Dicerna Presents Data From Phase 1 Trial of Belcesiran at American Association for the Study of Liver Diseases (AASLD) The Liver Meeting® 2021

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– Belcesiran Was Shown to Be Safe and Well Tolerated in Phase 1 Trial and Demonstrated Robust, Dose-Dependent Reductions in Serum Alpha-1 Antitrypsin –

– Enrollment in ESTRELLA Phase 2 Study of Belcesiran Is Ongoing; Global Rollout to Additional Trial Sites Continues –

LEXINGTON, Mass.--(BUSINESS WIRE)--Nov. 12, 2021-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today presented results from its Phase 1 double-blind, placebo-controlled, randomized trial of belcesiran, an investigational GalXC™ RNAi therapeutic in development for the treatment of alpha-1 antitrypsin (AAT) deficiency-associated liver disease (AATLD). These data expand upon interim results announced in July 2021, demonstrating the safety and tolerability of single ascending doses of belcesiran in healthy volunteers (up to and including the final 12 mg/kg dose cohort) and further reaffirming the dosing regimen established for the ESTRELLA Phase 2 study of belcesiran. In addition, the data demonstrated robust, dose-dependent reductions in serum AAT through the 6 mg/kg dose level, with a maximum individual reduction of 91%. The data were presented in a poster at The Liver Meeting® 2021, the annual meeting of the American Association for the Study of Liver Diseases (AASLD).

“In people with AATLD, misfolded AAT aggregates in the liver and causes liver injury that may progress to liver fibrosis, cirrhosis and hepatocellular carcinoma. Liver transplantation is currently the only option for individuals with this rare condition who progress to liver failure, underscoring the need for a safe and effective therapeutic approach that can reduce the production and aggregation of toxic protein in the liver,” said Shreeram Aradhye, M.D., Executive Vice President and Chief Medical Officer at Dicerna. “Belcesiran is designed to reduce the production of abnormal AAT. We are pleased by the results from the first clinical trial of belcesiran, which achieved our goals of demonstrating safety and establishing a dosing regimen for our ESTRELLA Phase 2 study of belcesiran, which is underway. We are confident in the dosing regimen that was selected for ESTRELLA and the profile that we expect it to generate.”

“The results from this first-in-human trial showed clear reduction in serum AAT with belcesiran administration,” said Edward Gane, M.D., MBChB, FRACP, MNZ, Auckland City Hospital and University of Auckland, Auckland, New Zealand, and investigator in the Phase 1 trial. “The results from this trial support further evaluation of belcesiran as a potential therapy for AATLD.”

“Enrollment in the ESTRELLA trial continues to progress as we bring more clinical trial sites online in multiple countries,” Dr. Aradhye continued. “We also look forward to expanding our inclusion criteria for ESTRELLA in the near-term to include patients on augmentation therapy – a key area of interest to us as patients with the liver manifestation can also present with AAT deficiency-associated lung disease.”

The Phase 1 trial was designed to evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of a single subcutaneous dose of belcesiran 0.1, 1.0, 3.0, 6.0 or 12.0 mg/kg compared to placebo (n=6, 2:1 randomization per cohort) in 30 adult healthy volunteers. A validated, standard-of-care quantitative nephelometry assay was used to measure serum AAT levels. Repeat measurements of spirometry and diffusing capacity of the lungs for carbon monoxide (DLCO) were performed to monitor pulmonary function. All participants completed their treatment periods (through Day 57). All participants receiving belcesiran and who met certain criteria entered conditional follow-up post Day 57.

Results

- Robust, dose-dependent reductions in serum AAT were observed up to 6 mg/kg following a single dose of belcesiran, with the 6 mg/kg and 12 mg/kg cohorts achieving similar AAT reductions. Mean serum AAT reductions from baseline at end of treatment for doses greater than 0.1 mg/kg were 48% (1.0 mg/kg), 67% (3.0 mg/kg), 77% (6.0 mg/kg) and 78% (12.0 mg/kg), with maximum reductions occurring approximately eight weeks post-dose.
    - Two participants achieved a maximum serum AAT reduction of approximately 90%; both participants received belcesiran 6 mg/kg.
- No severe or serious treatment-emergent adverse events (TEAEs) were reported. Most TEAEs were mild (39) or moderate (3 in two participants; common cold, gastroenteritis and staphylococcal folliculitis) and were determined to be unrelated to belcesiran treatment. No dose-dependent increases in frequency or severity of TEAEs, or abnormalities in safety labs, ECGs, physical exams or vital signs were observed.
- Normal lung function was maintained. There were no dose-dependent changes in spirometry measurements, and percent predicted DLCO repeat measurements remained within normal limits.
- No clinically significant changes in laboratory safety tests, including liver function tests, were reported for any belcesiran dose.

