Allena Pharmaceuticals Reports Positive Reloxaliase Topline Results from URIROX-1 Trial and from Study 206

November 7, 2019

Phase 3 URIROX-1 Trial Achieves Primary Endpoint with Statistically Significant Reduction in Urinary Oxalate in Patients with Enteric Hyperoxaluria

Phase 2 Study 206 Trial Demonstrates Substantial Plasma Oxalate Reduction in Patients with Enteric Hyperoxaluria and Advanced Chronic Kidney Disease

Allena to Present Results at the American Society of Nephrology Kidney Week 2019

Allena to Host Conference Call Today at 8:30 a.m. EST

NEWTON, Mass., Nov. 07, 2019 (GLOBE NEWSWIRE) -- Allena Pharmaceuticals, Inc. (NASDAQ: ALNA), a late-stage, biopharmaceutical company dedicated to developing and commercializing first-in-class, oral enzyme therapeutics to treat patients with rare and severe metabolic and kidney disorders, today announced positive topline results from URIROX-1, its first Phase 3 pivotal trial evaluating reloxaliase in patients with enteric hyperoxaluria (EH), as well as additional data from Study 206, its Phase 2 trial evaluating reloxaliase in high-risk patients with EH and advanced chronic kidney disease (CKD). In both studies, treatment with reloxaliase led to substantial reductions in measures of oxalate burden. URIROX-1 met its primary endpoint, demonstrating a statistically significant change from baseline in 24-hour urinary oxalate (UOx) excretion compared to placebo (p=0.004).

“We are excited to present positive results from two separate trials of reloxaliase at ASN. The demonstration of reloxaliase’s ability to consistently and significantly reduce UOx for patients in URIROX-1, and also reduce plasma oxalate (POx) in patients with EH and advanced CKD in Study 206, is an important step in the development of reloxaliase as a potential first-in-class therapy for people living with EH,” said Louis Brenner, MD, President and Chief Executive Officer of Allena Pharmaceuticals. “Sharing positive Phase 3 data from our study for a patient population with a high disease burden and without a currently available treatment option represents a key milestone for Allena and the patients we serve. We are grateful for the continued support of our patients, investigators, and partners.”

Dr. Brenner continued, “We look forward to analyzing the full datasets from URIROX-1 and Study 206. We plan to apply these insights to our ongoing clinical development of reloxaliase, including potentially the adaptive design elements of URIROX-2, as we pursue an accelerated approval regulatory strategy. In addition, based on the robust reduction of POx demonstrated in Study 206, we also plan to explore a registrational path for reloxaliase as a potential treatment for patients with EH and advanced CKD, a life threatening condition.”

URIROX-1 Results:

URIROX-1 is a multicenter, global, randomized, double-blind, placebo-controlled study conducted to evaluate the safety and efficacy of reloxaliase in 115 patients for a four-week treatment period. Patients were randomized 1:1 to receive either reloxaliase or placebo and took ~240 mg (equivalent to 7,500 units) of reloxaliase or placebo with each meal or snack three to five times per day.

The study achieved its primary endpoint, with a mean reduction of 22.6% in average 24-hour UOx excretion measured during Weeks 1-4 among patients treated with reloxaliase, compared to 9.7% in the placebo group (least square (LS) mean treatment difference of -14.3%, p=0.004). Additionally, in a pre-specified secondary endpoint, the stratified analysis of the primary endpoint in bariatric surgery patients (68% of the total study population), patients treated with reloxaliase achieved a mean reduction of 21.2% in average 24-hour UOx excretion, compared to 6.0% for patients treated with placebo (LS mean difference of -16.2%, p=0.01).

The lead secondary endpoint evaluated the proportion of patients on reloxaliase with a ≥20% reduction from baseline in 24-hour UOx excretion during Weeks 1-4. Across the full study population, the proportion of patients treated with reloxaliase who achieved a ≥20% reduction from baseline in 24-hour UOx excretion was 48.3%, compared to 31.6% for patients on placebo (p=0.06). In another pre-specified secondary endpoint, the stratified analysis of the key secondary endpoint in bariatric surgery patients, the proportion of patients on reloxaliase with a ≥20% reduction from baseline in 24-hour UOx excretion during Weeks 1-4 was 50.0%, compared to 28.9% for patients on placebo (p=0.036).

