Allena Pharmaceuticals Announces Streamlined Design for URIROX-2, Second Pivotal Clinical Trial of Reloxaliase for Enteric Hyperoxaluria

February 12, 2020

-- Reducing Target Enrollment to 200 Subjects --
-- Conducting Earlier Interim Analysis, Expected in Q3 2021 --
-- Company to Host Conference Call at 8:30 a.m. ET Today --

NEWTON, Mass., Feb. 12, 2020 (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 that it has reached agreement in principle with the U.S. Food and Drug Administration (FDA) on a streamlined design for URIROX-2, the second pivotal clinical trial for reloxaliase, a potential first-in-class, non-absorbed, orally administered enzyme for the treatment of severe hyperoxaluria.

URIROX-2 is designed to incorporate adaptive design elements that could allow for changes to sample size and duration of treatment based on accrued kidney stone (KS) disease progression rates and the conditional probability of achieving ultimate statistical success for KS disease progression in the long-term follow-up phase of the trial.

Based on the higher-than-projected KS event rate and the urinary oxalate (UOx) results observed in the completed URIROX-1 trial, the first pivotal Phase 3 clinical trial for reloxaliase, and subsequent engagement with the FDA, Allena now plans to:

- Reduce the target enrollment from 400 subjects to 200 subjects to support a potential Biologics License Application (BLA) filing for accelerated approval;
- Conduct the first sample size reassessment (SSR) based on total accrued KS events once 130 subjects, rather than 240, have reached six months of treatment; and
- Include a new sponsor-blinded estimation of the conditional probability of achieving the study's primary and key secondary UOx endpoints at the time of the first SSR.

These revisions are expected to streamline URIROX-2, potentially reducing the target length and cost of the trial. The company plans to submit a protocol amendment and associated study documents for the revised trial design in the first quarter of 2020. The interim analysis is projected for the third quarter of 2021.

"We are encouraged by recent progress across our URIROX program. Our analysis of the URIROX-1 clinical results confirmed a significant KS and chronic kidney disease burden among patients with enteric hyperoxaluria and a correlation between KS risk and UOx levels. Based on this observation, coupled with constructive input from the FDA on the design of our pivotal program, we are now in a position to streamline URIROX-2, reducing target enrollment and introducing an earlier interim analysis," said Louis Brenner, M.D., President and Chief Executive Officer of Allena Pharmaceuticals. "We believe the modified design of URIROX-2 will allow us to more efficiently advance reloxaliase toward a potential accelerated approval, and also demonstrate its potential long term clinical benefits. We look forward to working with the physician and patient communities to enroll and conduct URIROX-2. Longer term, we hope the URIROX-2 trial results will allow us to offer reloxaliase as the first pharmacologic treatment for people living with enteric hyperoxaluria."

The adaptive design of URIROX-2 retains a second KS-based SSR, now planned once 200 subjects, rather than 400 subjects, have reached six months of treatment. Analyses at that point will start with estimation of the conditional probability of achieving the primary long-term endpoint of KS disease progression, followed by confirmation of the relationship between UOx and KS events, and also safety and UOx efficacy data for the one month primary and six month secondary endpoints.

Allena plans to file a BLA with the FDA for reloxaliase using the accelerated approval regulatory pathway based on the URIROX-1 trial results and the data package from the second SSR in URIROX-2, pending positive results. Patients would then continue on therapy in URIROX-2 to confirm clinical benefit during the long-term follow-up phase of the trial. Subject to positive results, topline data to support a potential BLA filing are currently expected in the first quarter of 2022.

In November 2019, Allena announced positive topline results from URIROX-1. The study achieved its primary endpoint, demonstrating a statistically significant reduction in UOx, as well as a favorable tolerability profile. Additionally, data from URIROX-1 highlight the increased KS risk associated with high UOx: patients with a higher UOx at baseline had experienced a significantly greater number of KS within five years prior to enrollment, and the mean baseline UOx among patients who experienced a KS event during the URIROX-1 trial was substantially higher than the baseline UOx among patients who did not.

Conference Call Information

Allena will host a live conference call and webcast at 8:30 a.m. ET today to discuss the details of the design of the Phase 3 URIROX-2 trial and also review the results from the completed Phase 3 URIROX-1 clinical trial. James Lingeman, M.D., Professor of Clinical Urology at Indiana University

School of Medicine and the founding director of the International Kidney Stone Institute, will also speak on the call. Dr. Lingeman is an internationally acclaimed expert in kidney stone disease and minimally invasive urologic technologies, who is expert in both state-of-the-art techniques for kidney stone removal and in understanding and preventing kidney stone formation.

The conference call may be accessed by dialing (866) 521-3704 (domestic) or (210) 874-7779 (international) and referring to conference ID 1899236. A webcast of the conference call will be available under “Events and Presentations” in the Investors section of the Company’s website at www.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 Reloxaliase

Reloxaliase is an orally-administered, recombinant oxalate-degrading enzyme that is being developed for the treatment of hyperoxaluria. Reloxaliase targets oxalate in the gastrointestinal 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 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. The URIROX program will support a BLA submission for reloxaliase in patients with enteric hyperoxaluria using the accelerated approval regulatory pathway.

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 200 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 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 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 planned amended trial design for URIROX-2 and agreement in principle with the FDA about the amended design, the timing of sample size reassessments and interim analyses during the URIROX-2 trial, Allena’s ability to utilize the accelerated approval regulatory pathway for reloxaliase, and the timing and nature of regulatory submissions for reloxaliase, and statements concerning the future clinical, regulatory and commercial potential of reloxaliase. The planned amended trial design for URIROX-2 will be subject to a protocol amendment and associated study documents, which Allena plans to submit to the FDA shortly, and additional modifications to URIROX-2 may be required, which modifications could be material. The FDA has advised Allena that, while it agrees in principle with the planned revisions to URIROX-2, certain details, to be specified in the protocol amendment and associated study documents for the revised trial design, remain subject to further clarification and confirmation with the FDA. 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 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 September 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.

Investor Contact

Hannah Deresiewicz
Stern Investor Relations, Inc.
212-362-1200
hannah.deresiewicz@sternir.com

Media Contact

Adam Daley
Berry & Company Public Relations
212-253-8881
adaley@berrypr.com

Source: Allena Pharmaceuticals, Inc.