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At Beyond Genome, Dicerna Calls Virology, Oncology, Metabolic Disease Focus Areas

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SAN FRANCISCO — About seven months after it closed a \$13 million Series A private-equity financing round, RNAi drugs startup Dicerna Pharmaceuticals has disclosed details about its drug-development pipeline, which will focus on virologic, oncologic, and metabolic diseases.

The company is taking aim at hepatitis C, solid tumors, type II diabetes, and hyperlipidemia, Roberto Guerciolini, Dicerna co-founder and senior vice president of pharmaceutical development, said at Cambridge Healthtech Institute's Beyond Genome conference, held here this week.

For HCV, Dicerna will “go after those very conserved regions of the [virus] genome, which are more slowly mutated,” he said during a corporate presentation at the event. The diabetes program, meanwhile, will focus on “targets associated with insulin signaling and, even more relevant, targets involved with gluconeogenesis ... which is the key element supporting fasting hypoglycemia, a hallmark of type II diabetes.”

As for oncology, “we’re interested in solid tumors and we’re interested in going after those targets that have been elusive for the past decade and are exquisitely amenable to RNAi — targets [that] are not druggable by conventional methods ... are difficult to target ... and [are] uniquely mutated into neoplastic tissue,” Guerciolini said.

On the sidelines of Beyond Genome, Guerciolini said that Dicerna is currently conducting animal studies to support all three programs, but declined to provide timelines for when the company may be ready to file an investigational new drug application for any of the programs.

“Right now, we have tremendous data *in vitro* [but] limited data *in vivo*,” he said. “We really want to validate our platform *in vivo* [and] that will trigger the pre-IND work preparation. At the present time, it’s too early to say” when an IND might be filed with US regulators.

Guerciolini said that previous experience at Sirna Therapeutics, where he was CMO, “suggests that you can actually go from clinical candidate to IND in 18 months,” although he stressed that Dicerna has not committed itself to this kind of timeline.

Late last year, however, Dicerna co-founder and CEO James Jenson told *RNai News* that he expected the company to file its first IND within two years (see [RNai News, 11/8/2007](#)).

Guerciolini also declined to name any of the specific targets the company is focusing on in its three therapeutic programs.

He did note, however, that all of Dicerna’s drug candidates are expected to be systemically delivered, and that the company intends to look outside of its own labs for the technology to do so.

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Discussions are ongoing with a number of companies regarding RNAi delivery collaborations, Guercioli said. He added that Dicerna expects to ink deals for multiple delivery technologies rather than commit to a single approach.

Discerning Potency

Invented by Dicerna scientific co-founders John Rossi, who is also a City of Hope researcher and co-founder of RNAi drugs shop Calando Pharmaceuticals, and Mark Behlke, vice president of molecular genetics at Integrated DNA Technologies, Dicer-substrates are essentially 27-nucleotide long RNA duplexes that have been [shown](#) to be up to 100 times more effective at silencing genes than conventional 21 nucleotide-long siRNAs without inducing an interferon response or activating protein kinase R in cells.

Dicerna holds an exclusive license to use the technology therapeutically against all but five undisclosed targets, which were exclusively licensed to MDRNA, formerly Nastech Pharmaceutical, in 2006 (see [RNAi News, 11/9/2006](#)). MDRNA also has a non-exclusive access to the technology for all other mammalian targets.

During his presentation at Beyond Genome, Guercioli noted that the apparent high potency of Dicer-substrates, which he said has been confirmed by animal data in at least four published papers and two currently under review, is expected to give Dicerna an edge over rivals in the RNAi drug field because the doses of Dicer-substrates needed to effect a therapeutic response are likely to be lower than siRNA-based drugs.

“You can imagine, from a drug-development point of view, the difference even a five-fold [increase in potency] would have in terms of cost of goods, in terms of formulation work, in terms of drug supply, [and] in terms of safety,” he said.

Further, the unique structure of Dicer-substrates, as well as the fact that these oligos mediate gene silencing through Dicer rather than RISC, is expected to allow Dicerna to have the freedom to operate without requiring licenses to RNAi intellectual property held by such heavyweights as Alnylam Pharmaceuticals and Merck’s Sirna Therapeutics subsidiary.

“We are comfortable that [our] patent estate allows us the freedom to operate and convert this promising technology into therapeutic applications,” Guercioli said.

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