Dicerna Presents PHYOX™2 and Primary Hyperoxaluria Healthcare Utilization Data at American Society of Nephrology (ASN) Kidney Week 2021

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– Nedosiran Achieved Primary Endpoint Demonstrating Statistically Significant Sustained Reduction in Urinary Oxalate Excretion and Showed Robust Efficacy in PH1 –

– Real-World Healthcare Utilization Data Showed Delayed Diagnosis in More Than 50% of Patients, High Rates of Healthcare Use and Substantial Costs Following Start of Dialysis –

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 4, 2021-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced results of the PHYOX™2 pivotal clinical trial of nedosiran, an investigational GalXC™ RNAi candidate for the treatment of primary hyperoxaluria (PH), in a late-breaker poster presentation at the American Society of Nephrology (ASN) Kidney Week 2021.

In the PHYOX2 pivotal trial, which included patients with PH type 1 (PH1) and PH type 2 (PH2), nedosiran demonstrated a statistically significant reduction from baseline in urinary oxalate (Uox) excretion compared to placebo ($p<0.0001$). Additionally, a significantly higher proportion of patients treated with nedosiran achieved and sustained normal or near-normal Uox at two or more consecutive visits after Day 90 compared to placebo ($p=0.0025$). A post hoc subgroup analysis in participants with high baseline Uox (at least one value ≥ 1.6 mmol) also showed significantly greater Uox reduction in those treated with nedosiran ($p=0.0186$). These robust and sustained Uox reduction results observed in PHYOX2 were primarily driven by response to nedosiran in the PH1 subgroup, which met both primary and key secondary endpoints based on a post hoc analysis. There was no consistent pattern of Uox reduction observed in participants with PH2.

“Our pivotal PHYOX2 data emphasize the potential of nedosiran to be a safe and effective therapy option for people with PH1,” said Shreeram Aradhye, M.D., Executive Vice President and Chief Medical Officer at Dicerna. “Primary hyperoxaluria can lead to life-threatening kidney damage, and there continues to be an urgent need to provide the medical community with new therapeutic options and build an understanding of disease biology across the PH subtypes.”

“For people with primary hyperoxaluria, excessive oxalate production compromises kidney function and can have severe consequences,” said David Goldfarb, M.D., Clinical Chief of Nephrology at NYU Langone Health and co-director of its Kidney Stone Prevention Program. “More than 80% of people with PH1 taking nedosiran achieved normal or near-normal urinary oxalate excretions at Day 180 in the PHYOX2 trial. These data underscore the potential of nedosiran to be a meaningful treatment option for those affected by PH1, if approved.”

Separately, findings from a real-world study examining de-identified electronic medical record (EMR) data, including demographics, clinical characteristics and healthcare utilization among 47 patients with PH pre- and post-dialysis treatment were also presented at the conference. The study showed high rates of costly healthcare utilization, including emergency and inpatient visits, and confirmed that healthcare costs continued to be substantial, exceeding $200,000, in the first year following dialysis initiation. More than half of patients had no recorded PH diagnosis until after initiating dialysis.

“These healthcare utilization findings confirm what many of us know to be true – that people living with PH endure a high frequency of doctor visits. Over the course of the study, more than half of patients needed multiple emergency room visits and 70% had one or more hospital stays, which are even more expensive and disruptive to daily life,” Dr. Aradhye continued. “Of significant concern was the high rate of delayed diagnosis. More than half of patients did not receive a PH diagnosis until after their kidney function declined to the point of dialysis, underscoring the need for better education and understanding of the signs and symptoms of PH.”

PHYOX2 Detailed Results

PHYOX2 (NCT03847909), a placebo-controlled, double-blind, multicenter, pivotal study, was designed to evaluate the efficacy, safety and tolerability of nedosiran over six months in participants with PH1 or PH2 aged six years and older across 11 countries, including the U.S., Japan and Europe. Participants were randomized 2:1 to a fixed dose of nedosiran or placebo administered once monthly by subcutaneous injection.

