Dicerna Announces Positive Clinical Data for Investigational Treatments RG6346 for Chronic Hepatitis B Virus and Nedosiran for Primary Hyperoxaluria, and Presents Preclinical Data Applying RNAi Technology in New Tissues

August 6, 2020

– In the Ongoing Phase 1 Proof-of-Concept Trial Multidose Group, RG6346 1.5, 3.0 and 6.0 mg/kg Dosing Cohorts Reached Mean HBsAg Reduction From Baseline of 1.39, 1.80 and 1.84 Log10 IU/mL, Respectively, at Day 112 End-of-Treatment; Data for Earliest-Dose Cohort of 1.5 mg/kg Showed Durability of Response Through Day 336 –

– Self-Resolving ALT Elevations With Preserved Liver Function in Several Participants Treated With RG6346 Suggest ALT Flares Potentially as a Result of Treatment-Induced Enhanced Immune Responses –

– In the Ongoing PHYOX™3 Multidose, Open-Label Extension Trial of Nedosiran, 82% (Nine of 11 Participants) Achieved Normal or Near-Normal Levels of Key Primary Hyperoxaluria Measure at Day 120 –

– Company Presents for First Time Preclinical Data of Proprietary RNAi Technology in Extrahepatic Tissues –

– Company to Host Virtual R&D Event Today at 10:00 a.m. ET –

LEXINGTON, Mass.--(BUSINESS WIRE)--Aug. 6, 2020-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) (the “Company” or “Dicerna”), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced positive data from its Phase 1 proof-of-concept trial of RG6346, an investigational candidate for the treatment of chronic hepatitis B virus (HBV) infection in development in collaboration with Roche, and from its PHYOX3 open-label trial of nedosiran, an investigational candidate for the treatment of primary hyperoxaluria (PH). These data will be highlighted today as part of the Company’s virtual R&D Day event taking place from 10:00 a.m. to noon ET. Today’s event will also feature the Company’s first public presentation of preclinical data highlighting Dicerna’s proprietary RNAi technology in multiple new tissue types.

“The data presented today represent a cross-section of early- to late-stage results that highlight the power and significant potential of Dicerna’s RNAi technology platform, the benefit of innovative and thoughtfully designed development strategies, and our ability to generate a pipeline of potentially best-in-class new therapies for rare and prevalent diseases,” said Douglas Fambrough, Ph.D., president and chief executive officer of Dicerna. “I am very excited by the results we are seeing across our portfolio, demonstrating the strength of our RNAi technology platform and clinical enterprise, which together form the strong foundation upon which we are building our business to evolve into a fully integrated, commercial-stage biopharmaceutical company.”

RG6346 Phase 1 Proof-of-Concept Trial for Treatment of Chronic Hepatitis B Virus Infection

RG6346 is an investigational GalXC™ RNAi therapeutic candidate in Phase 1 for the treatment of chronic HBV infection. The ongoing Phase 1 proof-of-concept trial in adults comprises three groups: Group A, a dose-ranging cohort with healthy volunteers, which was completed last year; Group B, composed of newly diagnosed participants not on any antiviral therapy who received a single dose of RG6346; and Group C, which includes participants concurrently receiving nucleoside analog (NUC) therapy and four monthly doses of one of three dose levels of RG6346. In the Phase 1 study, nine of 10 participants who received RG6346 and have completed the treatment period in Group C achieved ≥1.0 log10 IU/mL reduction in hepatitis B surface antigen (HBsAg) at Day 112 and continued in the extended follow-up period. At Day 112, the mean reduction in HBsAg was 1.39 log10 IU/mL (n=4) for the 1.5 mg/kg cohort, 1.80 log10 IU/mL (n=4) for the 3.0 mg/kg cohort, and 1.84 log10 IU/mL (n=2) for the 6.0 mg/kg cohort; two participants have not yet reached Day 112. Of these 10 participants who received RG6346 and completed the treatment period, six had HBsAg <100 IU/mL at the last reported visit. Mean HBsAg reductions have been sustained through the extended follow-up period. The maximum HBsAg change observed was a 2.7 log10 IU/mL reduction on and after Day 112 end-of-treatment in a patient given 3.0 mg/kg of RG6346. The first patient dosed 1.5 mg/kg in the study has reached Day 392 with a 2.21 log10 IU/mL reduction in HBsAg (<100 IU/mL).

In addition, after a single 3.0 mg/kg dose of RG6346, two participants in Group B experienced protocol-defined transient alanine aminotransferase (ALT) flares, and one patient experienced a near-flare, each coinciding with a drop in HBsAg and preserved synthetic and excretory liver function, suggesting a potential enhanced immune response. One patient receiving 6.0 mg/kg of RG6346 in Group C demonstrated a similar self-resolving response.