Consistent with prior clinical experience, reloxaliase was well tolerated in the URIROX-1 trial. 114 of 115 patients completed the study, and there were no adverse events leading to treatment discontinuation in the reloxaliase group.

“Patients living with EH can experience painful kidney stone episodes and develop deposits of calcium oxalate crystals over time, both of which damage the kidney and can ultimately progress to CKD. The URIROX-1 results demonstrate that reloxaliase degrades oxalate via its gastrointestinal mechanism and has the potential to provide a significant reduction of the oxalate burden on the kidney, a key outcome for patients with EH,” said David S. Goldfarb, M.D., Professor of Medicine and Physiology and Clinical Chief of Nephrology at NYU Langone Health. “With reloxaliase’s favorable tolerability profile and clinically meaningful effect on UOx levels, this novel therapy, if approved, could potentially transform the treatment landscape for EH patients.”

Study 206 Results:

Study 206 is a multi-center, open-label, single-arm Phase 2 clinical trial designed to enroll between 15 and 20 patients in the United

States and Europe aged 12 and older. Patients orally administer ~240 mg (equivalent to 7,500 units) of reloxaliase with each meal or snack five times a day, for 12 consecutive weeks.

Study 206 has enrolled patients with EH and advanced CKD, which can lead to systemic oxalosis, a potentially life-threatening condition. This includes end stage renal disease patients who are on dialysis and patients who have undergone kidney transplantation.

- Two patients with CKD Stage 3 demonstrated a substantial reduction in 24-hour UOx excretion over Weeks 4 to 12 (reductions of 29% and 42%). These patients also showed a substantial reduction in POx (reductions of 42% and 16%, respectively).
- Six patients with CKD Stage 5, including five patients on dialysis, demonstrated substantial reductions in POx levels over Weeks 4 to 12 (reductions ranged from 19% to 68%).
- Consistent with prior clinical experience, reloxaliase was generally well tolerated in this population with treatment out to 12 weeks.

"I am incredibly encouraged by these data from Study 206, which build on the interim data reported earlier this year and suggest that reloxaliase improves the outlook for patients with EH and advanced CKD, who are often stuck in a vicious and fatal cycle of kidney damage, dialysis and transplantation," said Craig Langman, M.D., Head of the Division of Kidney Diseases, Ann & Robert H. Lurie Children's Hospital of Chicago and Isaac A. Abt, M.D. Professor of Kidney Diseases and Pediatrics at Northwestern University Feinberg School of Medicine. "To my knowledge, this is the first demonstration of a successful pharmacologic strategy for POx reduction in patients with EH. I look forward to partnering with Allena as we explore opportunities to potentially expand reloxaliase's reach to address the full spectrum of EH, including people living with the most severe forms of the disease."

Data from URIROX-1 and Study 206 will be presented in poster presentations at the ASN Annual Meeting this week in Washington, D.C.

Details are as follows:

- **A phase 3, randomized, placebo-controlled trial of reloxaliase in enteric hyperoxaluria (URIROX-1): Clinical characteristics and burden of illness (Abstract SA-PO278)** The session containing this poster is scheduled for Saturday, November 9, 2019, from 10:00am-12:00pm ET.
- **Pilot study of reloxaliase in subjects with severe enteric hyperoxaluria and hyperoxalemia: A pro tem analysis of study ALLN-177-206 (Abstract FR-PO316)** The session containing this poster is scheduled for Friday, November 8, 2019, from 10:00am-12:00pm ET.

Conference Call Information:
Allena Pharmaceuticals will host a live conference call and webcast at 8:30 a.m. ET today to discuss these clinical data. The conference call may be accessed by dialing (866) 521-3704 (domestic) and (210) 874-7779 (international) and referring to conference ID 3040287. A webcast of the conference call will be available in the Investors section of the Allena website at ir.allenapharma.com. The archived webcast will be available on Allena's website approximately two hours after the conference call and will be available for 90 days following the call.