These results were presented at AASLD by Dr. Gane as a narrated poster (Poster #27962) titled, “Belcesiran Was Well Tolerated and Reduced Serum AAT Levels in Healthy Volunteers.” The poster will be made available on the Events and Presentations page of Dicerna’s website.

About Alpha-1 Antitrypsin (AAT) Deficiency and Alpha-1 Antitrypsin Deficiency-Associated Liver Disease (AATLD)

Alpha-1 antitrypsin (AAT) deficiency is a rare genetic condition caused by mutations in the *SERPINA1* gene that results in disease of the liver and lungs. AAT protein is produced in hepatocytes and circulates in the bloodstream; AAT protects the lungs and other parts of the body by neutralizing

neutrophil elastase, an enzyme that fights infection but can also damage healthy tissues if not adequately regulated by AAT. The majority of people with severe AAT deficiency are homozygous for the Z allele (PiZZ genotype).[1] In the liver, misfolding of the mutant Z-AAT protein causes the protein to aggregate in liver cells, leading to liver injury, including fibrosis, cirrhosis and hepatocellular carcinoma. An estimated 10% or more of adults with AAT deficiency develop clinically meaningful liver disease.[2,3] People with AAT deficiency may also develop lung disease, including emphysema.

About Belcesiran

Belcesiran is a clinical-stage, subcutaneously administered, investigational GalXC™ RNAi therapy targeting alpha-1 antitrypsin (AAT) that is in development for the treatment of AAT deficiency-associated liver disease (AATLD). Belcesiran is designed to target the gene responsible for production of the abnormal AAT protein in order to reduce AAT production in the liver. Dicerna is currently investigating the use of belcesiran for the treatment of AATLD in the SHINE clinical development program.

About the ESTRELLA Trial

ESTRELLA (NCT04764448) is a randomized, multidose, double-blind, placebo-controlled Phase 2 trial evaluating the safety, tolerability, pharmacokinetics and pharmacodynamics of belcesiran in participants with alpha-1 antitrypsin deficiency-associated liver disease (AATLD). The study includes a 24-week cohort and a 48-week cohort to be conducted in participants who have a diagnosis of PiZZ-type AAT deficiency and AATLD. The ESTRELLA clinical trial is part of Dicerna's SHINE clinical development program to evaluate the safety and efficacy of belcesiran, formerly known as DCR-A1AT, for the treatment of AATLD.

About RNAi and Dicerna's GalXC™ RNAi Platform

Ribonucleic acid interference, or RNAi, provides a unique advantage to other disease inhibitor technologies, like small-molecule pharmaceuticals or monoclonal antibodies. Instead of targeting proteins after they have been produced and released, RNAi silences the genes themselves via the specific destruction of the messenger RNA (mRNA) made from the gene. Rather than seeking to inhibit a protein, the RNAi approach can prevent a disease-causing protein's creation, directly impacting disease manifestation.

Dicerna's proprietary GalXC™ RNAi platform aims to advance the development of next-generation RNAi-based therapies. Investigational therapeutics developed using our flagship GalXC technology utilize a proprietary *N*-acetyl-D-galactosamine (GalNAc)-mediated structure of double-stranded RNA molecules that are designed to bind specifically to receptors on liver cells, leading to selective hepatocyte internalization and access to the RNAi machinery within the cells. Dicerna is continuously innovating and exploring new applications of RNAi technology beyond GalNAc-mediated delivery to the liver, including alternative RNA structures and fully synthetic ligands that target other tissues and cell types and enable new therapeutic applications, referred to as GalXC-Plus™.

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 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, 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: the belcesiran development program, including the results from our clinical trials and the potential impact thereof, the potential of belcesiran as a treatment for alpha-1 antitrypsin deficiency-associated liver disease (AATLD), and the planned progression of our clinical trials, such as for our Phase 2 trial of belcesiran. The process by which investigational therapies 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, interim 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 unpredictability of the duration and results of the regulatory review of Investigational New Drug (IND) applications and Clinical Trial Applications (CTAs) that are necessary to continue to advance and progress the Company's clinical programs and the regulatory review of INDs and CTAs; 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.

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2. Tanash & Piitulainen. J Gastroenterol. 2019 Jun;54(6):541-548. doi: 10.1007/s00535-019-01548-y. Epub 2019 Jan 24.

3. Clark et al. J Hepatol. 2018 Dec;69(6):1357-1364. doi: 10.1016/j.jhep.2018.08.005. Epub 2018 Aug 21.

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