“We are very encouraged by these early results from the RG6346 trial,” said John Young, global head of infectious diseases at Roche Pharma Early Research & Development. “Curing HBV infection requires development of a finite-duration therapeutic regimen that leads to sustained loss of circulating viral DNA and S-antigen in the bloodstream of patients. The level and durability of HBsAg reduction seen in this trial is of great interest, and we look forward to further evaluating the potential of RG6346 in an HBV therapeutic cure regimen.”

No serious adverse events (SAEs) were observed with RG6346 treatment in any group. The most commonly reported adverse events were mild or moderate injection-site events. No dose-limiting toxicities were observed, and there were no safety-related discontinuations. No dose-/exposure-dependent increases in frequency or severity of safety parameters were noted, and participants with ALT/AST (alanine aminotransferase and aspartate aminotransferase) or GGT (gamma-glutamyl transferase) elevations are all self-resolving, with preserved liver synthetic and excretory function.

“We took a unique and unconventional approach in our development of RG6346 by targeting just the conserved S region for the treatment of HBV,” commented Ralf Rosskamp, M.D., chief medical officer of Dicerna. “Our preclinical models showed that by sparing the X-gene, we could produce a therapy with a strong reduction in HBsAg and a long and stable duration of activity. The early data that we are now seeing from the RG6346 Phase 1 trial align with our predictions and signal its potential for the dual benefits of strong and sustained HBsAg knockdown in patients with HBV.”

Participants within Groups B and C were randomized 5:3 and 2:1, respectively, active versus placebo. Participants in Groups B and C are eligible to enter into an extended follow-up observation period if they achieve a reduction of ≥1.0 log10 IU/mL of HBsAg from baseline at the end of the treatment period (12 weeks/85 days for Group B and 16 weeks/112 days for Group C). Enrollment was completed in June 2020, and results summarized below were as of June 25, 2020. Two participants have not yet reached Day 112, and the study is ongoing.

Under the terms of the agreement between the companies, Roche will be responsible for initiating Phase 2 development of RG6346.

Nedosiran PHYOX3 Multidose Open-Label Extension Trial Interim Analysis

The PHYOX3 trial (ClinicalTrials.gov: NCT04042402) is an ongoing open-label extension study evaluating nedosiran's long-term safety and efficacy in participants with any of the three known types of primary hyperoxaluria – PH1, PH2 or PH3 – a family of ultra-rare, life-threatening genetic disorders that initially manifest with recurrent renal stones and can lead to kidney failure. The PHYOX3 trial is open to participants six years of age or older with PH who have participated in any previous PHYOX clinical development program trial, as well as their siblings with PH. All PHYOX3 participants who reached Day 120 and were evaluated in this interim analysis had previously completed the PHYOX1 single-ascending-dose Phase 1 trial. Of the 11 participants (eight PH1 and three PH2) who had reached Day 120 receiving once-monthly nedosiran, nine participants (82%) had achieved normal or near-normal urinary oxalate (Uox) levels, defined as below 0.46 mmol/1.73m^2 body surface area adjusted (BSA)/24 hr (laboratory assay upper limit of normal [ULN]) and from 0.46 to 0.6 mmol/1.73m^2 BSA/24 hr (1.3xULN, defined per protocol as near-normal), respectively.

"The ultimate goal in treating patients with any PH type is to reduce their urinary oxalate levels to a normal range and give them the independence to not only live their life more free from the daily burden of hyperhydration, but even more importantly, with some reassurance that their PH won't eventually lead to severe consequences such as chronic kidney failure or systemic oxalosis," said Bernd Hoppe, M.D., vice president, global medical affairs at Dicerna and head, German Hyperoxaluria Center, Bonn, Germany. "As of this interim analysis, 82% of participants treated with five once-monthly doses of nedosiran reached normal or near-normal urinary oxalate levels. Five participants in the trial achieved these levels at three consecutive visits, making them eligible for weaning from hyperhydration disease management. The results observed so far in the PHYOX3 trial are very encouraging, and we look forward to seeing a more complete picture of nedosiran's therapeutic profile as additional data from this trial and the PHYOX program become available."

