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Dicerna Announces First Human Dosed in Phase 1 Clinical Trial of DCR-PHXC for Treatment of All Forms of Primary Hyperoxaluria

Clinical Proof-of-Concept Data for First GalXC™ RNAi Product Candidate Expected in Second Half of 2018

CAMBRIDGE, Mass.--(BUSINESS WIRE)-- Dicerna Pharmaceuticals, Inc. (NASDAQ:DRNA), a leading developer of RNA interference (RNAi) therapeutics, today announced the dosing of the first human in DCR-PHXC-101, a Phase 1 clinical trial of DCR-PHXC, the Company's most advanced GalXC™ product candidate. Dicerna is investigating DCR-PHXC for the treatment of primary hyperoxaluria (PH), a group of severe, rare, inherited disorders of the liver that often result in kidney failure. The Company anticipates that human proof-of-concept data from the Phase 1 trial will be available in the second half of 2018.

"Dosing of the first human in the DCR-PHXC-101 trial is a major milestone for Dicerna and our GalXC technology platform, as we seek to develop innovative RNAi therapeutics targeting disease-driving genes in the liver," said Ralf Rosskamp, M.D., chief medical officer of Dicerna. "Primary hyperoxaluria is a family of devastating diseases for which there are currently no approved treatment options. Based on our encouraging preclinical data, and the high unmet need in this underserved patient population, we are excited to embark on this Phase 1 clinical trial and look forward to working closely with the physician and the patient communities to advance clinical development of DCR-PHXC."

The DCR-PHXC-101 clinical trial is a 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 Phase 1 study in NHVs; Group B is an open-label, multi-center study in patients with PH types 1 (PH1) and 2 (PH2). The primary objective for the trial is to evaluate the safety and tolerability of single doses of DCR-PHXC in both groups. Secondary objectives are to characterize the pharmacokinetics (PK) of single doses of DCR-PHXC in NHVs and patients with PH, and to evaluate the pharmacodynamic (PD) effects of single doses of DCR-PHXC on biochemical markers including, but not limited to, changes in urine oxalate concentrations. The Company expects to dose the first patient in Group B in the first quarter of 2018.

In patients with PH, the liver over-produces oxalate, a metabolite that can accumulate throughout the body and particularly in the kidneys, often resulting in end-stage renal disease (ESRD) and the need for both kidney and liver transplants. DCR-PHXC, the lead product candidate in Dicerna's pipeline of RNAi therapies addressing rare diseases of the liver, targets the lactate dehydrogenase A (*LDHA*) gene, a gene that the Company has identified as potentially being an optimal therapeutic target in patients with PH. DCR-PHXC yields potent, liver-specific *LDHA* inhibition in animal models of PH, an effect that reduces oxalate to near-normal levels, which may prevent the damage to the kidneys and other organs caused by oxalate accumulation.

"Initiation of dosing in the DCR-PHXC-101 clinical trial is good news for the primary hyperoxaluria community, which has been waiting a long time for a potentially meaningful therapeutic option," said Bernd Hoppe, M.D., one of the investigators in the DCR-PHXC clinical trial and head of the Division of Pediatric Nephrology in the Department of Pediatrics at the University of Bonn, Germany. "Given the encouraging inhibitory activity of DCR-PHXC in animal studies, as well as its favorable preclinical safety and tolerability profile, we hope to observe positive results in the DCR-PHXC-101 trial, first in normal healthy volunteers and then in patients with primary hyperoxaluria types 1 and 2."

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 should 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 in the U.S. or the EU.

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 US and EU have the disease.[4] The median age at the first appearance of PH1 symptoms is 5.8 years.[5] 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.[6] 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, 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. 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 GalXC™; (ii) research and development plans related to GalXC; 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 could potentially lead to an approved product is long and subject to highly significant risks, particularly with respect to a pre-clinical research collaboration. Applicable risks and uncertainties include those relating to our preclinical research and other risks identified under the heading "Risk Factors" included in our most recent Form 10-Q 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.

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