Dicerna™ Presents Additional Data from PHYOX™1 Study of DCR-PHXC in Patients with Primary Hyperoxaluria Type 1 (PH1) and Type 2 (PH2)

June 21, 2019

—Researchers Report Substantial Oxalate Reduction Following Single-Dose Administration of DCR-PHXC in Additional Patients with PH2—

—Enrollment Underway in Pivotal PHYOX2 Trial of DCR-PHXC—

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jun. 21, 2019-- Dicerna™ Pharmaceuticals, Inc. (Nasdaq: DRNA) (the "Company" or "Dicerna"), a leading developer of ribonucleic acid interference (RNAi) therapies, today announced updated data from its ongoing PHYOX™1 Phase 1 clinical trial evaluating DCR-PHXC, the Company's lead GalXC™ product candidate. Investigators reported additional results evaluating DCR-PHXC in patients with primary hyperoxaluria type 1 (PH1) and type 2 (PH2), building on previously disclosed data showing substantial reductions in 24-hour urinary oxalate levels following a single-dose of DCR-PHXC. Researchers continue to characterize DCR-PHXC as well-tolerated. The results will be presented at the Oxalosis & Hyperoxaluria Foundation (OHF) International Hyperoxaluria Workshop in Boston on June 22.

"The substantial reduction in urinary oxalate following single-dose administration of DCR-PHXC is a promising sign of its potential potency and duration of action in patients with primary hyperoxaluria," said Bernd Hoppe, M.D., lead investigator of the PHYOX1 study and professor of Pediatrics in the Department of Pediatrics at the University of Bonn, Germany. As separately announced, Dr. Hoppe will join Dicerna as vice president and global head of medical affairs, effective July 1. "The positive results reported today in patients with PH2 are especially encouraging because DCR-PHXC is the only therapy in development for this type of PH. We look forward to further evaluating DCR-PHXC as we begin the PHYOX2 pivotal trial and the PHYOX3 long-term extension study."

In their poster presentation, Dr. Hoppe and other investigators reported the following results based on data analyzed through May 1, 2019:

- A single 3.0-mg/kg dose of DCR-PHXC was associated with a mean maximal reduction of 24-hour urinary oxalate of 71% (range: 62% to 80%) in participants with PH1. The 3.0-mg/kg dose brought urinary oxalate levels into the normal range (defined as 24-hour excretion <0.46 mmol) at one or more post-dose time points in four of six participants with PH1, and to near-normalization (defined as 24-hour excretion <0.6 and ≥0.46 mmol) in one participant with PH1 receiving this dose.
- Among the four participants with PH1 dosed at 6.0 mg/kg, the mean maximal reduction in urinary oxalate was 66% (range: 35% to 100%); one participant in this cohort reached normalization at more than one post-dose time points; two others achieved near-normalization.
- Additionally, the investigators also reported a mean maximal reduction in urinary oxalate of 48% (range: 28% to 59%) among participants with PH1 receiving a single 1.5-mg/kg dose, which led to normalization or near-normalization in three of five participants.

The PHYOX1 investigators also reported that the three participants with PH2 (one of whom received a single 1.5-mg/kg dose of DCR-PHXC; the other two received a 3.0 mg/kg dose) achieved a mean maximal reduction of 24-hour urinary oxalate of 42% (range: 22% to 66%) with one participant reaching normalization. All three participants with PH2 have reached Day 57 post-dosing and one is still in follow-up.

"The latest data from PHYOX1 provide more information on the effects of DCR-PHXC in individuals with PH1 as well as individuals with PH2. DCR-PHXC is the only RNAi-based therapy designed for the treatment of patients with all forms of PH and this data cut further strengthens the therapeutic rationale for this compound," said Ralf Rosskamp, M.D., chief medical officer of Dicerna. "Based on the observed 24-hour reductions in urinary oxalate, along with the safety and tolerability data reported thus far, we expect that a multi-dose regimen of DCR-PHXC may offer the potential for more pronounced and sustained reductions in urinary oxalate. We eagerly anticipate further results from PHYOX1, as well as from the PHYOX2 and PHYOX3 trials, which are investigating a multi-dose regimen of DCR-PHXC."

In the overall study population, most plasma oxalate values were within the normal range, and the values in two patients with elevated plasma oxalate normalized at one or more time points.

In terms of safety, the investigators reported that DCR-PHXC was generally well-tolerated, based on data from 18 participants (15 adults and three adolescents [participants 12-17 years old]) with PH1 (n=15) and PH2 (n=3) and 25 adult healthy volunteers (HVs). To date, four serious adverse events (SAEs) have occurred in three participants, though none were deemed related to the study drug, and all four SAEs have resolved. A total of nine participants dosed with DCR-PHXC experienced mild or moderate injection site reactions (ISRs), all of which resolved without intervention within 96 hours. The investigators observed no clinically meaningful safety signals including from liver function tests.

About the PHYOX1 Trial

The primary objective of the PHYOX1 Phase 1 trial (ClinicalTrials.gov: NCT03392896) is to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of single-ascending doses of DCR-PHXC. Secondary endpoints include the change in 24-hour urinary oxalate excretion from baseline, defined as the mean of two 24-hour collections during screening. The trial is divided into two groups:

- Group A is placebo-controlled, single-blind and includes 25 HVs enrolled at a single site in the United Kingdom with five cohorts dosed at 0.3, 1.5, 3.0, 6.0 or 12.0 mg/kg of DCR-PHXC or placebo (3:2 randomization).
- Group B is open-label and includes 18 participants with PH, including three cohorts of participants with PH1 dosed at 1.5, 3.0 and 6.0 mg/kg of DCR-PHXC, and a fourth cohort with flexible dosing. Group B participants are enrolled among five

sites in the European Union and one site in the United States.

The Company initiated the PHYOX1 Phase 1 trial in HVs in the fourth quarter of 2017 and dosed the first participant with PH in May 2018.

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).[1,2]

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 DCR-PHXC

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

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 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 potential for more pronounced and sustained 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. Oxalosis & Hyperoxaluria Foundation. Overview of hyperoxaluria. 2017. Available at: https://ohf.org/overview/. Accessed July 6, 2017.
2. Rare Kidney Stone Consortium. Primary hyperoxaluria. 2010. Available at: http://www.rarekidneystones.org/hyperoxaluria/physicians.html. Accessed July 6, 2017.
3. 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.
4. 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.
5. 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/20190621005066/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