Dicerna Reports Positive Top-Line Results From PHYOX™2 Pivotal Clinical Trial of Nedosiran for the Treatment of Primary Hyperoxaluria

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– Nedosiran Achieved Primary Endpoint, Demonstrating Statistically and Clinically Significant Sustained Reduction in Urinary Oxalate Excretion; Key Secondary Endpoint Also Achieved; Robust Efficacy Seen in PH1 Participants –

– Nedosiran Was Generally Well Tolerated in PHYOX2 With a Safety Profile Similar to Previously Reported PHYOX Trial Results –

– Results Further Validate GalXC™ RNAi Technology Platform and its Ability to Silence Disease-Driving Genes –

– Management to Host Conference Call and Webcast Today at 4:30 p.m. ET –

LEXINGTON, Mass.--(BUSINESS WIRE)--Aug. 5, 2021-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) (the "Company" or "Dicerna"), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced positive top-line results from the Company's PHYOX™2 pivotal clinical trial of nedosiran, which is in development as a once-monthly treatment for primary hyperoxaluria (PH), a family of ultra-rare, life-threatening genetic disorders that initially manifest with complications in the kidneys. Nedosiran is Dicerna's lead GalXC™ RNAi therapeutic candidate and is designed to inhibit 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. The PHYOX2 clinical trial included participants with PH subtypes 1 and 2 (PH1 and PH2).

Nedosiran achieved the primary endpoint in the PHYOX2 trial, demonstrating a statistically significant reduction from baseline in urinary oxalate (Uox) excretion compared to placebo ($p<0.0001$). The study also achieved the key secondary endpoint, with a significantly higher proportion of patients given nedosiran achieving and sustaining normal or near-normal Uox at two or more consecutive visits after Day 90 compared to placebo ($p=0.0025$). Uox reductions were significant in participants with PH1 while participants with PH2 (5 nedosiran and 1 placebo) showed inconsistent results in this trial. Nedosiran was generally well tolerated in the study with an overall adverse event (AE) profile consistent with previously reported data from PHYOX trials.

"We believe the reduction in Uox excretion seen in patients with PH1 showed that nedosiran knocks down *LDHA* in the liver and reconfirms the ability of Dicerna's GalXC RNAi technology to silence disease-driving genes, de-risking our growing pipeline of GalXC product candidates," said Shreeram Aradhye, M.D., Executive Vice President and Chief Medical Officer at Dicerna. "The heterogeneity of Uox response seen in participants with PH2, despite *LDHA* inhibition in the liver and in contrast to prior clinical experience, suggests more complexity in the PH2 disease biology than has been previously understood and will require further evaluation.

"The results reinforce nedosiran's potential to be a therapeutic option for patients with PH1, if approved," Dr. Aradhye continued. "Our New Drug Application to the U.S. Food and Drug Administration, expected to be submitted in the fourth quarter of 2021, will reflect the results reported today and a strategy to pursue approval of nedosiran for the treatment of PH1 for the near-term. We are extremely grateful to the patients, caregivers, physicians and healthcare professionals who participated in our trial and look forward to continuing to work with the PH community."

PHYOX2 Top-Line Results and PHYOX Development Program

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 aged six years and older across 11 countries, including the U.S., Japan and Europe, who have PH1 or PH2. Participants were randomized 2:1 to a fixed monthly dose of nedosiran or placebo administered once monthly by subcutaneous injection. 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 approximately 1.33 mmol/day (SD=0.47) and 1.96 mmol/day (SD=0.71) for the nedosiran and placebo groups, respectively.

The primary endpoint of the study was the percent change from baseline in 24-hour urinary oxalate excretion, as assessed by area under the curve (AUC) from Day 90 to Day 180. The primary endpoint of the study was met, with nedosiran resulting in a statistically significant reduction in Uox ($p<0.0001$). In the overall trial, nedosiran resulted in a 57.5% greater daily average reduction over Day 90 to Day 180 compared to placebo.

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) on at least two consecutive visits from Day 90 to Day 180. Nedosiran achieved statistically significant results ($p=0.0025$) in the study, with 50% of nedosiran-treated patients reaching normal or near-normal Uox on at least two consecutive visits, compared to 0% for those receiving placebo.

