Dicerna Receives Orphan Drug Designation From U.S. Food and Drug Administration for DCR-A1AT for Treatment of Alpha-1 Antitrypsin Deficiency

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LEXINGTON, Mass.--(BUSINESS WIRE)-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) (the “Company” or “Dicerna”), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced that the U.S. Food and Drug Administration (FDA) has granted orphan drug designation (ODD) to Dicerna’s DCR-A1AT for the treatment of alpha-1 antitrypsin (A1AT) deficiency. A1AT deficiency is a genetic disorder that can cause lung and liver disease. Children with the liver manifestations of the disease may present with yellowing of the skin and whites of the eyes (jaundice) and may progress to forming scar tissue in the liver (cirrhosis). Adults with the liver disease may also develop cirrhosis, progress to liver failure or develop a type of liver cancer called hepatocellular carcinoma.[1]

“The FDA’s orphan drug designation is an important milestone in our development plan for DCR-A1AT for alpha-1 antitrypsin deficiency-associated liver disease and underscores the treatment need that exists for this complex disorder,” said Ralf Rosskamp, M.D., chief medical officer of Dicerna. “RNAi technology has shown significant potential in the treatment of liver-related diseases, and we look forward to continuing to investigate DCR-A1AT’s potential to make a meaningful difference for this underserved patient population.”

In June 2019, the Company submitted a clinical trial application to the Swedish Medical Products Agency for DCR-A1AT for the treatment of patients with A1AT deficiency-associated liver disease and began enrolling healthy volunteers in the Phase 1/2 trial of DCR-A1AT (EudraCT number 2019-001999-11) in the fourth quarter of 2019. The Company expects to dose the first patient in the second half of 2020.

Orphan drug status is intended to advance drug development for rare diseases. The FDA provides ODD to drugs and biologics that demonstrate promise for the diagnosis and/or treatment of rare diseases or conditions that affect fewer than 200,000 people in the U.S. The designation can provide development and commercial incentives for designated compounds and medicines, including eligibility for a seven-year period of market exclusivity in the U.S. after product approval, FDA assistance in clinical trial design and an exemption from FDA user fees.

In December 2019, the European Commission granted ODD to DCR-A1AT for the treatment of congenital alpha-1 antitrypsin deficiency based on a positive opinion from the Committee for Orphan Medicinal Products of the European Medicines Agency.

About DCR-A1AT
DCR-A1AT is a subcutaneously administered ribonucleic acid interference (RNAi) therapeutic that is being investigated for the treatment of liver disease in patients with alpha-1 antitrypsin (A1AT) deficiency. A1AT is a protein primarily produced in and released from the liver. A1AT plays a role in several biological functions, including regulating the activity of neutrophil elastase, which helps the body fight infection. In A1AT deficiency, the *SERPINA1* gene encodes a mutated form of A1AT, the majority of which cannot be released from the liver. As a result, insufficient levels of A1AT are available to protect the lungs from harmful effects of neutrophil elastase. Additionally, the accumulation of mutated A1AT in the liver can lead to liver disease. There are currently no approved therapies to treat A1AT deficiency-associated liver disease. DCR-A1AT, which incorporates Dicerna’s proprietary GalXC™ technology, is designed to target *SERPINA1,* reducing production of abnormal A1AT in the liver. A clinical trial program investigating the safety and efficacy of DCR-A1AT is currently underway.

About Alpha-1 Antitrypsin (A1AT) Deficiency
Alpha-1 antitrypsin (A1AT) deficiency is an inherited disorder that can lead to liver disease in children and adults, and lung disease in adults. The disorder is caused by mutations in a gene called *SERPINA1*. When functioning normally, this gene provides instructions for making a protein called A1AT, which protects the body from an enzyme called neutrophil elastase. This enzyme is released from white blood cells to fight infection, but it can attack normal tissues if not tightly controlled by A1AT. Mutations in the *SERPINA1* gene can result in a deficiency, or shortage, of functional A1AT and an abnormal form of the protein that cannot control neutrophil elastase. Uncontrolled neutrophil elastase can destroy alveoli (small air sacs in the lungs) and cause lung disease.[1] In the liver, the accumulation of abnormal A1AT can trigger an injury cascade, which can lead to liver injury.[2]

About 10% of adults with A1AT deficiency develop cirrhosis, or liver damage, due to formation of scar tissue in the liver.[3] Individuals affected by A1AT deficiency are also at risk of developing hepatocellular carcinoma, a type of liver cancer. People with A1AT deficiency may develop the first symptoms of lung disease between the ages of 20 and 50 years. Symptoms can include shortness of breath following mild activity, reduced ability to exercise, wheezing, unintended weight loss, recurring respiratory infections, fatigue and rapid heartbeat upon standing. Some individuals with A1AT deficiency develop emphysema, a lung disease caused by damage to the alveoli. [1]

A1AT deficiency occurs all over the world, though its prevalence varies by population. The disorder affects roughly one in 1,500 to 3,500 individuals with European ancestry and is uncommon in people of Asian descent.[1] Congenital A1AT deficiency is estimated to affect 2.4 people out of every 10,000 in the European Union.[4] Many individuals with A1AT deficiency are thought to be undiagnosed, particularly those who also have chronic obstructive pulmonary disease (COPD). Some people with A1AT deficiency are misdiagnosed with asthma.[1]

About Dicerna's GalXC™ RNAi Technology Platform
Dicerna’s proprietary ribonucleic acid 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 and other body systems. Liver-targeted GalXC-based compounds enable subcutaneous delivery of RNAi therapies that are designed to specifically bind 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 reducing the level of disease-causing proteins in the hepatocytes of the liver, Dicerna's GalXC has the potential to safely target conditions that are difficult to treat with other modalities. Continually innovating, Dicerna is also exploring new applications of 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. and Boehringer Ingelheim International GmbH. Between Dicerna and our collaborative partners, we currently have more than 20 active discovery, preclinical or clinical programs focused on rare, cardiometabolic, viral-infectious, 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. 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) research and development plans and timelines related to DCR-A1AT and the potential of DCR-A1AT to treat A1AT or liver disease; (ii) the potential of Dicerna's technology and drug candidates in the Company's research and development pipeline; and (iii) the receipt of orphan drug designation from applicable regulatory authorities and the intended benefits from such designation. The process by which an early-stage investigational therapy such as DCR-A1AT and an early-stage platform such as GalXC™ could potentially lead to an approved product or have a major impact on liver disease is a long-term effort 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 filing on Form 10-K 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 unpredictability of the duration and results of the regulatory review of Investigational New Drug applications (INDs) and Clinical Trial Applications that are necessary to continue to advance and progress the Company's clinical programs and the regulatory review of marketing applications in the future; 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 research and development; our ability to maintain and realize the intended benefits of orphan drug designation; 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.

References

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4. Based on Dicerna internal estimates.

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