Evaluate the Safety and Efficacy of ALLN-177 in Patients with Enteric Hyperoxaluria (uriROX-1)

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Hyperoxaluria (HOx) & Kidney Damage

- Oxalate is an end-product of carbohydrate and amino acid metabolism, and it is also absorbed from the diet. There is no known physiological requirement for oxalate, and the metabolic and dietary oxalate load is excreted unchanged in the urine.
- Hyperoxaluria (HOx) is a serious metabolic disorder and one of the major risk factors for progression of kidney stone disease and can also lead to chronic kidney disease and end-stage kidney disease.
- Enteric HOx refers to excessive urine oxalate (UOx) excretion that is a complication of increased intestinal oxalate absorption due to an underlying gastrointestinal (GI) condition associated with malabsorption (e.g., bariatric surgery, short bowel syndrome, inflammatory bowel disease, etc.) with UOx levels often approaching levels in primary hyperoxaluria.
- There are no approved pharmacological therapies for HOx. Current management consists of recommendations to restrict dietary oxalate and increase calcium and fluid intake, but these may be difficult to sustain or may be of limited efficacy.
- A Phase 2 randomized clinical trial (NCT02547805) in patients with secondary HOx showed that reloxaliase (ALLN-177) was well-tolerated and led to a meaningful reduction in 24-hr UOx excretion, particularly in patients with enteric HOx, with 24h UOx decreasing 36.25% relative to placebo.

Reloxaliase (ALLN-177): Crystalline Formulation of Oxalate Decarboxylase

- Reloxaliase (ALLN-177) is a first-in-class oral enzyme therapy that specifically targets oxalate:
  - Rapidly degrades oxalate within the GI tract, resulting in less oxalate available for systemic absorption, thereby reducing UOx excretion
  - Reloxaliase is not systemically absorbed to any meaningful extent

Phase 3 Study: uriROX-1 (ALLN-177-301)

Study Objectives

- Determine the efficacy of reloxaliase in reducing UOx excretion in subjects with enteric HOx
- Evaluate the safety of reloxaliase in subjects with enteric HOx

Study Design

- uriROX-1 (NCT03456830) is a global study being conducted at > 30 participating sites in Canada, France, Germany, Italy, Spain, United Kingdom, and United States
- Phase 3, multi-center, randomized, double-blind, placebo-controlled study
- 124 subjects will be randomized 1:1 to either reloxaliase or placebo
- Dose regimen:
  - reloxaliase (3,750 units/capsule) or matching placebo
  - 2 capsules, 3-5 times per day with each meal/snack for 4 weeks
- Two 24-hour urine collections each week during treatment
- 90% power to show ≥ 20 percentage point difference (reloxaliase vs. placebo) in primary efficacy endpoint

Screening: 4 Weeks	Treatment Period: 4 Weeks				Follow-Up: 4 Weeks
Key Entry Criteria	Week 1	Week 2	Week 3	Week 4	Safety Assessments
• Adults with enteric HOx • UOx ≥ 50 mg/24h • eGFR ≥ 30 mL/min/1.73 m²	Reloxaliase 2 capsules (7,500 u) with meal/snack 3-5 times per day Placebo 2 capsules with meal/snack 3-5 times per day				• Physical exam • Clinical labs • Adverse events
1 x UOx, 2 x UOx	2 x UOx	2 x UOx	2 x UOx	2 x UOx	

Continue recommended diet and medications for management of kidney stone risk factors

Key Inclusion Criteria

- 18 years of age or older
- History of HOx, secondary to a known underlying enteric disorder associated with malabsorption (e.g., bariatric surgery, Crohn's disease, short bowel syndrome, or other malabsorption syndrome)
- Has adequate 24-hour urine collection at Screening, with resulting UOx ≥ 50 mg/24hr
- Two adequate 24-hour urine collections at Baseline, with average UOx ≥ 50 mg/24hr (and neither is < 40 mg/24hr)
- If taking concomitant medications for management of kidney stone risk factors, dose regimen must be stable for ≥ 8 weeks

Key Exclusion Criteria

- Has > 30% variability in the ratio of creatinine (mg)/body weight (kg) among the three 24-hour urine samples collected prior to randomization (1 at Screening, 2 at Baseline)
- Unable or unwilling to discontinue Vitamin C supplementation
- Is in acute renal failure or has an estimated glomerular filtration rate (eGFR) < 30 mL/minute/1.73 m² at Screening
- Has an active autoimmune disorder or other condition requiring therapy with high doses of systemic steroids (i.e., > 10 mg/day prednisone or equivalent) or intensification of other immunosuppressant therapy within 4 weeks prior to or during Screening
- Has received study drug (reloxaliase or placebo) in any other ALLN-177 clinical study, or participation in another drug or device clinical trial within 30 days prior to or during Screening

Key Efficacy Endpoints

- **Primary Endpoint:** Percent change from Baseline in 24-hour UOx excretion during Weeks 1-4 (average)
- **Secondary Endpoints:**
  - Proportion of subjects with a ≥ 20% reduction from Baseline in 24-hour UOx excretion during Weeks 1- 4
  - Analysis of efficacy parameters by bariatric surgery vs. other enteric condition subgroup
- **Exploratory Endpoint:** Change from Baseline to Week 4 in urine supersaturation of calcium oxalate

Safety Endpoints

- Treatment-emergent adverse events (TEAEs)
- AEs of special interest (passage of kidney stones, procedures, hospitalizations, or emergency room visits related to kidney stones)
- Subgroup analyses of TEAEs and other selected safety parameters by underlying condition

Trial Information

Global study in >30 participating sites in Canada, France, Germany, Italy, Spain, UK, and USA

Sponsor: Allena Pharmaceuticals
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For information about recruitment and participating research centers:
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