Dicerna Announces Positive Updated Data From Phase 1 Trial of RG6346 for Treatment of Chronic Hepatitis B Virus (HBV) Infection at AASLD's The Liver Meeting® Digital Experience™ 2020

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– Data Presentations Show Treatment With Up to Four Monthly Doses of RG6346 Resulted in Substantial and Durable Reductions in HBsAg Levels Lasting Up to One Year After Last Dose –

– RG6346 Was Shown to be Safe and Well Tolerated in This Trial –

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 16, 2020-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) (the "Company" or "Dicerna"), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced positive updated data from its Phase 1 double-blind, placebo-controlled, proof-of-concept trial of RG6346, an investigational GalXC™ RNAi therapeutic that Dicerna is developing in collaboration with Roche for the treatment of chronic hepatitis B virus (HBV) infection. The data, presented in a late-breaker poster and oral session at The Liver Meeting® Digital Experience™ 2020 hosted by the American Association for the Study of Liver Diseases (AASLD), expand upon the interim results presented by the Company in August 2020 and demonstrate that four monthly doses of RG6346 treatment resulted in substantial and durable reductions in biomarkers of HBV disease activity as measured by reductions in hepatitis B surface antigen (HBsAg) levels lasting up to one year following the last dose. RG6346 was also shown to have a favorable safety and tolerability profile in the trial.

In trial participants who were treated with four monthly doses of RG6346 added to nucleos(t)ide (NUC) antiviral therapy (Group C), 11 of 12 (92%) had mean HBsAg reductions from baseline greater than 1.0 $\log_{10}$ IU/mL by Day 112 (one month after last dose). Seven of the 12 participants (58%) also achieved HBsAg levels below 100 IU/mL – a level that is associated with a reduced risk of progression to cirrhosis and hepatocellular carcinoma. Durability of HBsAg reductions was observed up to Day 448 (one year after the last dose). Among participants eligible to continue in long-term follow-up after the dosing period in the longest-observed cohort (1.5 mg/kg; n=3), the mean reduction in HBsAg from baseline was 1.40 $\log_{10}$ IU/mL at Day 448; one of these participants maintained greater than a 2.0 $\log_{10}$ IU/mL reduction in HBsAg level from baseline at Day 448.

"We are pleased by the magnitude and sustainability of HBsAg suppression with RG6346 seen in our latest Phase 1 results, lasting up to one year after the last dose administered," said Shreeram Aradhye, M.D., Executive Vice President and Chief Medical Officer at Dicerna. "RNAi is a modality that holds significant promise in HBsAg suppression, and the results we have seen thus far with RG6346 are very encouraging, suggesting it could be a strong foundation for a combination therapy approach with the potential to achieve functional cures in people with chronic HBV infection."

Additional data highlights from Group C participants treated with RG6346 plus NUC therapy (data cutoff October 2020) included:

- 75% (9 of 12) experienced HBsAg reductions of ≥1.5 $\log_{10}$ IU/mL.
- At Day 112, the mean reduction in HBsAg was 1.39 (SE 0.19) $\log_{10}$ IU/mL for the 1.5 mg/kg cohort (n=4); 1.80 (SE 0.28) $\log_{10}$ IU/mL for the 3.0 mg/kg cohort (n=4); and 1.64 (SE 0.30) $\log_{10}$ IU/mL for the 6.0 mg/kg cohort (n=4).
- The maximum HBsAg reduction from baseline was 2.7 $\log_{10}$ IU/mL in a participant given 3.0 mg/kg of RG6346.
- 83% (10 of 12) entered conditional follow-up. Participants were eligible to enter the conditional follow-up period if they had HBsAg reductions from baseline of ≥1.0 $\log_{10}$ IU/mL at the end of the treatment period.
- 67% (8 of 12) entered conditional follow-up and had ≥1.0 $\log_{10}$ IU/mL HBsAg reduction from baseline at the last observed time point, which ranged from Day 140 to Day 448.
- Similar mean maximum HBsAg $\log_{10}$ IU/mL reductions were observed independent of hepatitis B e-antigen status (HBeAg levels are an indicator of active HBV replication and high infectivity).

