Dicerna™ Submits Updated IND Application for DCR-PHXC for Treatment of Primary Hyperoxaluria (PH) for the PHYOX™2 Pivotal Trial

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– Update Reflects Alignment with FDA on Path to Full Approval for Treatment of PH1 and Discussions Now Focusing on Appropriate Endpoints for PH2 and PH3 –

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 2, 2019-- Dicerna™Pharmaceuticals, Inc. (Nasdaq:DRNA) (the “Company” or “Dicerna”), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced the submission of an updated investigational new drug (IND) application to the U.S. Food and Drug Administration (FDA) for DCR-PHXC, the Company’s lead GalXC™ product candidate for the treatment of all forms of primary hyperoxaluria (PH). The update reflects agreement on the primary endpoint for the PHYOX™2 pivotal clinical trial, which is enrolling patients with PH type 1 (PH1) and PH type 2 (PH2), and alignment with the FDA regarding the path to full approval for the treatment of patients with PH1, as conveyed during a recent FDA Type A meeting. The Company will continue its ongoing dialogue with the FDA regarding endpoints for studies involving patients with PH2 and PH3, as part of the PHYOX clinical development program for DCR-PHXC.

“We are pleased by the positive and constructive discussion with the FDA regarding our DCR-PHXC program. The agency’s confirmation of the primary endpoint for our pivotal trial provides a clear path forward to achieve full approval of DCR-PHXC for the treatment of PH1,” said Ralf Rosskamp, M.D., chief medical officer of Dicerna. “We also look forward to continuing discussions with the FDA regarding the primary and secondary endpoints in patients with PH2 and PH3, less prevalent subtypes of primary hyperoxaluria for which there are relatively little natural history data. We will continue to report our progress as the PHYOX trials move forward.”

For the forthcoming pivotal PHYOX2 study, Dicerna reached agreement with the FDA on a primary endpoint of 24-hour urinary oxalate burden, expressed as the time-weighted standardized (TWS) area under the curve (AUC) from Day 90 to 180, based on percent change from baseline. Dicerna recently announced initiation of participant screening in the PHYOX2 trial, which will evaluate a multi-dose regimen of DCR-PHXC in individuals with PH1 and PH2. The Company expects to begin enrolling patients to the PHYOX2 trial in the second quarter of 2019.

“Urinary oxalate burden is increasingly recognized as an important issue for patients with primary hyperoxaluria, as overproduction of oxalate is implicated in all types of this devastating disease, for which there are no approved therapies,” commented Craig Langman, M.D., a pediatric nephrologist and the Isaac A. Abt, M.D. Professor of Kidney Diseases at the Feinberg School of Medicine, Northwestern University and Head, Kidney Diseases, at Lurie Children's Hospital. “We expect that the PHYOX trials will demonstrate reduction of oxalate, by targeting the lactate dehydrogenase A enzyme, in the pathogenesis of PH2 and PH3.”

Dicerna recently presented updated data from the ongoing PHYOX1 Phase 1 clinical trial of DCR-PHXC, which showed post-dose reductions in 24-hour urinary oxalate levels in adult and adolescent study participants with PH1 and PH2. The PHYOX1 data also showed that a single dose of DCR-PHXC led to normalization or near-normalization of urinary oxalate levels in a majority of patients and was generally well-tolerated.

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 lactate dehydrogenase A enzyme, or 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 may 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 organs 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 "no mutation detected" (NMD) PH or idiopathic PH (IPH). 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), and
- 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 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, 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. Dicerna has strategic collaborations with Eli Lilly and Company, Alexion Pharmaceuticals, Inc. and Boehringer Ingelheim International GmbH. For more information, please visit www.dicerna.com.

Cautionary Note on Forward-Looking Statements
This press release includes forward-looking statements. 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 future discussions the Company plans to have with the FDA regarding clinical endpoints for PH2 and PH 3 in the PHYOX clinical trial; (ii) the monitoring and ultimate outcome of the PHYOX clinical trial in PH1, PH2 and PH2 patients; research and development plans and timelines related to DCR-PHXC; and (iii) the potential of Dicerna™'s technology and DCR-PHXC in the Company's research and development pipeline. The process by which an early stage investigational therapy such as DCR-PHXC and an early stage platform such as GalXC could potentially lead to an approved product is long and subject to highly significant risks. Applicable risks and uncertainties include those relating to Dicerna's clinical 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 Securities and Exchange Commission. These risks and uncertainties include, among others, the cost, timing and results of preclinical studies and clinical trials and other development activities; the likelihood of Dicerna's clinical programs being executed within timelines provided and reliance on the Company's contract research organizations and predictability of timely enrollment of subjects and patients to advance Dicerna's clinical trials; the potential for future data to alter initial and preliminary results of early stage clinical trials; the unpredictability of the duration and results of the regulatory review of Investigational New Drug Applications (NDAs) and Clinical Trial Applications that are necessary to continue to advance and progress the Company's clinical programs and the regulatory review of 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 that could emerge as new data are generated in research and development, 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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