# Dicerna's GalXC-Plus™ RNAi Technology Delivers Target Knockdown Across CNS and to Specific CNS Cell Types in Preclinical Studies

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LEXINGTON, Mass.--(BUSINESS WIRE)--Mar. 30, 2021-- Dicerna Pharmaceuticals, Inc. (Nasdaq: DRNA) (the "Company" or "Dicerna"), a leading developer of investigational ribonucleic acid interference (RNAi) therapeutics, today announced new data from preclinical studies of its GalXC-Plus™ RNAi technology demonstrating its potential to deliver deep and sustained messenger RNA (mRNA) knockdown against prespecified gene targets across the central nervous system (CNS) and to specific CNS cell types. By interfering with mRNA of a target gene, Dicerna's proprietary GalXC-Plus RNAi technology is designed to silence disease-causing genes across multiple therapeutic areas and expands on the functionality and application of the Company's flagship liver-targeted GalXC™ RNAi technology.

"The results from these preclinical applications of our GalXC-Plus technology demonstrate its flexibility and clear ability to target mRNA knockdown across the CNS as well as to specific, specialized cells within the CNS," said Bob D. Brown, Ph.D., Chief Scientific Officer and Executive Vice President of Research and Development at Dicerna. "The depth and distribution across the brain and spinal cord in each of these trials reinforce the degrees of saturation and specificity that customizable GalXC-Plus structures can deliver to multiple CNS cell types. We are excited about the potential broad applicability of Dicerna's GalXC-Plus technology to treat a broad range of CNS and other diseases."

Data from a preclinical mouse study showed that a single dose of an unconjugated GalXC-Plus molecule engineered to silence mRNA produced by the *ALDH2* gene, a widely occurring and common genetic test target, resulted in dose-dependent reductions of up to 92% knockdown in target mRNA across the CNS that lasted through the trial conclusion at 28 days. GalXC-Plus delivered similar mRNA reductions in non-human primate (NHP) studies after a single dose, resulting in up to 90% target mRNA silencing after 28 days. There were no adverse observations for any GalXC-Plus cohort in these trials.

Additional preclinical data demonstrated the degree and distribution of GalXC-Plus silencing of β-tubulin III (TUBB3 gene; expressed in neurons and associated with various cancers) and two undisclosed gene targets expressed by astrocytes and oligodendrocytes, respectively, using unconjugated and various conjugated GalXC-Plus payloads.

- **Oligodendrocytes**: There was a clear reduction of target mRNA in oligodendrocytes across the brain and spinal cord of rodents following a single, lumbar intrathecal or intracisternal GalXC-Plus dose with up to 80% target mRNA silencing after seven days. In NHPs, there was a clear dose-related relationship between GalXC-Plus intracisternal administration and target mRNA reduction with up to 85% target mRNA reduction maintained for approximately three months. There were no adverse observations for any GalXC-Plus cohort in these trials.
- **Astrocytes**: GalXC-Plus demonstrated a clear reduction in target mRNA in mouse astrocytes after a single lumbar intrathecal injection. An ongoing preclinical study also shows durable control of target mRNA expression, with up to 80% target mRNA reduction maintained for at least 160 days. The durability in rodents was independent of the initial magnitude of target knockdown.
- **Neurons**: The flexibility of the GalXC-Plus technology enabled additional conjugations to optimize delivery to neuronal cells, resulting in clear, CNS-wide reductions (up to 95%) in neuronal-specific *Tubb3* mRNA after a single lumbar intrathecal dose in mice. Comparisons of target knockdown potency across astrocyte and neuronal cells using multiple GalXC-Plus conjugate modifications indicated the potential for complementary and tunable knockdown across multiple CNS cell types.

The data were presented as part of the sixth annual Oligonucleotide and Precision Therapeutics (OPT) Virtual Congress. "GalXC-Plus: Cell-Type Targeted Therapeutic Oligonucleotide Delivery in the CNS," was presented by Maire Osborn, Ph.D., Associate Director of Neuro Discovery at Dicerna. The slide presentation will be made available on the Events & Presentations page of Dicerna's corporate website.

**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 targeted destruction of the messenger RNA (mRNA) made from the gene. Rather than seeking to inhibit a protein directly, 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 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 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 rare, 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 pertaining to the Company's GalXC-Plus technology and its clinical or commercial potentials, other discovery and development data presented at the Oligonucleotide and Precision Therapeutics Virtual Congress, which may include discussion of the Company's business and operations, including the discovery, development and commercialization of potential product candidates and technologies, and the therapeutic potential thereof, and the success of our collaborations with partners and any potential future collaborations. 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. Applicable risks and uncertainties include those relating to our preclinical research and clinical programs and other risks identified under the heading "Risk Factors" included in our most recent Form 10-Q and Form 10-K filings and in other future filings with the SEC. 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.



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