# Dicerna Receives Recommendation from EMA Committee to Designate DCR-PHXC an Orphan Medicinal Product for the Treatment of Primary Hyperoxaluria (PH) in the EU

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*COMP Opinion Cites Encouraging Preclinical Data and Chronically Debilitating and Life-threatening Nature of PH*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 11, 2018--

Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced that the European Medicines Agency's (EMA) Committee for Orphan Medicinal Products (COMP) has recommended designating DCR-PHXC, the Company's lead GalXC™ product candidate, as an orphan medicinal product for the treatment of primary hyperoxaluria (PH) in the European Union (EU). The European Commission (EC) is expected to review the COMP opinion and issue a final ruling within 30 days of receipt. Separately, Dicerna recently announced that the U.S. Food and Drug Administration (FDA) granted Orphan Drug Designation to DCR-PHXC for the treatment of PH.

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 Phase 1 clinical trial of DCR-PHXC in normal healthy volunteers in the fourth quarter of 2017 and dosed the first patient with PH in May 2018, with clinical proof-of-concept data anticipated in the second half of 2018.

"We are gratified to see regulators recognize the urgent need for a safe and effective therapy for primary hyperoxaluria, as well as the encouraging preclinical data for DCR-PHXC in various mouse models of PH," said Ralf Rosskamp, M.D., chief medical officer of Dicerna. "This positive recommendation, as well as the Orphan Drug Designation from the FDA, acknowledges the needs of this underserved patient population."

The EMA grants orphan medicinal product designation to investigational drugs intended to treat, prevent or diagnose a life-threatening or chronically debilitating disease affecting fewer than five in 10,000 people in the EU, and for which no satisfactory treatment is available. Orphan medicinal product designation provides regulatory and financial incentives for companies to develop and market therapies, including market exclusivity, protocol assistance, fee reductions, and EU-funded research.

In examining the orphan medicinal product application for DCR-PHXC, the COMP concluded that Dicerna established the following:

- The intention to treat PH with DCR-PHXC is justified based on reduction of urine oxalate concentration and kidney oxalate crystal deposits in a non-clinical model of the condition;
- The condition is chronically debilitating and life-threatening, in particular because of nephrolithiasis (presence of kidney stones) and nephrocalcinosis (calcification in the renal parenchyma, the functional part of the kidney) leading to renal damage. The majority of patients with PH reach end-stage renal disease (ESRD) during the third to fifth decade of life;
- The condition was estimated to affect fewer than five per 10,000 persons in the EU at the time the application was submitted.

**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 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 U.S. and EU 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 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, 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 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). 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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