Dicerna Announces FDA Clearance of Investigational New Drug (IND) Application for DCR-AUD for the Treatment of Alcohol Use Disorder

July 29, 2021

– Novel ALDH2*-Targeting GalXC™ RNAi Candidate Designed to Address a Highly Prevalent and Undertreated Disorder[1] –*

– Dicerna Expects to Initiate Phase 1 Clinical Trial of DCR-AUD in the Third Quarter of 2021 –

LEXINGTON, Mass.--(BUSINESS WIRE)--Jul. 29, 2021-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) ("Company" or "Dicerna"), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced the U.S. Food and Drug Administration ("FDA") clearance of its Investigational New Drug (IND) application for DCR-AUD, the Company's investigational RNAi candidate for the treatment of alcohol use disorder (AUD).

AUD is a medical condition characterized by the inability to stop or control alcohol use despite social, occupational or health consequences.[2] Aldehyde dehydrogenase 2, or ALDH2, is an enzyme that plays a key role in metabolizing alcohol. DCR-AUD has been shown to induce long-lasting liver-specific ALDH2 messenger RNA (mRNA) knockdown in nonclinical studies. By silencing ALDH2 in the liver and interrupting the alcohol metabolic pathway, DCR-AUD has the potential to induce real-time physiological feedback to help individuals seeking treatment for AUD regain control over harmful levels of alcohol use.

"The key to developing a successful treatment for the more than 14 million people affected by AUD is finding a way to help individuals regain control over their alcohol use," said Bob D. Brown, Ph.D., Chief Scientific Officer and Executive Vice President of R&D at Dicerna. "We believe that RNAi may be ideally suited to do this. RNAi's long duration of effect and target specificity can achieve liver-specific reduction of ALDH2, which could be an effective strategy to reduce alcohol consumption. We've performed extensive screening and optimization of GalXC™ RNAi molecules targeting human ALDH2 to identify DCR-AUD and believe DCR-AUD has the potential to improve health outcomes for those with AUD."

Dr. Brown continued, "We would also like to acknowledge the financial support we received from the National Institutes of Health in the form of a cooperative Small Business Innovation Research grant that has contributed to the development of DCR-AUD. The grant reviewers and the agency's votes of confidence in Dicerna's drug development capabilities and the liver-specific RNAi mechanism of action of GalXC have helped make our DCR-AUD program possible."

Dicerna plans to initiate a 24-week, randomized, double-blind, placebo-controlled Phase 1 trial in the third quarter of 2021 to evaluate the safety and tolerability, pharmacokinetics and pharmacodynamics of single-ascending doses of DCR-AUD in healthy volunteers. The trial will also assess the interaction between DCR-AUD treatment and alcohol consumption using standardized Ethanol Interaction Assessments.

About Alcohol Use Disorder (AUD)

Alcohol use disorder, or AUD, is a chronic disorder characterized by the inability to stop or control alcohol use despite social, occupational or health consequences. AUD presents as a problematic pattern of alcohol use leading to clinically significant impairment or distress. Symptoms can include compulsive drinking, loss of control over alcohol use and negative emotions when not drinking.[2] AUD is one of the most common psychiatric disorders, affecting more than 14 million adults in the U.S. annually, and it is one of the leading causes of preventable death. Globally, AUD affects approximately 283 million people, according to the World Health Organization.[3] AUD is often undiagnosed and untreated. Of the estimated 14 million individuals in the U.S. with AUD, fewer than 1.4 million received AUD treatment of any kind, including psychosocial support, and only a fraction of these 1.4 million received medication to treat this disorder.[1,4]

About DCR-AUD

DCR-AUD is Dicerna's GalXC™ RNAi investigational candidate designed to silence ALDH2 (aldehyde dehydrogenase 2) messenger RNA (mRNA) expression in the liver. DCR-AUD has been shown to induce long-lasting liver-specific ALDH2 mRNA knockdown in nonclinical studies. Some individuals are born with naturally occurring mutations in one or both gene copies that encode the ALDH2 enzyme. In these people with *ALDH2* mutations, alcohol consumption can result in uncomfortable physiological effects that occur soon after drinking. These effects are thought to be the reason people with *ALDH2* mutations are much less likely to be affected by AUD. Dicerna designed DCR-AUD based on human genetic data that suggest knocking down ALDH2 mRNA in individuals with AUD may provide similar physiological feedback that is protective against harmful levels of alcohol consumption. Preclinical research for DCR-AUD was supported by a grant from the National Institute on Alcohol Abuse and Alcoholism of the National Institutes of Health (NIH), under Award Number U44AA027404.

About RNAi and Dicerna's GalXC™ RNAi Platform Technologies

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 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 potential of DCR-AUD for the treatment of alcohol use disorder; market size for people affected by AUD; and timing of initiating a Phase 1 clinical trial of DCR-AUD in healthy volunteers. 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 applications (INDs) 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. Substance Abuse and Mental Health Services Administration. Results from the 2019 National Survey on Drug Use and Health. Accessed on July 28, 2021.
2. National Institute on Alcohol Abuse and Alcoholism. Understanding Alcohol Use Disorder. Alcohol Facts and Statistics. Accessed July 28, 2021.
3. World Health Organization. *Global Status Report on Alcohol and Health*, 2018. Accessed July 27, 2021.
4. Grant et al., JAMA Psychiatry 2015.

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Media:
Amy Trevvett
+1 617-612-6253
atrevvett@dicerna.com

Investors:
Janhavi Mohite
+1 212-362-1200
ir@dicerna.com

Source: Dicerna Pharmaceuticals, Inc.