The primary endpoint of the study was the percent change from baseline in 24-hour Uox excretion, as assessed by area under the curve (AUC) from Day 90 to Day 180. The key secondary endpoint was percentage of patients (PH1 and PH2) achieving normalization (defined as Uox level below 0.46 mmol adjusted per 1.73 m^2 body surface area in participants younger than 18 years when collected over 24 hours) or near-normalization (defined as 1.3 times the upper limit of normal; 0.60 mmol) on at least two consecutive visits from Day 90 to Day 180.

Of the 35 patients randomized (23 nedosiran and 12 placebo; 29 with PH1 and 6 with PH2), 34 participants had at least one efficacy assessment after Day 90 (modified intent-to-treat population; mITT). Baseline mean estimated glomerular filtration rate (eGFR; a measure of kidney function) was 89.5 mL/min/1.73 m^2 (SD=37.5) for participants given nedosiran and 82.0 mL/min/1.73 m^2 (SD=30.0) for participants given placebo. Baseline mean Uox values were 1.33 mmol/day (SD=0.47) and 1.96 mmol/day (SD=0.71) for the nedosiran and placebo groups, respectively.

Nedosiran achieved the primary endpoint showing a statistically significant reduction from baseline in Uox excretion compared to placebo ($p<0.0001$). PHYOX2 also achieved its key secondary endpoint, with a significantly higher proportion of patients treated with nedosiran achieving and sustaining normal or near-normal Uox at two or more consecutive visits after Day 90 compared to placebo (50% vs. 0%; $p=0.0025$). Of the participants treated with nedosiran, 73% achieved normalization or near-normalization at least once during the study.

The significant and sustained Uox reduction observed in PHYOX2 was primarily driven by response to nedosiran in participants with PH1. There was no consistent pattern of Uox reduction observed in participants with PH2. Based on further analysis of the data by PH subtype, patients with PH1

treated with nedosiran achieved statistically significant differences from placebo for both the primary (p<0.0001) and the key secondary (p=0.0006) efficacy endpoints of the trial.

Among study participants assessed for plasma oxalate (Pox), where mean baseline Pox values were <10 µmol/L in both groups, those treated with nedosiran showed a median decrease of 25% at Day 180 (p=0.0264; ns); based on a post hoc analysis, Pox reduction of 25% in nedosiran-treated participants with PH1 was statistically significant compared to placebo (p=0.0168).

Nedosiran was generally well tolerated in the study with an overall adverse event (AE) profile consistent with previously reported data from PHYOX trials. The most common AEs in the trial were mild, self-resolving injection-site reactions (two patients given nedosiran and zero given placebo). There were three reported kidney stone AEs in participants given nedosiran (13%) and five in participants given placebo (42%).

Dicerna's posters for ASN will be made available on the Company's website.

About Primary Hyperoxaluria (PH)

Primary hyperoxaluria (PH) is a family of ultra-rare, life-threatening genetic disorders that initially manifest with complications in the kidneys. There are three known subtypes of PH (PH1, PH2 and PH3), each resulting from a mutation in one of three different genes. These genetic mutations cause enzyme deficiencies that result in the overproduction of oxalate, which is an end-product of metabolism. Excess production and accumulation of oxalate leads to recurrent kidney stones, nephrocalcinosis and chronic kidney disease that may progress to end-stage renal disease requiring intensive dialysis. Compromised renal function eventually results in the accumulation of oxalate in a wide range of organs including the skin, bones, eyes and heart. In the most severe cases, symptoms start in the first year of life. A combined liver-kidney transplant may be undertaken to resolve PH1 or PH2, but it is an invasive solution with limited availability and high morbidity that requires lifelong immune suppression to prevent organ rejection. Genetic studies suggest approximately 8,500 people in the U.S. are affected by PH, and researchers estimate that more than 80% of patients remain undiagnosed.[1] There is currently only one approved therapy available that is limited to the treatment of patients with PH1.

