# Dicerna Doses First Primary Hyperoxaluria Patient with DCR-PHXC in Group B Portion of PHYOX Phase 1 Clinical Trial

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*FDA Grants Orphan Drug Designation for DCR-PHXC for the Treatment of Primary Hyperoxaluria*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 30, 2018-- Dicerna Pharmaceuticals, Inc. (Nasdaq:DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced that the Company has dosed the first primary hyperoxaluria (PH) patient with DCR-PHXC in the Group B portion of the PHYOX Phase 1 clinical trial. DCR-PHXC is an investigational GalXC™ product candidate in development 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 also announced that the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation to DCR-PHXC for the treatment of PH on May 15, 2018. Dicerna expects to have clinical proof-of-concept data from the PHYOX trial in the second half of 2018.

“The Orphan Drug Designation for DCR-PHXC for the treatment of primary hyperoxaluria and the dosing of the first primary hyperoxaluria patient in the Group B portion of the PHYOX trial are important milestones for the Company as we seek to develop the first GalXC-based RNAi therapeutic to treat patients with all forms of this serious, life-threatening disease,” said Ralf Rosskamp, M.D., chief medical officer of Dicerna. “While the PHYOX study remains blinded to treatment assignment, the early safety and tolerability data from healthy volunteers in Group A are encouraging. The advancement of DCR-PHXC demonstrates our commitment to progressing novel science that has the potential to make a meaningful difference for this underserved patient population.”

The PHYOX trial is a Phase 1, single-ascending dose study of DCR-PHXC in normal healthy volunteers (NHVs) and patients with PH. The study is divided into two groups: Group A is a placebo-controlled, single-blind, single-center study that has enrolled 25 NHVs; Group B is an open-label, multi-center study enrolling up to 16 patients with PH type 1 (PH1) and PH type 2 (PH2).

The primary objective of the PHYOX study is to evaluate the safety and tolerability of single doses of DCR-PHXC in both groups. The secondary objectives are to evaluate the pharmacodynamic effect of single doses of DCR-PHXC on biochemical markers, including but not limited to, changes in urine oxalate concentrations, and to characterize the pharmacokinetics of single doses of DCR-PHXC in NHVs and patients with PH.

“Primary hyperoxaluria is a family of devastating diseases for which there are currently no approved treatment options,” said Pierre Cochat, M.D., Ph.D., professor at the University of Lyon, France, and head of service at the Hôpital Femme Mère Enfant in Bron Cedex, France. “Patients with severe primary hyperoxaluria often undergo major surgical procedures, such as dual liver and kidney transplants, followed by a lifelong regimen of immunosuppressant drugs to avoid rejection. Given the extreme challenges faced by this population, we are excited to have begun dosing patients with DCR-PHXC in this important clinical study.”

The Company has completed the Group A portion of the PHYOX study. While the study is still blinded and only topline results from Group A are available, there were no serious adverse events (SAEs) and no discontinuations. Out of 25 participants, there have been two mild-to-moderate transient injection site reactions at doses of 6 and 12 mg/kg involving erythema and tenderness, lasting no more than 36 hours. The highest dose level in the Group A portion of the trial was 12 mg/kg, while the highest dose level in the Group B portion is 6 mg/kg.

Dicerna also recently announced that the Company received a notice from the FDA indicating that the DCR-PHXC Phase 1 study could proceed in the U.S., under an Investigational New Drug application (IND). In addition to this active IND, the Company has active Clinical Trial Applications (CTAs) in the United Kingdom, France, and Germany, having received the appropriate regulatory and ethical approvals for the trial in these countries. A CTA has been submitted and is pending approval in the Netherlands.

**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 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 affects an estimated 1 in 58,000 individuals around the world. PH1 is the most common form of the disease, accounting for approximately 80% of cases, whereas PH2 and PH3 each account for roughly 10% of cases.[3] The estimated genetic incidence of PH1 is 1 in 151,887 births, which implies more than 5,000 patients in the U.S. and EU have the disease.[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 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, including, for example, Dicerna's expected timeline and plans for development of DCR-PHXC and other pipeline programs, as well as expected regulatory results and timing. 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. Applicable risks and uncertainties include risks relating to Dicerna's clinical and preclinical 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 SEC. 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**


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