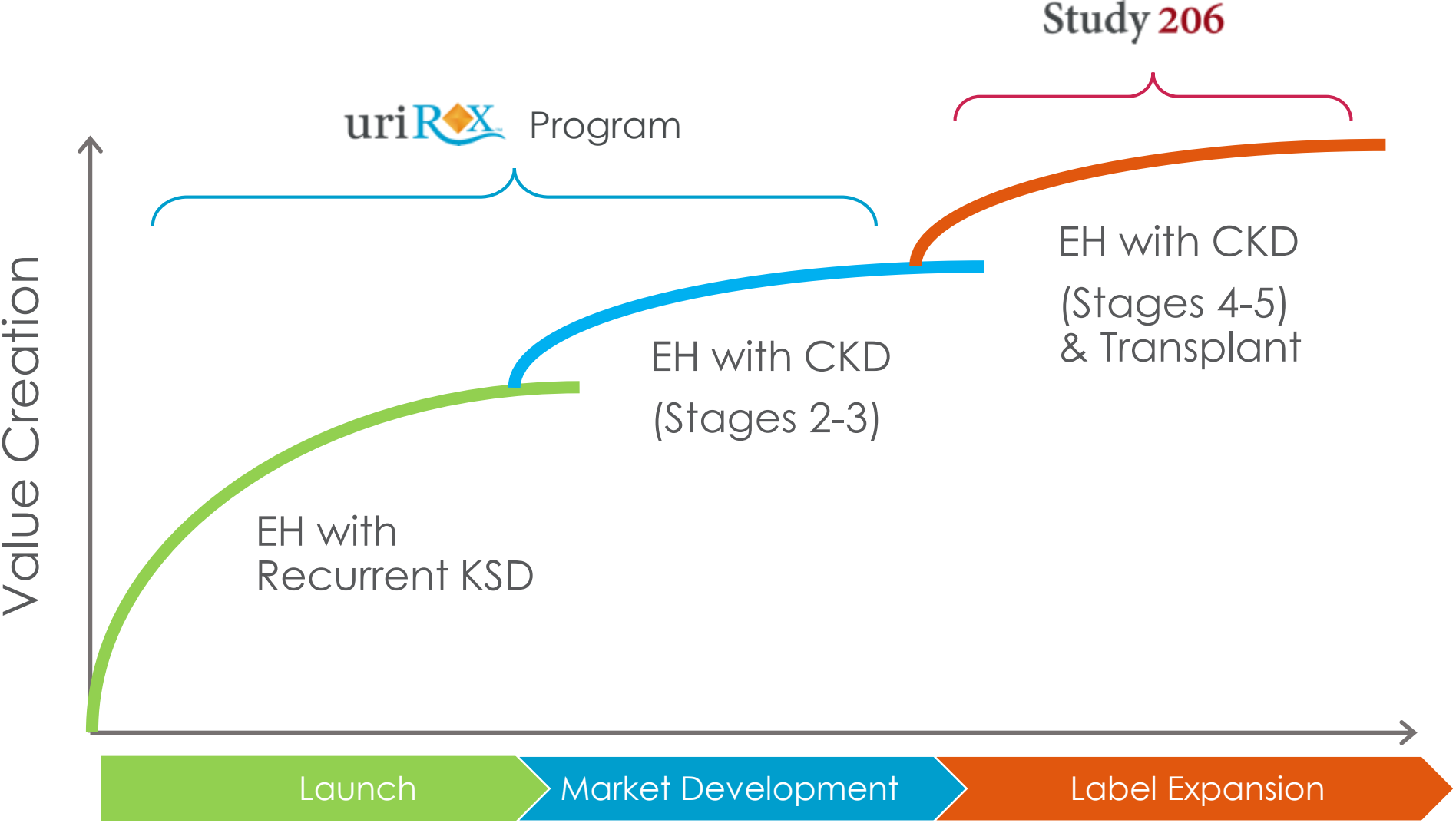
*“Anyone with recurrent stones would benefit from this.”*  
– Nephrologist

*“Recurrent stone formers are the ones who have a real risk in developing more stones or developing CKD. These are the patients I would prescribe this in.”*  
– Bariatric Surgeon



Source: Health Advances physician interviews and analysis.

# Clinical Program Designed to Facilitate Penetration in EH

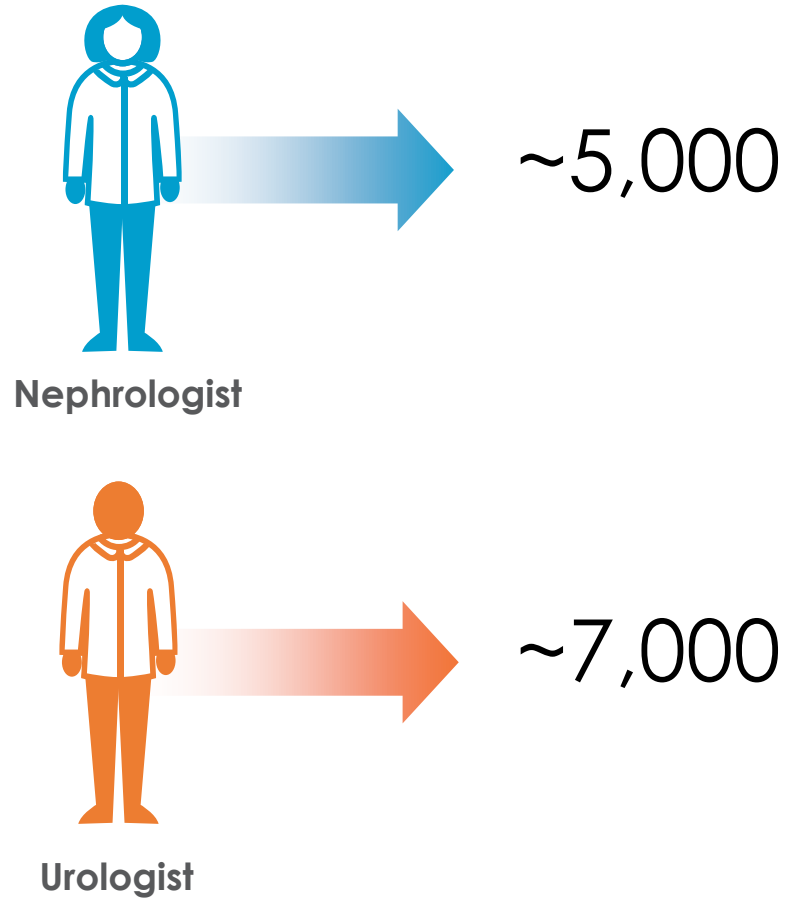


# US Commercialization Strategy

Allena Sales Force Target Audience

High Volume Prescribing Physicians, Treating the Majority of EH Patients with KSD and/or CKD

## Settings of Care



Kidney Stone Clinics



Nephrology and Urology Practices



Hospitals

Source: Health Advances Analysis, 2019

# Reloxaliase: Therapeutic Candidate with Blockbuster Potential

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- ▶ Novel Non-absorbed Oral Biologic
- ▶ Successful Completion of URIROX-1, First Pivotal Phase 3 Study
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- ▶ FDA Alignment on Accelerated Approval Strategy
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