Dicerna™ Announces the Presentation of Updated Data Demonstrating Utility of its Lead Compound DCR-PHXC in Treating Primary Hyperoxaluria Type 1 (PH1) and Type 2 (PH2)

March 29, 2019

—PHYOX™1 Investigators Reported Potent, Durable Response in Phase 1 Study in Patients with PH1 and PH2 at German Society of Pediatric Nephrology 50th Annual Meeting—

—Company Announces Initiation of Participant Screening for PHYOX2 Pivotal Trial in PH1 and PH2—

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Mar. 29, 2019-- Dicerna™Pharmaceuticals, Inc. (Nasdaq: DRNA), (the "Company" or "Dicerna") a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced the presentation of updated data from its ongoing PHYOX™1 Phase 1 clinical trial evaluating DCR-PHXC, the Company's lead GalXC™ product candidate. The data showed post-dose reductions in 24-hour urinary oxalate levels in adult and adolescent study participants with primary hyperoxaluria type 1 (PH1) and type 2 (PH2). Investigators reported that a single dose of DCR-PHXC led to normalization or near-normalization of urinary oxalate levels in a majority of participants and was generally well-tolerated. The data were presented in a poster on March 28 at the German Society of Pediatric Nephrology 50th Annual Meeting in Cologne, Germany.

"These latest results from PHYOX1 further support the potential potency and duration of action of DCR-PHXC in treating all types of primary hyperoxaluria," stated lead investigator Bernd Hoppe, M.D., head of the Division of Pediatric Nephrology in the Department of Pediatrics at the University of Bonn, Germany. "There is significant unmet medical need among patients suffering from primary hyperoxaluria, as their predisposition to the formation of stones in the urinary tract and kidneys often results in renal damage. Having already established the lactate dehydrogenase A enzyme, or LDHA, as a possibly ideal therapeutic target, PHYOX1 continues to demonstrate the potential ability of DCR-PHXC to improve clinical outcomes for these patients."

Dr. Hoppe and colleagues reported that a single 3.0-mg/kg dose of DCR-PHXC was associated with a mean maximal reduction of 24-hour urinary oxalate of 71% (range: 62% to 80%). The 3.0-mg/kg dose also brought urinary oxalate levels into the normal range (defined as 24-hour excretion <0.46 mmol) at one or more post-dose time points in four of five participants with PH1. The investigators also reported a mean maximal reduction in urinary oxalate of 51% (range: 28% to 72%) with a single 1.5-mg/kg dose, which led to near-normalization (defined as 24-hour excretion <0.6 and ≥0.46 mmol) in three of five participants with PH1. Additionally, among the three participants with PH1 dosed at 6.0-mg/kg, the mean maximal reduction in urinary oxalate was 76% (range: 58% to 100%); one participant in this cohort reached normalization at one or more post-dose time points; two are still in follow-up and may not yet have reached maximal 24-hour urinary oxalate reductions.

In their poster presentation, which is based on a data cut of March 14, 2019, the PHYOX1 investigators also reported that DCR-PHXC was generally well-tolerated in this ongoing study, based on data from 18 participants (15 adults and three adolescents [participants 12-17 years old]) with PH1 (n=15) and PH2 (n=3) and 25 adult healthy volunteers (HVs). To date, four serious adverse events (one mild, two moderate, and one severe) have occurred in three participants, though none were deemed related to the study drug. A total of nine participants (27%) dosed with DCR-PHXC experienced mild or moderate injection site reactions, all of which resolved without intervention within 96 hours.

"DCR-PHXC is the only therapy being investigated in the RNAi space that is designed for the treatment of patients with all forms of primary hyperoxaluria," said Ralf Rosskamp, M.D., chief medical officer of Dicerna. "By demonstrating marked 24-hour reductions in urinary oxalate, along with favorable tolerability, the latest data from PHYOX1 strengthen the rationale for a multi-dose regimen of DCR-PHXC, which we expect will show more pronounced and sustained reductions in the urinary oxalate burden. We are pleased to announce the start of participant screening in the pivotal PHYOX2 trial, which will evaluate a multi-dose regimen of DCR-PHXC in individuals with PH1 and PH2."

