Dicerna Initiates Patient Dosing in ESTRELLA Phase 2 Clinical Trial of Belcesiran for the Treatment of Alpha-1 Antitrypsin Deficiency-Associated Liver Disease

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LEXINGTON, Mass.--(BUSINESS WIRE)--Jun. 22, 2021-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) (the “Company” or “Dicerna”), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, announced it has initiated patient dosing in the Company’s Phase 2 ESTRELLA trial of belcesiran, an investigational GalXC™ RNAi therapeutic candidate for the treatment of alpha-1 antitrypsin (AAT) deficiency-associated liver disease (AATLD). AATLD is a rare genetic condition that can lead to liver fibrosis, cirrhosis and hepatocellular carcinoma.

“There are an estimated 183,000 people in Europe and the U.S. who carry a genetic mutation that can result in AAT deficiency and the associated liver and lung disease.[1] With no therapies available to specifically address AAT liver disease, liver transplantation remains the only option for these patients,” said Shreeram Aradhye, M.D., Executive Vice President and Chief Medical Officer at Dicerna. “Dicerna’s investigational RNAi therapeutic, belcesiran, is designed to silence the gene that produces the abnormal AAT protein. Reducing production of this protein in patients with AATLD has the potential to allow their livers to clear the accumulated abnormal protein and restore liver health. We are very pleased to have now begun patient dosing in our Phase 2 ESTRELLA trial to better understand belcesiran’s potential to treat the underlying cause of AATLD.”

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 AATLD. The study includes a 24-week cohort and a 48-week cohort to be conducted in parallel, each with up to 27 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. A Phase 1 trial of multiple doses of belcesiran in healthy volunteers is ongoing, with initial data from the Phase 1 trial expected in mid-2021.

About Alpha-1 Antitrypsin 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). 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 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 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 on the functionality and application of our flagship liver-targeted GalXC technology, 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 the belcesiran development program and the potential of belcesiran as a treatment for alpha-1 antitrypsin deficiency-related liver disease (AATLD). 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 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.

1. Blanco et. al. Int J Chron Obstruct Pulmon Dis. 2017; 12: 561–569.
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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