Dicerna Receives Breakthrough Therapy Designation for DCR-PHXC for Treatment of Primary Hyperoxaluria Type 1 (PH1)

July 15, 2019

—Designation Follows Recently Reported PHYOX™1 Phase 1 Data Showing Positive Clinical Responses to DCR-PHXC–

—FDA Recognizes Primary Hyperoxaluria Types 2 and 3 (PH2 and PH3) as Meeting Criteria for a Serious or Life-Threatening Disease or Condition—

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 15, 2019-- Dicerna™ Pharmaceuticals, Inc. (Nasdaq: DRNA) (the "Company" or "Dicerna"), a leading developer of ribonucleic acid interference (RNAi) therapies, today announced that the U.S. Food and Drug Administration (FDA) has granted a Breakthrough Therapy Designation (BTD) to DCR-PHXC for the treatment of patients with primary hyperoxaluria type 1 (PH1). DCR-PHXC is the only RNAi investigational therapy in development for the treatment of all types of PH, a family of severe, rare, inherited disorders of the liver that often result in kidney failure.

In its communication to Dicerna, the FDA also conveyed its determination that PH type 2 (PH2) and PH type 3 (PH3) meet the criteria for a serious or life-threatening disease or condition, based on the Agency's standards. The Company will continue its ongoing dialogue with the FDA regarding endpoints for studies of DCR-PHXC in patients with PH2 and PH3, as part of the PHYOX™ clinical development program.

"By granting Breakthrough Therapy Designation, the FDA recognizes both the urgent need to develop a therapy for primary hyperoxaluria type 1 and the encouraging preliminary data from the PHYOX1 clinical trial of DCR-PHXC in these patients," said Ralf Rosskamp, M.D., Dicerna's chief medical officer. "We look forward to continuing our dialogue with the FDA as we advance DCR-PHXC as quickly as possible as a potential therapeutic option for all persons living with primary hyperoxaluria."

The FDA's BTD is intended to expedite the development and review of a drug candidate that is planned for use to treat a serious or life-threatening disease or condition when preliminary clinical evidence indicates that the drug may demonstrate substantial improvement over existing therapies on one or more clinically significant endpoints. The BTD offers companies the opportunity for increased communication with FDA and an organizational commitment involving more intensive guidance from FDA senior managers.

Dicerna recently presented updated data from the PHYOX1 Phase 1 clinical trial of DCR-PHXC, which reported substantial post-dose reductions in 24-hour urinary oxalate levels in adult and adolescent study participants with PH1 and PH2. The updated PHYOX1 data, presented at the Oxalosis and Hyperoxaluria Foundation's International Workshop on June 22, 2019, 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.[1] For more information about the PHYOX clinical development program, please visit www.phyoxtrials.com.

About DCR-PHXC

DCR-PHXC is the only RNAi investigational drug in development for the treatment of all types 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.

Dicerna is evaluating DCR-PHXC in the PHYOX™ clinical trial program. Interim results from the ongoing PHYOX1 Phase 1 study have demonstrated normalization or near-normalization of urinary oxalate levels in a majority of participants receiving DCR-PHXC, as well as a favorable tolerability profile.

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. The accumulation of oxalate can result in severe damage to the kidneys and other organs.

There are three known genetic types of PH, each of which results from a mutation in a specific gene. In each type, the mutation decreases the activity of an enzyme in the liver, leading to an increase in the production of oxalate.

- PH type 1, or PH1, is caused by a mutation in the AGXT gene. This causes a deficiency of the enzyme alanine:glyoxylate-aminotransferase (AGT).
- PH type 2, or PH2, is caused by a mutation in the GRHPR gene. This causes a deficiency of the enzyme glyoxylate/hydroxypyruvate reductase (GR/HPR).
- PH type 3, or PH3, is caused by a mutation in the HOGA1 gene, causing a deficiency of the enzyme 4-hydroxy-2-oxoglutarate aldolase (HOGA).[2,3]

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.[4] 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.[4] The estimated genetic prevalence of PH2 is 1 in 310,055 and that of PH3 is 1 in 135,866.[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 by their mid-30s.[3]

About Dicerna™ Pharmaceuticals, Inc.

Dicerna™ Pharmaceuticals, Inc., is a biopharmaceutical company using RNA interference, or RNAi, to create medicines that silence genes that cause disease. The Company's proprietary GalXC™ technology is intended to amplify its ability to create potent, selective and safe RNAi therapies to treat diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases and viral infectious diseases. Dicerna aims to restore health by addressing the underlying causes of illness with capabilities that extend beyond the liver to address a broad range of diseases, focusing on target genes where connections between gene and disease 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 potential for confirmation of reductions in urinary oxalate in future data from DCR-PHXC clinical trials; (ii) research and development plans and timelines related to DCR-PHXC; and (iii) the potential of Dicerna™'s technology and drug candidates 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-Q 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.

References

1. Dicerna Press Release. Dicerna™ Presents Additional Data from PHYOX™1 Study of DCR-PHXC in Patients with Primary Hyperoxaluria Type 1 (PH1) and Type 2 (PH2). Available at: http://investors.dicerna.com/news-releases/news-release-details/dicernatm-presents-additional-data-phyoxtm1-study-dcr-phxc. Accessed July 11, 2019.
2. Oxalosis & Hyperoxaluria Foundation. Overview of hyperoxaluria. 2017. Available at: https://ohf.org/overview/. Accessed July 6, 2017.
3. Rare Kidney Stone Consortium. Primary hyperoxaluria. 2010. Available at: http://www.rarekidneystones.org/hyperoxaluria/physicians.html. Accessed July 6, 2017.
4. Hopp, K, Cogal, A, Bergstralh, E, et al. Phenotype-genotype correlations and estimated carrier frequencies of primary hyperoxaluria. Journal of the American Society of Nephrology 2015; 26(10):2559-2570.
5. van der Hoeven SM, van Woerden CS, Groothoff JW. Primary hyperoxaluria type 1, a too often missed diagnosis and potentially treatable cause of end-stage renal disease in adults: results of the Dutch cohort. Nephrology, Dialysis, Transplantation 2012; 27(10):3855-3862.
6. Tang X, Bergstrath EJ, Mehta RA, Vrtiska TJ, Milliner DS, Lieske JC. Nephrocalcinosis is a risk factor for kidney failure in primary hyperoxaluria. Kidney International 2015; 87:623-631.

View source version on businesswire.com: https://www.businesswire.com/news/home/20190715005117/en/

Source: Dicerna™ Pharmaceuticals, Inc.

Investors:
Stern Investor Relations, Inc.
Lauren Stival, 212-698-8646
Lauren.stival@sternir.com

Media:

SmithSolve
Alex Van Rees, 973-442-1555 ext. 111
Alex.vanrees@smithsolve.com