

## FOR IMMEDIATE RELEASE

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### **Dicerna Pharmaceuticals Announces Preclinical Findings Highlighting Novel Approach to Maximizing Dicer-Substrate Small Interfering RNAs (DsiRNAs) in Rheumatoid Arthritis; Data Appear Published by *Molecular Therapy***

CAMBRIDGE, Mass., October 1, 2008 –Dicerna Pharmaceuticals, Inc. ([www.dicerna.com](http://www.dicerna.com)), a second generation RNA interference company developing novel therapeutics utilizing proprietary Dicer Substrate Technology™, announced today a paper appearing in the advance online publication of *Molecular Therapy* which describes the therapeutic potential for Dicer-substrate small interfering RNAs (DsiRNAs) in the treatment of rheumatoid arthritis in a murine model of arthritis.

Rheumatoid arthritis is a chronic inflammatory disease affecting approximately one percent of the population. Joint destruction associated with this autoimmune condition results from synovial infiltration by various classes of immune cells which cause inflammation and joint destruction. This strong inflammatory response is predominantly driven by secretion of the cytokine tumor necrosis factor  $\alpha$  (TNF $\alpha$ ) by macrophages. The paper presents the first demonstration of a novel anti-inflammatory treatment for rheumatoid arthritis, where intraperitoneal administration of DsiRNA complexed with a chitosan nanoparticle achieved reduction of TNF $\alpha$  levels at affected joints and resulted in reduced inflammation and reduced joint damage. Secretion of TNF $\alpha$  by macrophages plays a prominent role in the development and progression of rheumatoid arthritis, and this strategy allows delivery into the peritoneal cavity, which is a major reservoir for macrophages.

“These findings underscore the potency of the Dicer Substrate Technology in that we were able to suppress expression of a targeted gene using a total cumulative dose of only 0.25 – 0.5 mg/kg,” stated co-author and Dicerna co-founder Mark Behlke, M.D., Ph.D., vice president of molecular genetics and biophysics and chief scientific officer at Integrated DNA Technologies. “Furthermore, our research using DsiRNA/chitosan delivery systems suggests the onset of arthritis could be delayed using a preventative dosing regime. This work demonstrates nanoparticle-mediated TNF $\alpha$  knockdown as a method to reduce both local and systemic inflammation presenting a novel strategy for arthritis treatment.”

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 other 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 continues to demonstrate utility in a broad range of therapeutic areas by offering a novel path to gene silencing, and engaging new scientific approaches in the development of novel, potent, and selective drugs for unmet medical needs. This proof-of-concept work bolsters the growing body of data that is driving our Dicer Substrate Technology research, and provides further evidence that chemically modified DsiRNAs may be more effective therapeutics than non-modified DsiRNAs."

Online copies of the article can be found at:

- *Molecular Therapy*: "Chitosan/siRNA nanoparticle-mediated TNF $\alpha$  knockdown in peritoneal macrophages for anti-inflammatory treatment in murine arthritis model," by Howard et al., <http://www.nature.com/mt/journal/vaop/ncurrent/> (subscription required)

### **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](http://www.dicerna.com).

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