As of the July 10, 2020 interim analysis:

- 16 of the 18 participants in the PHYOX1 trial had enrolled in PHYOX3.
- 11 participants had received at least five monthly doses of 170 mg of nedosiran delivered subcutaneously (Days 1, 30, 60, 90 and 120).
- There was an extended washout period between participants' completion of PHYOX1 during which participants were anticipated to return to 80% of their Uox PHYOX1 baseline prior to starting in PHYOX3. Some patients did not return to this range and were permitted to enroll in PHYOX3 with lower baseline levels. The mean BSA-adjusted baseline Uox of these 11 participants in PHYOX1 was 1.323 mmol/1.73m^2 BSA/24 hr, and the mean BSA adjusted observable baseline Uox levels for these same participants initiating PHYOX3 and included in this analysis was 0.926 mmol/1.73m^2 BSA/24 hr.
- 100% of PH1 participants (eight of eight) that had rolled over from PHYOX1 and received five doses of nedosiran in the PHYOX3 study had achieved normalization or near-normalization at Day 120; of these, normalization was reached in 63% of the PH1 participants (five of eight).
- For PH1 participants, the mean Uox level achieved was within the normal range (mean Uox= 0.404 mmol/1.73m^2 BSA/24 hr).
- All PH2 participants who had rolled over from PHYOX1 have received at least five doses of nedosiran. 33% of PH2 participants (one of three) achieved normalization at Day 120.
- Five of the 17 participants enrolled in PHYOX3 had achieved and maintained normal Uox concentrations on at least three consecutive visits, making them eligible for gradual reduction in fluid intake.

In this interim analysis, nedosiran appeared generally well tolerated, with three injection-site reactions in the 16 enrolled patients and no drug-related severe adverse events. The overall adverse event profile was comparable to that observed in the PHYOX1 Phase 1 clinical trial. There was one participant who experienced a serious adverse event that was determined by the investigator to be unrelated to the study drug. Based on the cumulative number of days participants have participated in the PHYOX3 trial, total patient exposure to monthly dosing of nedosiran delivered subcutaneously has reached 5.8 years.

The results of this interim analysis comprised data from participants in the previously completed PHYOX1 single-dose Phase 1 trial. The study's primary endpoint will evaluate annual rate of decline in estimated glomerular filtration rate (eGFR), a measure of kidney function and nedosiran's ability to preserve remaining kidney function. Also, the PHYOX3 trial will evaluate nedosiran's long-term effect on new stone formation, nephrocalcinosis, and the durability of reducing Uox levels, as well as its potential to enable the gradual decrease or elimination of their disease management practices.

Going Beyond GalXC: Dicerna's Technology in New Tissues

Dicerna also announced preclinical data demonstrating expansion of its technology and discovery efforts beyond its hepatocyte-focused GalXC RNAi technology to central nervous system (CNS), skeletal muscle and adipose tissues. Among the key highlights were:

- Results from preclinical assays demonstrated consistent and durable CNS-wide target mRNA knockdown using novel constructs regardless of route of administration (intrathecal [IT] or intracisterna magna [ICM]); and
- Reduction in target mRNA (messenger RNA) in skeletal muscle and adipose tissue using optimized chemistries, resulting in equivalent and potentially highly durable target knockdown regardless of dosing regimens.

"We are very excited to present for the first time today preclinical data demonstrating the potential application of our technology platform beyond the

liver," said Bob D. Brown, chief scientific officer and executive vice president of R&D at Dicerna. "With the discovery and early success of GalXC– the technology platform underpinning our lead candidate nedosiran, core pipeline candidates, and our collaborations – we have continued to innovate and evolve our technology to provide flexibility for medicinal chemistry optimization and expansion. The preclinical data shown today generated by structurally and chemically modified and/or alternatively conjugated forms of our foundational GalXC technology can exhibit the potential to deliver therapeutic nucleic acids with potent and sustained activity in central nervous system, skeletal muscle and adipose tissues, as well as other tissues."

Dr. Fambrough concluded, "The interim data today from our PHYOX3 study of nedosiran reinforce its potential to meaningfully interfere with the overproduction of urinary oxalate that can lead to serious systemic impacts in patients with PH, including kidney failure. The data from our Phase 1 study of RG6346 highlight its potential to be an important RNAi therapy in the treatment of HBV, with strong HBsAg knockdown sustained over a long duration. The preclinical data emerging from our labs supporting the extension of our technology to potential new therapeutic categories beyond the liver are demonstrating precisely the outcomes we intended. It's an exciting time at Dicerna. I am energized by the caliber of data emerging from our preclinical and clinical programs and look forward to presenting the data in greater detail later today."

Virtual Webcast Details

The virtual webcast presentation to discuss these data will begin at 10:00 a.m. ET and may be accessed by visiting the "Investors & Media" section of the Dicerna website, www.dicerna.com. A conference line can be accessed by dialing (800) 708-4539 or +1 (847) 619-6396 and referencing conference ID 49860522. A replay of the webcast will be archived on Dicerna's website following the conclusion of the live event.