The primary objective of the PHYOX1 Phase 1 trial (ClinicalTrials.gov: NCT03392896) is to evaluate the safety, tolerability, pharmacokinetics, and pharmacodynamics of single-ascending doses of DCR-PHXC. Secondary endpoints include the change in 24-hour urinary oxalate excretion from baseline, defined as the mean of two 24-hour collections during screening. The trial is divided into two groups:

- Group A is placebo-controlled, single-blind and includes 25 HVs enrolled at a single site in the United Kingdom with five cohorts dosed at 0.3, 1.5, 3.0, 6.0 or 12.0 mg/kg of DCR-PHXC or placebo (3:2 randomization).
- Group B is open-label and includes 18 participants with PH, including three cohorts of participants with PH1 dosed at 1.5, 3.0 and 6.0 mg/kg of DCR-PHXC, and a fourth cohort with flexible dosing. Group B participants are enrolled among five sites in the European Union and one site in the United States.

The Company initiated the PHYOX1 Phase 1 trial in HVs in the fourth quarter of 2017 and dosed the first participant with PH in May 2018.

About DCR-PHXC

DCR-PHXC is an investigational drug in development for the treatment of all forms of primary hyperoxaluria (PH), and the most advanced product candidate utilizing Dicerna's GalXC™technology. GalXC is a proprietary platform invented by Dicerna scientists to discover and develop next-generation RNAi-based therapies designed to silence disease-driving genes in the liver. In animal models of PH, DCR-PHXC selectively silences lactate dehydrogenase A enzyme, or LDHA, in the liver, blocking the excess production of oxalate, a hallmark of the disease. In preclinical studies of DCR-PHXC, the compound was well tolerated with no adverse effects in the liver. Studies have shown that people who are completely deficient in LDHA show no liver dysfunction and can lead normal lives. LDHA deficiency in the liver may be beneficial for patients with PH, as the *LDHA* enzyme is implicated in the abnormal production of oxalate in PH, which in turn is responsible for the severe damage to kidneys and other organs in patients with PH.

About Primary Hyperoxaluria (PH)

Primary hyperoxaluria (PH) is a family of severe, rare, genetic liver disorders characterized by overproduction of oxalate, a natural chemical in the body that is normally eliminated as waste through the kidneys. In patients with PH, the kidneys are unable to eliminate the large amount of oxalate that is produced, and the accumulation of oxalate can result in severe damage to the kidneys and other organs. Currently, there are no approved therapies for the treatment of PH. There are three known types of PH, each of which results from a mutation in a specific gene, as well as PH for which the molecular basis remains unknown, often referred to as "no mutation detected" (NMD) PH or idiopathic PH (IPH). The known PH mutations cause a decrease in the activity of a specific enzyme in the liver, triggering an increase in oxalate production. In each case the decreased enzyme activity changes the balance of intermediary metabolites, resulting in overproduction of oxalate. The three genetically known types of PH are: [1,2]

- PH1, which is caused by a mutation in the AGXT gene, causing a deficiency of the enzyme alanine:glyoxylate-aminotransferase (AGT),
- PH2, which is caused by a mutation in the GRHPR gene, causing a deficiency of the enzyme glyoxylate/hydroxypyruvate reductase (GR/HPR), and
- PH3, which is caused by a mutation in the HOGA1 gene, causing a deficiency of the enzyme 4-hydroxy-2-oxoglutarate aldolase (HOGA).

Patients with severe PH often undergo both liver and kidney transplants, which are major surgical procedures, and subsequently must take immunosuppressant drugs for the rest of their lives. Patients with decreased renal function may also experience oxalosis, which involves a build-up of oxalate in other organs such as the bone, skin, heart, and retina, possibly causing other concomitant, debilitating complications.

PH occurs in an estimated 1 in 120,000 live births around the world.[3] The estimated genetic prevalence of PH1 is 1 in 151,887 births, which implies more than 5,000 patients in the United States and European Union have the disease.[3] The estimated genetic prevalence of PH2 is 1 in 310,055 and that of PH3 is 1 in 135,866.[3] The median age at the first appearance of PH1 symptoms is 5.8 years.[4] The median age at diagnosis of PH1 is between 4.2 and 11.5 years, depending on whether nephrocalcinosis (calcification in the renal parenchyma, the functional part of the kidney) is present.[5] Fifty percent of patients with PH1 reach end-stage renal disease by their mid-30s.[2]

About Dicerna ™Pharmaceuticals, Inc.