In three of six NUC-naïve participants treated with a single 3.0 mg/kg dose of RG6346 (Group B), transient alanine aminotransferase (ALT) elevations, or flares (defined in the study protocol as more than three times baseline or post-baseline nadir value and more than seven times the upper limit of normal), were observed during the treatment period. These were associated with concomitant viral marker reductions and preserved liver function, suggesting beneficial treatment-induced immune-mediated responses to HBV. No protocol-defined ALT flares were observed in Group C (NUC-suppressed) participants, most likely reflecting therapeutic NUC suppression and further demonstrating RG6346 safety in combination therapy for HBV.

No serious adverse events (SAEs) were reported for participants treated with RG6346, and there were no dose-limiting toxicities or safety-related discontinuations. The most commonly reported adverse events were mild or moderate injection-site events. There were no dose-exposure or regimen-dependent increases in frequency or severity of adverse events, safety lab values, electrocardiogram readings or vital signs.

"The data presented show for the first time the depth of HBsAg reduction achieved by all treated patients during the full RG6346 treatment period, as well as post-dose duration of HBsAg knockdown lasting up to one year," commented Man-Fung Yuen, D.Sc., M.D., Ph.D., Chief of the Division of Gastroenterology & Hepatology and Deputy Head of the Department of Medicine at Queen Mary Hospital at The University of Hong Kong, and investigator in the Phase 1 proof-of-concept trial. "The substantial and durable HBsAg knockdown seen to date in this trial, together with evidence suggestive of beneficial ALT flare immune responses in participants naïve to antiviral therapy, demonstrate RG6346's significant potential as a viable RNAi therapy for the treatment of chronic HBV infection. With supportive safety and tolerability data, I am encouraged by the potential for this investigational therapy to induce functional cures in patients as a part of a combination treatment regimen."

"We continue to be very encouraged by results seen with RG6346," said John Young, Global Head of Infectious Diseases at Roche Pharma Early Research & Development. "The level and duration of HBV surface antigen reduction with RG6346 treatment, as well as decreases in viral DNA,

suggest the potential for strong synergy as part of a combination regimen for HBV. We look forward to the further characterization of RG6346 as part of a combination therapeutic approach in a planned Phase 2 trial."

The results of this Phase 1 trial will be presented live on Nov. 16, 2020 at 2:20 p.m. ET during the Late-Breaking Oral Session 2 by Dr. Yuen. The poster and slides will also be made available on the Events & Presentations page of Dicerna's corporate website after their presentation at the conference.

About the RG6346 Phase 1 Proof-of-Concept Trial

The RG6346 Phase 1 proof-of-concept trial comprises three groups of adult participants: Group A, composed of 30 healthy volunteers who received single RG6346 doses up to 12.0 mg/kg (completed 2019); Group B, composed of nine participants who were newly diagnosed with chronic HBV and naive to any NUC antiviral therapy, randomized 5:3[1] to a single 3.0 mg/kg dose of RG6346 or placebo, respectively (completed early 2020); and Group C, composed of 18 participants who were diagnosed with chronic HBV and actively receiving NUC therapy, randomized 2:1 to four monthly doses of 1.5, 3.0 or 6.0 mg/kg of RG6346 or placebo, respectively. The last participant visit in the double-blind period up to Day 112 for Group C occurred in October 2020. Participants in Groups B and C were eligible to enter an extended follow-up observation period if they achieved an HBsAg reduction from baseline of ≥1.0 $\log_{10}$ IU/mL at the end of the treatment period (12 weeks/85 days for Group B; 16 weeks/112 days for Group C).

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. [2] According to the Hepatitis B Foundation, 30 million people become newly infected with HBV each year, and it is estimated that more than 880,000 people die annually from hepatitis B and related complications such as liver cancer.[3]

About RG6346

RG6346 is an investigational GalXC™ RNAi therapeutic candidate in development in collaboration with Roche for the treatment of chronic hepatitis B virus (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 nucleos(t)ide 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 RNAi to knock down selectively 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, we believe RG6346 has the potential to provide a functional cure as part of a combination regimen for patients living with chronic HBV.

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 silence selectively 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 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: 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. The process by which investigational therapies, such as RG6346, 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] One additional subject was enrolled in Group B (total n=9) to replace a subject determined to be ineligible after the study dose had been administered.

[2] Polaris Observatory Collaborators. Global prevalence, treatment, and prevention of hepatitis B virus infection in 2016: a modelling study. *The Lancet Gastroenterology and Hepatology*. 2018;3(6):383-403.

[3] Hepatitis B Foundation. Facts and Figures. Available at: http://www.hepb.org/what-is-hepatitis-b/what-is-hepb/facts-and-figures/. Accessed on Oct. 25, 2020.

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