Nedosiran was generally well tolerated in this study with an AE profile consistent with that observed in the PHYOX1 Phase 1 study and from previous interim analyses from the ongoing PHYOX3 open-label trial. The most common AEs in the trial were mild, self-resolving injection-site reactions (2 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%). Of the 35 participants enrolled in the trial, two discontinued, with one withdrawing from the study due to declining renal function (a participant who was receiving placebo) and one discontinuing due to self-resolving, benign palpitations considered to be unrelated to study drug by external experts.

Additional analyses of the Uox data for nedosiran-treated patients with PH1 demonstrated:

- 59% greater reduction from baseline in 24-hour Uox averaged over Day 90 to Day 180 for nedosiran compared to placebo;
- 68% (SD=14.6) mean maximum percent reduction in 24-hour Uox from baseline with nedosiran treatment at any time point;
- 81% of participants achieved normal or near-normal Uox at Day 180;
- 44% of participants had normal Uox at Day 180; and
- 65% of participants had normal Uox on one or more visits during the 180-day period.

We expect the results from the PHYOX2 trial to support marketing authorization applications in the U.S. and other major markets.

Dicerna intends to present full results from PHYOX2 at an upcoming medical congress, subject to abstract acceptance.

PHYOX2 is part of the broader PHYOX clinical trial program designed to evaluate nedosiran in participants with PH1, PH2 and PH3. Data from PHYOX1, a single-dose Phase 1 trial in healthy volunteers and participants with PH1 or PH2; PHYOX2; PHYOX4, a single-dose safety and tolerability study in participants with PH3; and the ongoing PHYOX3 open-label extension study, are expected to support the nedosiran New Drug Application (NDA) submission, which is planned for the fourth quarter of 2021.

Conference Call and Webcast

Management will host a conference call and webcast at 4:30 p.m. ET today to discuss the PHYOX2 top-line results. The conference call can be accessed by dialing (855) 453-3834 or +1 (484) 756-4306 (international) and referencing conference ID 2845518 prior to the start of the call. A webcast presentation will also be available under the “Investors & Media” section of the Dicerna website, www.dicerna.com. A replay of the call will be available approximately two hours after the completion of the call. To access the replay, please dial (855) 859-2056 or +1 (404) 537-3406 and refer to conference ID 2845518. The webcast will also be archived on Dicerna’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 an end-product of metabolism called oxalate. Abnormal 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 the only RNAi drug candidate in development for primary hyperoxaluria (PH) types 1, 2 and 3 and is Dicerna’s most advanced product candidate utilizing the proprietary GalXC™ RNAi technology platform. 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 PH1, PH2 or PH3. Dicerna is evaluating the safety and efficacy of nedosiran in patients with all known subtypes of PH as part of its PHYOX™ clinical development program.

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 and potential impact of the results from the PHYOX2 trial of nedosiran as well as from the broader PHYOX clinical development program; the therapeutic potential of our product candidates, such as nedosiran; the Company’s regulatory plans and timelines for nedosiran, including our planned submission of a New Drug Application (NDA) for nedosiran and the indication(s) expected to be pursued in the near term; 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; the likelihood

of Dicerna's clinical programs being executed on timelines provided; our reliance on the Company's contract research organizations; the predictability of timely enrollment of subjects and patients to advance Dicerna's clinical trials; positive data from preclinical studies and earlier clinical trials may not be predictive of results from subsequent preclinical studies and clinical trials; the reliance of Dicerna on contract manufacturers to supply its products for research, development and commercialization and the risk of supply interruption from one or more such contract manufacturers; the potential for additional or future data to alter initial, interim and preliminary results of clinical trials; the results of clinical trials may produce negative, inconclusive or uncompetitive results; the impact of the ongoing COVID-19 pandemic on our business operations, including the conduct of our research and development activities; the regulatory review and unpredictability of the duration and results of the regulatory review of Investigational New Drug applications (INDs) and Clinical Trial Applications (CTAs) that are necessary to continue to advance and progress the Company's clinical programs; the timing, plans and reviews by regulatory authorities of marketing applications such as NDAs and comparable foreign applications for one or more of Dicerna's product candidates; alignment with the FDA on the regulatory pathway to approval for nedosiran; the ability to secure, maintain and realize the intended benefits of collaborations with partners; market acceptance for approved products and innovative therapeutic treatments; 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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