Dicerna™Pharmaceuticals, Inc., is a biopharmaceutical company focused on the discovery and development of innovative, subcutaneously delivered RNAi-based therapeutics for the treatment of diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases and viral infectious diseases. Dicerna is leveraging its proprietary GalXC™ RNAi technology platform to build a broad pipeline in these core therapeutic areas, focusing on target genes where connections between target gene and diseases are well understood and documented. Dicerna intends to discover, develop and commercialize novel therapeutics either on its own or in collaboration with pharmaceutical partners. Dicerna has strategic collaborations with Eli Lilly and Company, Alexion Pharmaceuticals, Inc. and Boehringer Ingelheim International GmbH. For more information, please visit www.dicerna.com.

Cautionary Note on Forward-Looking Statements

This press release includes forward-looking statements. Forward-looking statements are subject to risks and uncertainties that could cause actual results to differ materially from those expressed or implied in such statements. Examples of forward-looking statements include, among others, statements we make regarding: (i) the therapeutic and commercial potential of DCR-PHXC, DCR-HBVS and the GalXC™ platform; (ii) research and development plans and timelines related to DCR-PHXC, DCR-HBVS, and GalXC; and (iii) the potential of Dicerna™'s technology and drug candidates in the Company's research and development pipeline. The process by which an early stage investigational therapy such as DCR-PHXC and an early stage platform such as GalXC could potentially lead to an approved product is long and subject to highly significant risks. Applicable risks and uncertainties include those relating to Dicerna's clinical research and other risks identified under the heading "Risk Factors" included in the Company's most recent Form 10-K filing and in other future filings with the Securities and Exchange Commission. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities; the likelihood of Dicerna's clinical programs being executed within timelines provided and reliance on the Company's contract research organizations and predictability of timely enrollment of subjects and patients to advance Dicerna's clinical trials; the potential for future data to alter initial and preliminary results of early stage clinical trials; the unpredictability of the duration and results of the regulatory review of Investigational New Drug Applications (NDAs) and Clinical Trial Applications that are necessary to continue to advance and progress the Company's clinical programs and the regulatory review of NDAs; market acceptance for approved products and innovative therapeutic treatments; competition; the possible impairment of, inability to obtain and costs of obtaining intellectual property rights; and possible safety or efficacy concerns that could emerge as new data are generated in research and development, general business, financial and accounting risks and litigation. The forward-looking statements contained in this press release reflect Dicerna's current views with respect to future events, and Dicerna does not undertake and specifically disclaims any obligation to update any forward-looking statements.

References

1. Oxalosis & Hyperoxaluria Foundation. Overview of hyperoxaluria. 2017. Available at: https://ohf.org/overview/. Accessed July 6, 2017.

2. Rare Kidney Stone Consortium. Primary hyperoxaluria. 2010. Available at: http://www.rarekidneystones.org/hyperoxaluria/physicians.html. Accessed July 6, 2017.

3. Hopp, K, Cogal, A, Bergstralh, E, et al. Phenotype-genotype correlations and estimated carrier frequencies of primary hyperoxaluria. Journal of the American Society of Nephrology 2015; 26(10):2559-2570.

4. van der Hoeven SM, van Woerden CS, Groothoff JW. Primary hyperoxaluria type 1, a too often missed diagnosis and potentially treatable cause of end-stage renal disease in adults: results of the Dutch cohort. Nephrology, Dialysis, Transplantation 2012; 27(10):3855-3862.

5. Tang X, Bergstrath EJ, Mehta RA, Vrtiska TJ, Milliner DS, Lieske JC. Nephrocalcinosis is a risk factor for kidney failure in primary hyperoxaluria. Kidney International 2015; 87:623-631.

View source version on businesswire.com: https://www.businesswire.com/news/home/20190329005064/en/

Source: Dicerna Pharmaceuticals, Inc.

Rebecca Peterson
Head of Corporate Communications
Dicerna Pharmaceuticals, Inc.
PH: 617-642-6235
rpeterson@dicerna.com