About the URIROX Program
Allena's URIROX program consists of two pivotal Phase 3 trials, URIROX-1 and URIROX-2, which are designed to evaluate the safety and efficacy of reloxaliase in patients with enteric hyperoxaluria.

URIROX-2 is a multicenter, global, randomized, double-blind, placebo-controlled study designed to evaluate the safety and efficacy of reloxaliase in patients with enteric hyperoxaluria, over a minimum treatment period of two years. The trial is designed to enroll 400 patients with 24-hour UOx excretion greater than or equal to 50 mg and a history of kidney stones, and will include patients with normal kidney function as well as chronic kidney disease.

The primary efficacy endpoint of URIROX-2 is the percent change from baseline in 24-hour UOx excretion during Weeks 1-4, comparing reduction in the average UOx excretion across Weeks 1-4 with reloxaliase to placebo, the same primary endpoint as URIROX-1. Secondary endpoints in URIROX-2 include the proportion of subjects with a ≥ 20% reduction from baseline in 24-hour UOx excretion during Weeks 1-4 and percent change from baseline in 24-hour UOx excretion during Weeks 16 to 24. The primary long-term efficacy endpoint to confirm clinical benefit is the proportion of subjects with kidney stone disease progression, defined as a composite of either symptomatic kidney stones or finding of new or enlarged kidney stones using imaging, over a minimum treatment period of two years. Secondary long-term efficacy endpoints to confirm clinical benefit include change in eGFR from baseline and emergency room visits, hospitalizations or procedures for the management of kidney stones.

In January 2019, Allena announced that it reached alignment with the U.S. Food and Drug Administration (FDA) on both the design of URIROX-2 and its strategy to pursue a Biologics License Application (BLA) submission for reloxaliase in patients with enteric hyperoxaluria using the accelerated approval regulatory pathway.

In March 2019, Allena announced an agreement with the Duke Clinical Research Institute, a leading academic research institute within Duke University School of Medicine, to establish and lead an Academic Coordinating Center in support of the URIROX-2 Phase 3 clinical trial and preparation for the potential launch of reloxaliase.

About Study 206
Study 206 is a multi-center, open-label, single-arm Phase 2 clinical trial designed to enroll between 15 and 20 patients in the United States and Europe aged 12 and older. Patients orally administer ~240 mg (equivalent to 7,500 units) of reloxaliase with each meal or snack five times a day, for 12 consecutive weeks. The primary endpoints of the trial are change from baseline in 24-hour UOx excretion and POx levels. UOx is collected only for patients who are not on dialysis.

About Hyperoxaluria
Hyperoxaluria is a metabolic disorder characterized by significantly elevated oxalate levels in the urine, due to either overproduction of oxalate by the

liver from a genetic defect, called primary hyperoxaluria, or from the excess absorption of oxalate from the diet, called secondary hyperoxaluria. Secondary hyperoxaluria is further characterized either as enteric, resulting from a chronic and unremediable underlying gastrointestinal disorder associated with malabsorption, such as bariatric surgery complications or Crohn's disease, which predisposes patients to excess oxalate absorption, or idiopathic, meaning the underlying cause is unknown. Kidney stones, typically the first sign of hyperoxaluria, are often painful and may require interventional procedures. Severe hyperoxaluria in settings of enteric and primary hyperoxaluria may also lead to kidney damage (nephrocalcinosis), chronic kidney disease and end-stage renal disease, which may lead to death.

EH is the more severe subset of secondary hyperoxaluria. Allena estimates that there are approximately 250,000 EH patients with kidney stones and/or CKD in the United States.

About Reloxaliase
Reloxaliase is an orally-administered, recombinant oxalate-degrading enzyme that is being developed for the treatment of hyperoxaluria. Reloxaliase targets oxalate in the GI tract in an effort to reduce the burden of both dietary and endogenously produced oxalate. Reloxaliase has the potential to decrease the oxalate available systemically for deposition as calcium oxalate crystals or stones in the kidneys, as well as reduce long-term kidney complications. In addition, reloxaliase has been granted separate orphan drug designations by the FDA for the treatment of primary hyperoxaluria and for the treatment of pediatric hyperoxaluria. The European Commission has granted orphan drug designation for reloxaliase for the treatment of primary hyperoxaluria.

