Dicerna Files Clinical Trial Application for DCR-PHXC, the Company's Most Advanced GalXC™ Product Candidate, for Phase 1 Study in Primary Hyperoxaluria (PH)

The Company Expects to Initiate Clinical Dosing in Q1 2018

CAMBRIDGE, Mass., October 16, 2017 -- Dicerna Pharmaceuticals, Inc. (NASDAQ: DRNA), a leading developer of investigational RNA interference (RNAi) therapeutics, today announced the first submission of a clinical trial application (CTA) to the Medicines and Healthcare products Regulatory Agency (MHRA) in the United Kingdom to initiate a Phase 1 clinical trial of DCR-PHXC, the company's most advanced GalXC™ product candidate, for the potential treatment of primary hyperoxaluria (PH). PH is a group of severe, rare, inherited disorders of the liver that often result in kidney failure. Once the CTA is authorized by the MHRA and local ethics committees, Dicerna plans to begin its Phase 1 clinical study in healthy volunteers and in patients with PH types 1 and 2 at trial sites in the United Kingdom. The company plans to submit additional CTAs in other European countries.

"The filing of this CTA marks an important milestone for Dicerna, for our GalXC technology platform, and most importantly, for our pipeline of GalXC product candidates," said Douglas Fambrough, Ph.D., president and chief executive officer of Dicerna. "Specifically, the filing signals our readiness to begin GalXC-based clinical efforts as we further investigate a needed pharmaceutical treatment option for patients with PH, a family of severe disorders with a high unmet medical need. I want to thank the many Dicerna employees, external collaborators and the primary hyperoxaluria community, who have been instrumental in advancing our GalXC-based program for PH to this point. Pending CTA approval, we look forward to dosing the first person with DCR-PHXC and moving this program through clinical trials. We expect to present initial data from our Phase 1 proof-of-concept study in 2018."

Once the CTA is authorized by the MHRA, Dicerna plans to conduct the Phase 1 trial as a randomized, single-blind, placebo-controlled, single-ascending dose study, enrolling up to 25 healthy volunteer subjects and up to 16 patients with PH. The primary objective of the study is to evaluate the safety and tolerability of single doses of DCR-PHXC, with participants being enrolled into as many as five sequential cohorts of increasing doses. Patients with PH will be dosed after safety has been established at the same dose level in normal healthy volunteers. Secondary endpoints include the pharmacokinetics of DCR-PHXC and its pharmacodynamic effects on oxalate biomarkers in plasma and urine.

DCR-PHXC is the most advanced product candidate utilizing Dicerna's GalXC technology, 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. DCR-PHXC targets the lactate dehydrogenase A (*LDHA*) gene, a non-essential gene that Dicerna has identified as being a potentially optimal therapeutic target in patients with PH.

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.

“Based on pre-clinical data, *LDHA* has the potential to be an ideal therapeutic target in patients with PH and we hope to replicate the inhibitory effect on oxalate production in human clinical studies,” said Ralf Rosskamp, M.D., chief medical officer of Dicerna Pharmaceuticals. “Our research findings to date, along with the findings from our PHYOS observational study, have been instrumental in our understanding of PH and informing our clinical development plan. Preclinical studies have shown that DCR-PHXC results in the potent, durable, and consistent knockdown of *LDHA* and reduces oxalate in multiple animal models of PH. We are committed to investigating a treatment option for patients with all forms of PH and are excited to begin the Phase 1 trial.”

“With this CTA filing, and the expected initiation of a first-in-human, proof-of-concept Phase 1 trial of DCR-PHXC once the MHRA authorizes the CTA, Dicerna is pursuing an exciting and important approach that may address a high unmet medical need in primary hyperoxaluria,” noted Craig B. Langman, M.D., The Isaac A Abt MD Professor of Kidney Diseases at the Feinberg School of Medicine at Northwestern University. “Given the lack of curative treatment options for individuals with this devastating family of diseases, a medication that suppressed oxalate production would be a welcome therapeutic solution for these patients.”

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 US 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 RNAi-based therapeutics for diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases, and viral infectious diseases. The Company 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. The Company 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. The process by which early clinical technology and product candidates such as DCR-PHXC could potentially lead to an approved product is long and subject to highly significant risks. 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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