About Chronic Hepatitis B Virus (HBV) Infection

Hepatitis B virus (HBV) is the world's most common serious liver infection and affects an estimated 292 million people worldwide. [1] Chronic HBV infection, a condition characterized by the presence of the HBV surface antigen (HBsAg) for six months or more, claims more than 887,000 lives annually.[2] HBV is also the primary cause of liver cancer (also known as hepatocellular carcinoma, or HCC), which is the second-leading cause of cancer deaths in the world.[1]

About RG6346

RG6346 is an investigational GalXC™ RNAi therapeutic candidate in development in collaboration with Roche for the treatment of chronic HBV infection. Dicerna is currently conducting a Phase 1 proof-of-concept trial of RG6346 in adult patients with non-cirrhotic chronic HBV infection. Current therapies for HBV, such as nucleoside analogs, can provide long-term viral suppression if taken continuously, but they rarely lead to long-term functional cures, as measured by the clearance of HBV surface antigen (HBsAg) and sustained HBV deoxyribonucleic acid (DNA) suppression in patient plasma or blood. By contrast, RG6346 is designed to employ RNA interference to selectively knock down specific genes involved in the creation of HBV messenger RNA (mRNA) and the entry of the virus into liver cells. Preclinical data have demonstrated greater than 99.9% reduction in circulating HBsAg, as observed in mouse models of HBV infection. Unlike current therapies that typically provide long-term suppression of the virus, RG6346 has the potential to provide a functional cure for patients living with chronic HBV.

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 types 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 a substrate 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 results eventually in the accumulation of oxalate in organs ranging from skin, bones, eyes and heart. In the most severe cases, symptoms start in the first year of life. A combined liver-kidney transplantation may be undertaken to resolve PH1 or PH2 but is an invasive solution with limited availability and high morbidity that requires lifelong immune suppression to prevent organ rejection. Currently, there is no approved therapy for the treatment of PH. Patients are limited to using hyperhydration and medication to attempt to increase solubility of oxalate in urine. Despite these interventions, oxalate may continue to accumulate in the kidneys, causing damage.

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 the lactate dehydrogenase (LDH) enzyme – an enzyme that catalyzes the final step in a common pathway resulting in oxalate overproduction in patients with PH1, PH2 and PH3. Dicerna is evaluating the safety and efficacy of nedosiran in patients with all known forms of PH as part of its PHYOX™ clinical development program.

About the GalXC™ RNAi Technology Platform

Dicerna's proprietary RNA interference (RNAi) technology platform, called GalXC™, aims to advance the development of next-generation RNAi-based therapies designed to silence disease-driving genes in the liver. GalXC-based compounds enable subcutaneous delivery of RNAi therapies that are designed to bind specifically to receptors on liver cells, leading to internalization and access to the RNAi machinery within the cells. The GalXC approach seeks to optimize the activity of the RNAi pathway so that it operates in the most specific and potent fashion.

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 selectively silence genes that cause or contribute to disease. Using our proprietary RNAi technology platform called GalXC™, 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 hepatocytes, Dicerna has continued to innovate and is exploring new applications of its RNAi technology beyond the liver, targeting additional tissues and enabling new therapeutic applications. 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 rare, cardiometabolic, viral, chronic liver and complement-mediated diseases, as well as neurodegeneration and pain. At

Dicerna, our mission is to interfere – to silence genes, to fight disease, to restore heath. 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: (i) Phase 1 proof-of-concept data for RG6346, an investigational GalXC™ RNAi treatment candidate for chronic hepatitis B virus (HBV) infection in development with Roche; (ii) multidose data from the PHYOX™3 trial of nedosiran, an investigational GalXC RNAi treatment candidate for primary hyperoxaluria (PH), (iii) first preclinical data on Dicerna's RNAi technology in extrahepatic tissues; (iv) the therapeutic and commercial potential of nedosiran and (v) clinical development timelines and review related to nedosiran and continued alignment on the regulatory pathway to approval. 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 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 reliance of Dicerna on contract manufacturers to supply its products for research and development and the risk of supply interruption from a contract manufacturer; the potential for future data to alter initial and preliminary results of early-stage clinical trials; 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 New Drug Applications (NDAs) and comparable foreign applications for one or more of Dicerna's product candidates; 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 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] Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. *The Lancet Gastroenterology and Hepatology*. Volume 3, Issue 6, June 2018, Pages 383-403.

[2] Hepatitis B Foundation. Facts and Figures. Available at: http://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/. Accessed on Aug. 4, 2020.

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