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Contacts:

Martin Williams, SVP & Chief Business Officer
Dicerna Pharmaceuticals
(617) 621-8097

Sheryl Seapy
Pure Communications Inc.
(949) 608-0841

Dicerna Pharmaceuticals' Co-founders Publish Studies Describing Novel Approaches to Maximizing Dicer-Substrate Small Interfering RNAs (DsiRNAs)

CAMBRIDGE, Mass., August 12, 2008 – Dicerna Pharmaceuticals, Inc. (www.dicerna.com), a second generation RNA interference company developing novel therapeutics utilizing proprietary Dicer Substrate Technology™, today announced key studies highlighting the therapeutic potential for Dicer-substrate small interfering RNAs (DsiRNAs).

The first study, co-authored by Dicerna co-founder John Rossi, Ph.D., professor in the Division of Molecular Biology and dean, Graduate School of Biological Sciences at City of Hope's Beckman Research Institute, which appears in the August 2008 issue (Volume 16 Number 8) of *Molecular Therapy*, demonstrates successful fusion of an aptamer to anti-HIV DsiRNAs leading to potent anti-HIV activity in HIV-1 infected cells. Aptamers are oligonucleic acid or peptide molecules that bind a specific target molecule, and the dual inhibitory function of the aptamer-DsiRNA delivery system offers a novel approach to treating HIV. This study also suggests that the Dicer-substrate 27mer RNAi molecule, which is longer than the conventional 21mer RNAi molecule, was more effective at inhibiting HIV replication than the 21mer.

Dr. Rossi commented, “This study reinforces that, by utilizing Dicer Substrate Technology, we can knock down the expression of a targeted gene in a way that is highly selective, specific and more potent than other RNAi approaches. Furthermore, our research suggests that aptamer-DsiRNA delivery systems may offer an important new approach to treating HIV and potentially other infectious diseases. In this particular study, although the aptamer provided some inhibitory function when tested in this setting alone, the DsiRNA chimeras provided more potent inhibition than the aptamer alone, thus suggesting cooperative action between the DsiRNA and aptamer portions in inhibiting replication and spread of HIV.”

The second study in Volume 18 Number 2 of the journal *Oligonucleotides*, co-authored by Dicerna co-founder Mark Behlke, M.D., Ph.D., vice president of molecular genetics and biophysics and chief scientific officer at Integrated DNA Technologies, explored chemical modification patterns compatible with high potency 27-mer DsiRNAs. This study showed that a modification pattern involving alternating 2'-O-methyl RNA bases generally retains high

potency when tested in different sites in different genes, evades activation of the innate immune system, and improves stability in serum.

“The goal of this study was to define modification patterns of 27-mer DsiRNAs that would be useful for research purposes and would remain active at most sites in different genes regardless of sequence context. Based on the chemical modifications we explored in this study, it appears that the 2'OMe modification may provide more generalized protection from immune responses than other 2'-modifications,” stated Dr. Behlke. “Modification patterns of this kind may be useful in therapeutic applications of Dicer substrate processed RNAi molecules. We expect that more extensively modified sequences could be developed for specific sites that would have increased nuclease stability and yet retain high potency, which are desirable for pharmaceutical applications such as we are pursuing at Dicerna.”

Dicerna's pipeline of RNAi-targeted drugs is focused in the therapeutic areas of oncology, metabolic diseases and hepatitis C infection (HCV). In addition to these internal focus areas, Dicerna expects to broadly utilize its Dicer Substrate Technology in several additional therapeutic areas, such as inflammation, immunology, cardiology, and others, through collaborations with pharmaceutical and biotechnology companies.

James C. Jenson, Ph.D., chief executive officer and co-founder of Dicerna, stated, “Dicerna's Dicer Substrate Technology offers a new avenue to harness gene silencing and address the entire transcriptome for drug development. These studies add to the growing body of data that will allow us to maximize the potential of this technology to develop novel, potent and selective drug candidates for important unmet medical needs.”

Online copies of the articles can be found at:

- *Molecular Therapy: Novel Dual Inhibitory Function Aptamer-siRNA Delivery System for HIV-1 Therapy*, by Zhou et al., <http://www.nature.com/mt/index.html> (subscription required)
- *Oligonucleotides: Chemical Modification Patterns Compatible with High Potency Dicer-Substrate Small Interfering RNAs*, by Collingwood, et al., <http://www.liebertonline.com/doi/pdfplus/10.1089/oli.2008.0123>,

About RNAi

First described in plants and then in worms, flies and higher organisms, RNAi works differently in mammals because of the activity of Dicer, a key enzyme involved in the processing of double-stranded RNA into siRNA. In humans, Dicer optimally processes double-stranded RNA oligonucleotides of 25 to 30 base pairs, resulting in a 5-to-100-fold more potent activity and longer duration of action.

About Dicerna

Dicerna Pharmaceuticals is a private, venture-backed RNAi-focused biopharmaceutical company developing novel therapeutic agents in multiple disease areas based on its proprietary Dicer Substrate Technology platform. Dicerna is developing novel RNAi-based therapies that use an earlier step in the gene silencing process, namely the engagement of the enzyme Dicer, which is a natural initiation point for the RNAi cascade. This approach results

in the knockdown of expression of a targeted gene in a way that is highly selective, specific and more potent than other RNAi approaches. The Dicer Substrate Technology is based on intellectual property that is both broadly enabling and distinct from other IP in the field. Dicerna is based in Cambridge, Massachusetts. For more information, please visit www.dicerna.com.

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