About Allena Pharmaceuticals
Allena Pharmaceuticals, Inc. is a late-stage biopharmaceutical company dedicated to developing and commercializing first-in-class, oral enzyme therapeutics to treat patients with rare and severe metabolic and kidney disorders. Allena's lead product candidate, reloxaliase, is a first-in-class, oral enzyme therapeutic for the treatment of hyperoxaluria, a metabolic disorder characterized by markedly elevated urinary oxalate levels and commonly associated with kidney stones, chronic kidney disease and other serious kidney disorders.

Forward-Looking Statements

This release contains "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding the topline data from the URIROX-1 clinical trial and Study 206, Allena's ongoing review of these data and implications for the future clinical, regulatory and commercial potential of reloxaliase, statements regarding the ability of reloxaliase to provide clinical benefit to patients, statements regarding future plans for the URIROX-2 clinical trial, including the adaptive design elements of this trial, statements regarding the future development of reloxaliase for patients with EH and advanced CKD, statements regarding the URIROX clinical program generally and alignment with the FDA, and statements regarding Allena's ability to utilize the accelerated approval regulatory pathway for reloxaliase. In addition, it should be noted that additional capital will be required to complete the planned URIROX-2 clinical trial, which capital may not be available to Allena on terms that are acceptable to it, if at all. If adequate funds are not available on a timely basis, Allena may be required to delay, limit, reduce or terminate its clinical development of reloxaliase. Any forward- looking statements in this press release are based on management's current expectations of future events and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: the risk that Allena's clinical and regulatory strategy for reloxaliase may evolve following further review of the topline data from the URIROX-1 clinical trial and Study 206, including without limitation, modifications or termination of the planned URIROX-2 clinical trial; the risk that the results of the URIROX-1 clinical trial may not be replicated in the URIROX-2 or other clinical trials of reloxaliase; the risk that the reduction in 24-hour UOx excretion observed in the placebo arm of the URIROX-1 trial may be observed in the URIROX-2 or other clinical trials of reloxaliase, which may have a negative impact on Allena's ability to secure regulatory approval for this product candidate; the risk that results of earlier studies, or interim results, may not be predictive of future clinical trial results, and planned and ongoing studies may not establish an adequate safety or efficacy profile for reloxaliase to support regulatory approval or the use of the accelerated approval regulatory pathway; risks related to Allena's ability to utilize the accelerated approval pathway for reloxaliase, including the risk that available data at the time of any sample size re-estimation or interim analysis conducted during the URIROX-2 trial may not be sufficient to demonstrate an increased probability of kidney stone events in patients with enteric hyperoxaluria and increasing UOx levels; the risk that the FDA may require that Allena increase the sample size or duration of treatment following the sample size reassessments to be conducted in accordance with the adaptive design element of the trial or otherwise collect additional clinical data from the URIROX-2 or other clinical trials prior to submitting a BLA for reloxaliase; risks associated with Allena's ability to enroll a sufficient number of patients to adequately power URIROX-2 in order to achieve ultimate statistical success for kidney stone disease progression in the long-term follow-up phase of the trial; risks related to Allena's use of UOx and/or POx as surrogate endpoints in its ongoing clinical trials, neither of which it believes have been previously utilized as biomarkers to support regulatory approval of other drug candidates, and the risks related to validating that reductions in UOx and/or POx correlate with meaningful clinical benefit; risks associated with obtaining, maintaining and protecting intellectual property; risks associated with Allena's ability to enforce its patents against infringers and defend its patent portfolio against challenges from third parties; the risk of competition from other companies developing products for similar uses; risk associated with Allena's financial condition and its need to obtain additional funding to support its business activities, including the future clinical development of reloxaliase; and risks associated with Allena's dependence on third parties. For a discussion of other risks and uncertainties, and other important factors, any of which could cause Allena's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Item 1A of Part II of Allena's Quarterly Report on Form 10-Q for the quarter ended June 30, 2019, as well as discussions of potential risks, uncertainties and other important factors in Allena's subsequent filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Allena undertakes no duty to update this information unless required by law.

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