About Nedosiran

Nedosiran is in development for the treatment of primary hyperoxaluria (PH) as part of the PHYOX clinical development program and is Dicerna’s most advanced RNAi drug candidate utilizing its proprietary GalXC RNAi technology. Nedosiran is designed to inhibit production of the hepatic lactate dehydrogenase (LDH) enzyme – an enzyme that catalyzes the final step in the glyoxylate metabolism pathway that can lead to oxalate overproduction in patients with PH.

About Dicerna Pharmaceuticals, Inc.

Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) is a biopharmaceutical company focused on discovering, developing and commercializing medicines that are designed to leverage ribonucleic acid interference (RNAi) to silence selectively genes that cause or contribute to disease. Using our proprietary GalXC™ and GalXC-Plus™ RNAi technologies, Dicerna is committed to developing RNAi-based therapies with the potential to treat both rare and more prevalent diseases. By silencing disease-causing genes, Dicerna’s GalXC platform has the potential to address conditions that are difficult to treat with other modalities. Initially focused on disease-causing genes in the liver, Dicerna has continued to innovate and is exploring new applications of its RNAi technology with GalXC-Plus, which expands on the functionality and application of our flagship liver-targeted GalXC technology to tissues and cell types outside the liver, and has the potential to treat diseases across multiple therapeutic areas. In addition to our own pipeline of core discovery and clinical candidates, Dicerna has established collaborative relationships with some of the world’s leading pharmaceutical companies, including Novo Nordisk A/S, Roche, Eli Lilly and Company, Alexion Pharmaceuticals, Inc., Boehringer Ingelheim International GmbH and Alnylam Pharmaceuticals, Inc. Between Dicerna and our collaborative partners, we currently have more than 20 active discovery, preclinical or clinical programs focused on cardiometabolic, viral, chronic liver and complement-mediated diseases, as well as neurodegenerative diseases and pain. At Dicerna, our mission is to interfere – to silence genes, to fight disease, to restore health. 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. Examples of forward-looking statements include, among others, statements we make regarding our product candidates and the development thereof, such as the Company’s PHYOX clinical development program for nedosiran in PH; the impact of the results from the PHYOX2 trial of nedosiran for the potential treatment of PH1; the therapeutic potential of our product candidates, such as nedosiran; our belief regarding the unmet need to provide new therapeutic options and to build an understanding of disease biology across the PH subtypes; the impact of data from the real-world healthcare; the Company’s refined near-term nedosiran strategy to focus primarily on the treatment of PH1; our business and operations, including the discovery, development and commercialization of our product candidates and technology platform, and the therapeutic potential thereof; our collaboration with partners and any potential future collaborations.

The process by which investigational therapies, such as nedosiran, 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 filings on Forms 10-K and 10-Q 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 by us and our collaborative partners and any potential future collaborations, including any potential commercialization partner(s) for nedosiran; the potential for additional or future data to alter initial, interim and preliminary results of clinical trials; the impact of the ongoing COVID-19 pandemic on our business operations and those of the third parties and collaboration partners with whom we engage; the timing, plans and reviews by regulatory authorities of our marketing applications, such as for our planned submission to the FDA of an NDA for nedosiran in PH1; the ability to secure, maintain and realize the intended benefits of collaborations with partners, including any commercialization partner(s) for nedosiran; market acceptance for approved products and innovative therapeutic treatments, such as nedosiran; competition; the possible impairment of, inability to obtain, and costs to obtain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in R&D and following commercialization; and 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.

1 Hopp K, et al. J Am Soc Nephrol. 2015;26(10):2559-2570 and U.S. Census Bureau population on a date: February 20, 2020. United States Census Bureau website, 2020.

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Media:
Amy Trevvett
+1 617-612-6253
atrevvett@dicerna.com

Investors:
Kristen K. Sheppard, Esq.
+1 617-514-2275
ksheppard@dicerna.com

Source: Dicerna Pharmaceuticals, Inc.