Dicerna Announces Late-Breaking Data Supporting Use of DCR-PHXC in Adults with Primary Hyperoxaluria Types 1 and 2 (PH1 and PH2)

October 25, 2018

Single-dose Data from Ongoing PHYOX Phase 1 Trial, Presented at ASN Kidney Week, Show Normalization or Near-normalization of Urinary Oxalate Levels in a Majority of Participants

Reductions in Urinary Oxalate, Combined with Favorable Safety/Tolerability Profile, Lay Groundwork for Planned DCR-PHXC Phase 2/3 Registration Trial, Anticipated to Begin in First Quarter of 2019

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 25, 2018-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced the presentation of late-breaking data from its ongoing PHYOX Phase 1 trial, in which single-dose administration of DCR-PHXC, the Company's lead GalXC™ product candidate, was associated with normalization or near-normalization of urinary oxalate levels in a majority of adult patients with primary hyperoxaluria types 1 and 2 (PH1 and PH2). In a poster presented at the American Society of Nephrology (ASN) Annual Kidney Week 2018 in San Diego, Calif., investigators reported that a single 3.0-mg/kg dose of DCR-PHXC 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 three of four participants, including a mean maximal reduction in 24-hour urinary oxalate of 65%. Investigators also reported that a single 1.5-mg/kg dose led to near-normalization (defined as 24-hour excretion <0.6 and ≥0.46 mmol) in three of four PH1 participants and led to a mean maximal reduction in urinary oxalate of 50% in the five patients dosed at that level, including one PH2 patient. All patients demonstrated a clinically significant reduction in urinary oxalate (defined as >30% reduction compared to baseline).

In their poster presentation, which is based on a data cut of October 1, 2018, the PHYOX investigators also reported that DCR-PHXC is safe and well-tolerated in this ongoing study, based on data from 12 adult participants with PH1 (n=11) and PH2 (n=1) and 25 adult normal healthy volunteers (NHVs). The ASN presentation follows Dicerna's announcement last month of preliminary proof-of-concept for DCR-PHXC, based on interim PHYOX data demonstrating substantial and clinically significant reductions in urinary oxalate in all assessed patients with PH.

"The observed reduction in 24-hour urinary oxalate following a single dose of DCR-PHXC in both PH1 and PH2 participants is a promising sign of this compound's potential potency and duration of action," said Ralf Rosskamp, M.D., chief medical officer of Dicerna. "Based on accumulated experience in animals and humans, we see a strong scientific rationale for a multi-dose regimen of DCR-PHXC, which we anticipate will show even more pronounced and sustained 24-hour urinary oxalate reductions, with potential utility in all types of primary hyperoxaluria. The encouraging findings from PHYOX thus lay the groundwork for Dicerna's planned Phase 2/3 registration trial for DCR-PHXC, which we aim to initiate in the first quarter of 2019, pending regulatory feedback."

"The PHYOX trial continues to generate meaningful and highly encouraging data on urinary oxalate reduction, and we look forward to gaining a more complete view of the magnitude of this effect as the trial progresses," noted PHYOX investigator Bernd Hoppe, M.D., head of the Division of Pediatric Nephrology in the Department of Pediatrics at the University of Bonn, Germany. "We are optimistic about attaining normalization or near-normalization of urinary oxalate in an even greater percentage of patients than we have seen thus far. Such an achievement would be a welcome development for the primary hyperoxaluria community, within which there is a significant unmet medical need."

Dicerna is investigating DCR-PHXC for the treatment of all forms of PH, a family of severe, rare, inherited disorders of the liver that often result in kidney failure. The Company initiated the PHYOX trial in NHVs in the fourth quarter of 2017 and dosed the first patient with PH in May 2018.

The primary objective of the PHYOX 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 a placebo-controlled, single-blind Phase 1 trial in 25 NHVs enrolled at a single site in the United Kingdom.
- Group B is an open-label, multi-center trial of DCR-PHXC in 16 patients with PH, including three cohorts of patients with PH1 dosed at 1.5, 3.0, and 6.0 mg/kg, and a fourth PH2-only cohort with flexible dosing. Group B patients are enrolled at five sites in the European Union (EU) and one site in the United States.

In terms of safety, no severe or serious adverse events have occurred as of the October 1 data cut, and there have been no clinically significant changes in electrocardiography (ECG), vital signs, laboratory or hematology values. Among the 27 participants dosed with DCR-PHXC in both Group A and B, the investigators observed a total of five participants with mild-to-moderate injection site reactions (19%), all of which were transient and resolved without intervention within 24 to 72 hours.

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 lactase dehydrogenase (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 might 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 organ systems 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 idiopathic PH (IPH) or "no mutation detected" (NMD) PH. 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)
- 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 (ESRD) 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, viral infectious diseases, chronic liver diseases, and cardiovascular 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. For more information, please visit www.dicerna.com.

Cautionary Note on Forward-Looking Statements

This press release includes forward-looking statements. Such 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 the GalXC™ platform, including DCR-PHXC; (ii) research and development plans related to GalXC,™ including DCR-PHXC; and (iii) the potential of our technology and drug candidates in our research and development pipeline. The process by which an early stage platform such as GalXC (including DCR-PHXC, our lead product candidate) could potentially lead to an approved product is long and subject to highly significant risks. In general, most earlier stage drug candidates do not ultimately become approved drugs. Applicable risks and uncertainties include those relating to Dicerna's clinical and preclinical research and others identified under the heading "Risk Factors" included in the Company's filings with the Securities and Exchanges Commission (SEC). These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities; the unpredictability of the duration and results of regulatory review of New Drug Applications and Investigational 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, 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.

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