Dicerna Announces Proof of Concept for DCR-PHXC in the Treatment of Primary Hyperoxaluria

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Initial 6-Week Data in PHYOX Phase 1 Trial Show Significant and Sustained Reduction in Urinary Oxalate Levels Following Single-Dose Administration in Adults with PH1 and PH2

A Detailed Data Readout of the PHYOX Trial is Anticipated in Q4 2018

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 5, 2018-- Dicerna Pharmaceuticals, Inc. (Nasdaq:DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced preliminary proof-of-concept data from its ongoing PHYOX Phase 1 clinical trial. A single-dose administration of DCR-PHXC, the Company's lead GalXC™ product candidate, brought urinary oxalate levels into the normal range (defined as 24-hour excretion ≤0.46 mmol) or near-normal range (defined as 24-hour excretion ≤0.6 mmol) in a majority of the eight assessed patients with primary hyperoxaluria type 1 and type 2 (PH1 and PH2). All of the assessed patients experienced substantial and clinically significant reductions in urinary oxalate (defined as >30% reduction compared to baseline). Assessed patients are those patients for whom data are available through Week 6, or Day 43. All assessed patients are adults and include seven patients with PH1 and one patient with PH2.

The interim PHYOX data constitute preliminary clinical proof of concept for DCR-PHXC. Moreover, the investigational agent was safe and well-tolerated during the period of initial observation. The interim data provide a promising indicator of DCR-PHXC's potential potency and duration of action following administration of a single dose, and are consistent with an anticipated once-quarterly administration. Dicerna intends to present a detailed data readout from the PHYOX trial in the fourth quarter of 2018, and plans to initiate a registration trial for DCR-PHXC pending regulatory feedback in the first quarter of 2019.

"We are encouraged to see such an early demonstration of proof of concept in the initial data readout from patients in the ongoing PHYOX trial," said Ralf Rosskamp, M.D., chief medical officer of Dicerna. "The magnitude of urinary oxalate reduction, coupled with the duration of action, appear to validate therapeutic targeting of lactase dehydrogenase, an enzyme involved in the ultimate step of hepatic oxalate production. Based on this novel mechanism of action, DCR-PHXC has the potential to work in all types of primary hyperoxaluria. We look forward to sharing additional results from the PHYOX trial once data from all patients become available."

"The substantial reductions in urinary oxalate appear to confirm that our GalXC platform may effectively reduce target gene expression in humans and suggest that our pioneering application of RNAi may treat all genetic variants of primary hyperoxaluria," said Bob D. Brown, Ph.D., chief scientific officer of Dicerna. "Our results from preclinical GalXC studies appear to have translated smoothly into patients with regards to potency, durability, and tolerability. Looking beyond our DCR-PHXC program, we are encouraged that our GalXC platform will continue to perform in upcoming Dicerna clinical programs, including those in other rare diseases, hepatitis B virus, and various cardiovascular and chronic liver diseases."

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 normal healthy volunteers (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 being enrolled at five sites in the European Union (EU) and one site in the United States.

Initial Results in PHYOX Phase 1 Trial Group B

In the first Group B cohort (1.5 mg/kg), preliminary results following a single administration of DCR-PHXC show that three of four adult patients had urinary oxalate levels in the near-normal range between Days 43 and 57, which are the latest observation days for those patients. The fourth adult, whose baseline urinary oxalate level was 2.28 mmol/24hr, is exhibiting substantial reductions, with the latest observation (Day 95) showing the maximal reduction for that patient (urinary oxalate <1.0 mmol/24hr).

In the second Group B cohort (3 mg/kg), two of four adult patients reached normal urinary oxalate concentrations (<0.46 mmol/24hr) by Day 43. Both of the other patients also have substantial oxalate reductions (one of which does not yet have Day 43 data).

The one adult patient with PH2 in the fourth Group B cohort has also experienced a substantial reduction in 24-hour urinary oxalate excretion.

The PHYOX investigators have observed three mild-to-moderate injection site reactions. All were transient and resolved without intervention.

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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