



## Dicerna Initiates Phase 1 Clinical Trial of DCR-AUD, a Novel Investigational GalXC™ RNAi Therapeutic Candidate for the Treatment of Alcohol Use Disorder

September 28, 2021

– Trial to Evaluate Safety and Tolerability of DCR-AUD in Healthy Volunteers –

– Trial Includes Ethanol Interaction Assessments to Evaluate Participants' Response to Alcohol After Receiving DCR-AUD –

LEXINGTON, Mass.--(BUSINESS WIRE)--Sep. 28, 2021-- [Dicerna Pharmaceuticals, Inc.](#) (Nasdaq: DRNA), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced that it dosed the first subjects in its Phase 1 clinical trial to assess DCR-AUD, Dicerna's investigational GalXC™ RNAi therapeutic in development for the treatment of alcohol use disorder (AUD). The study will evaluate the safety, tolerability, pharmacokinetics and pharmacodynamics of single ascending doses of DCR-AUD in healthy volunteers. The trial will also assess the interaction between DCR-AUD administration and alcohol consumption using standardized Ethanol Interaction Assessments (EIA) performed serially over the trial's duration.

AUD is characterized by the inability to stop or control alcohol use despite social, occupational or health consequences.<sup>1</sup> Treatment approaches include psychosocial support and pharmacotherapy, but many individuals with AUD do not receive treatment, and currently available pharmacotherapies are not widely prescribed.<sup>2</sup> Overall, of the estimated 14 million individuals in the U.S. with AUD, fewer than 1.4 million receive treatment of any kind.<sup>3,4</sup>

"We designed DCR-AUD leveraging our GalXC RNAi technology to serve as a potential therapeutic that offers real-time physiological feedback to complement the evidence-based psychosocial treatments used to help individuals with AUD," said Shreeram Aradhye, M.D., Executive Vice President and Chief Medical Officer at Dicerna. "We are pleased to initiate clinical development of DCR-AUD and look forward to sharing interim data later next year."

The randomized, double-blind Phase 1 clinical trial ([NCT05021640](#)) will evaluate single doses of DCR-AUD compared to placebo in up to 36 healthy volunteers over a 24-week observation period.

### 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.<sup>1</sup> 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.<sup>5</sup> 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 received medication to treat this disorder.<sup>3,4</sup>

### 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 Dicerna's GalXC RNAi Platform Technologies

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 for 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](http://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 our product candidates and the development thereof, including about the Company's Phase 1 clinical trial of DCR-AUD for the treatment of alcohol use disorder, including our trial design; expected timing of results from the Company's Phase 1 clinical trial of DCR-AUD; the Company's clinical development programs, including for DCR-AUD; the design and therapeutic potential of our product candidates, including DCR-AUD; the estimated market size for AUD and other diseases for which we are developing potential therapies to address; our business and operations, including the discovery, development and commercialization of our product candidates; the development of our RNAi technology platform, and the therapeutic potential thereof; and our collaboration with partners and any potential future collaborations.

The process by which investigational therapies, such as DCR-AUD, 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; reliance on the Company's contract research organizations (CROs); predictability of timely enrollment of subjects and patients to advance Dicerna's clinical trials; the reliance of Dicerna on contract manufacturers (CMOs) to supply its products for research, development and commercialization and the risk of supply interruption from a CMO; 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 and those of our CROs and CMOs, including the conduct of our research and development activities; the regulatory review and 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; 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; alignment with the FDA on the regulatory pathway to approval for our 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 and maintain intellectual property rights; possible safety or efficacy concerns that could emerge as new data are generated in R&D and following commercialization; 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. National Institute on Alcohol Abuse and Alcoholism. [Understanding Alcohol Use Disorder. Alcohol Facts and Statistics](#). Accessed on Sept. 27, 2021.
2. Witkiewitz, K. et al. Advances in the science and treatment of alcohol use disorder. *Sci Adv* 2019 Sep; 5(9): eaax4043.
3. Substance Abuse and Mental Health Services Administration. [Results from the 2019 National Survey on Drug Use and Health](#). Accessed on Sept. 27, 2021.
4. Grant et al., *JAMA Psychiatry* 2015.
5. World Health Organization. [Global Status Report on Alcohol and Health, 2018](#). Accessed on Sept. 27, 2021.

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