Dicerna™ to Begin Clinical Development of DCR-A1AT for Treatment of Patients with Alpha-1 Antitrypsin Deficiency-Associated Liver Disease

July 2, 2019

— Company Submitted Clinical Trial Application and Plans to Initiate Multicenter Phase 1/2 Trial in Third Quarter of 2019 —

— Alpha-1 Antitrypsin Deficiency-Associated Liver Disease Program Broadens Dicerna's Commitment to Addressing Chronic Liver Diseases—

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jul. 2, 2019-- Dicerna™ Pharmaceuticals, Inc. (Nasdaq: DRNA) (the "Company" or "Dicerna"), a leading developer of ribonucleic acid interference (RNAi) therapies, today announced it submitted a Clinical Trial Authorization (CTA) application to the Swedish Medical Products Agency (MPA) last week to conduct a first-in-human Phase 1/2 study of DCR-A1AT, an investigational therapy from the Company's GalXC™ technology platform, for the treatment of alpha-1 antitrypsin (A1AT) deficiency-associated liver disease. A1AT deficiency is a genetic disorder that can cause liver disease in children and adults, leading to complications such as weight loss, fatigue, jaundice and life-threatening conditions such as cirrhosis. Patients with A1AT deficiency are also at risk for developing hepatocellular carcinoma.[1]

"We are pleased to begin the clinical development phase of our A1AT deficiency-associated liver disease program, which serves two roles in Dicerna's portfolio," said Douglas Fambrough, president and chief executive officer of Dicerna. "First, A1AT deficiency-associated liver disease fits with our rare disease strategy as an indication with a significant unmet medical need and a clear biomarker, presenting a rapid development path to approval. Second, the program will inform and aid our efforts in the much broader chronic liver disease field, where we believe our GalXC platform can have a major impact, and which provides ample opportunities to collaborate with larger pharmaceutical company partners."

The proposed parallel-group, placebo-controlled, Phase 1/2 study will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of DCR-A1AT in adult healthy volunteers (HVs) and patients with A1AT deficiency-associated liver disease. The study will consist of two phases:

- Group A: a single ascending-dose phase in HVs, enrolling up to 36 participants in as many as six cohorts
- Group B: a multiple ascending-dose phase in patients with A1AT deficiency-associated liver disease, consisting of up to 24 participants in three or fewer cohorts

Pending approval from the Swedish MPA, Dicerna aims to initiate screening of HVs for Group A in the third quarter of 2019, and to begin enrolling Group B participants in the first quarter of 2020. Dicerna plans to conduct the study in up to 16 sites across Europe, with the first clinical trial site in Sweden.

"A1AT deficiency is a genetic condition that can lead to liver disease with potentially devastating complications including scarring of the liver and liver cancer," commented Jeffrey Teckman, M.D., professor of Biochemistry and Molecular Biology at Saint Louis University School of Medicine in St. Louis, MO. "With this CTA filing, and the expected initiation of a first-in-human Phase 1/2 clinical trial of DCR-A1AT once the MPA authorizes the CTA, Dicerna is pursuing an exciting and important approach that addresses a high unmet medical need in A1AT deficiency-associated liver disease."

"The launch of the DCR-A1AT clinical program is welcome news to the A1AT deficiency community, as there are currently no approved therapies that treat the liver manifestations of this condition," commented Miriam O'Day, president and chief executive officer of the Alpha-1 Foundation. "We look forward to working with Dicerna as they advance DCR-A1AT through clinical trials."

About DCR-A1AT and the GalXC™ Technology Platform

DCR-A1AT is a ribonucleic acid interference (RNAi) therapeutic being investigated for the treatment of liver disease in patients with alpha-1 antitrypsin (A1AT) deficiency. The compound incorporates Dicerna's proprietary GalXC™ technology, which amplifies the Company's ability to create selective and safe RNAi therapies that are specific and potent in the way they target disease. Dicerna scientists invented GalXC as a method to discover and develop next-generation RNAi therapies designed to silence disease-causing genes. With these therapies, we aim to restore health by addressing the underlying causes of disease. Drug candidates produced via GalXC are intended to be broadly applicable across multiple therapeutic areas with a current focus on diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases and viral infectious diseases. Data from clinical and preclinical studies suggest that GalXC may offer several distinct benefits for the treatment of disease, including:

- potency that has the potential to surpass comparable RNAi platforms;
- highly specific binding to disease-causing targets;
- long duration of action; and
- an infrequent dosing regimen via subcutaneous (under the skin) injection, which can minimize the treatment burden for patients.

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 (shortage) of 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]

Approximately 10% of infants with A1AT deficiency develop liver disease, which often causes jaundice (yellowing of the skin and whites of the eyes). About 15% of adults with A1AT deficiency develop cirrhosis (liver damage) due to formation of scar tissue in the liver. Individuals affected by A1AT deficiency are also at risk of developing hepatocellular carcinoma, a type of liver cancer. People with A1AT deficiency typically 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, unintentional 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. 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™ Pharmaceuticals, Inc.

Dicerna™ Pharmaceuticals, Inc., is a biopharmaceutical company using RNA interference, or RNAi, to create medicines that silence genes that cause disease. The Company's proprietary GalXC™ technology is intended to amplify its ability to create potent, selective and safe RNAi therapies to treat diseases involving the liver, including rare diseases, chronic liver diseases, cardiovascular diseases and viral infectious diseases. Dicerna aims to restore health by addressing the underlying causes of illness with capabilities that extend beyond the liver to address a broad range of diseases, focusing on target genes where connections between gene and disease are well understood and documented. Dicerna intends to discover, develop and commercialize novel therapeutics either on its own or in collaboration with pharmaceutical partners. Dicerna has strategic collaborations with Eli Lilly and Company, Alexion Pharmaceuticals, Inc. and Boehringer Ingelheim International GmbH. 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 liver disease; and (ii) the potential of Dicerna™'s technology and drug candidates in the Company's research and development pipeline. 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 Form 10-Q filing 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; the likelihood of Dicerna's clinical programs being executed within timelines provided and reliance on the Company's contract research organizations and predictability of timely screening and enrollment of subjects and patients to advance Dicerna's clinical trials; 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 (NDAs) and Clinical Trial Applications that are necessary to continue to advance and progress the Company's clinical programs and the regulatory review of NDAs; market acceptance for approved products and innovative therapeutic treatments; competition; the possible impairment of, inability to obtain and costs of obtaining intellectual property rights; and possible safety or efficacy concerns that could emerge as new data are generated in research and development, 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

1. Genetics Home Reference. Alpha-1 antitrypsin deficiency. Bethesda, Md.: U.S. Department of Health and Human Services, National Institutes of Health, National Library of Medicine; 2013. Available at: https://ghr.nlm.nih.gov/condition/alpha-1-antitrypsin-deficiency#genes. Accessed June 26, 2019.

2. Patel D, Teckman JH. Alpha-1-antitrypsin deficiency liver disease. Clinical Liver Disease. 2018;22(4):643-655.

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