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Dicerna Aims to Gain Foothold in RNAi World With More Potent, Longer-Lasting Gene Silencers

Luke Timmerman, 1/30/09

Most of the headlines in the RNA interference world go to Cambridge, MA-based Alnylam Pharmaceuticals (NASDAQ: ALNY). While that company says it has amassed enough intellectual property—and cash—to dominate this emerging field of gene-silencing technologies for years, they aren't the only game in town. One intriguing upstart of the RNAi field is a privately held company in Watertown, MA called [Dicerna Pharmaceuticals](#).

Xconomy first covered the Dicerna story when it started in November 2007, and the company first hit my radar screen in July, when it raised \$8.4 million to cap off a first-round financing of \$21.4 million. It got the cash from Abingworth, Oxford Bioscience Partners, and Skyline Ventures. These people aren't dabblers—Doug Fambrough of Oxford is a molecular biologist who invested in Sirna Therapeutics before that company was sold for \$1.1 billion to Merck in 2006, and Steve Hoffman of Skyline was a fellow Sirna investor who also bet early on Alnylam. So I figured it was worth hearing more from Dicerna CEO Jim Jen-

son a couple weeks ago at the JP Morgan Healthcare Conference in San Francisco.

The idea behind RNAi-based drug development is to shut down disease at its roots, by using specially engineered RNA molecules to shut down production of specific disease-causing proteins. Dicerna was founded on the belief that there's more than one way to achieve this; the company says it is working on a "second doorway" of RNA interference, by designing drugs that are a little longer than so-called small interfering RNA molecules being developed by Alnylam and others. The Dicerna method may have the added advantage of being more potent—meaning they can be given in lower doses, and could be cheaper to manufacture—and they may last longer in the body, meaning they could be given in fewer shots. Plus, they have a feature that will allow RNAi drugs to be bound together with other compounds like antibody fragments or peptides that could give them extra kick, say, against cancer cells.

All of this work is still being done in animals, so there's no proof



this works in people. But even with that limited evidence, and a grim investing climate, Jenson said he saw no shortage of interest among potential pharmaceutical partners at the JP Morgan meeting.

"It's the real deal, the next game changer in drug development," Jenson says. "Stay tuned, there is a very strong interest in our programs. Many people see the importance of this."

Most small interfering RNA drugs tend to be 21 nucleotides, or chemical letters, long. The Dicerna drugs are a little longer, 27 nucleotides. This enables Dicerna's compounds to interact with an enzyme called "Dicer," hence the company name. This is important because Dicer is involved at an earlier step in the RNA interference process than where other drugs come in, Jenson says—intervening earlier gives the firm's drugs increased

potency and duration of effect. The extra few nucleotides also give the drug extra precision in targeting diseased cells, he says.

The extra length also gives Dicerna the ability to attach other compounds like peptides or antibody fragments, and to make other modifications that could enable Dicerna to avoid the problems other drug developers have encountered in trying to deliver RNAi drugs, Jenson says. If given directly, most small RNAi drugs get flushed out via the kidneys in a few minutes—before they can do any good. Companies like Alnylam and others are

working on a host of delivery techniques to solve the problem.

The critical patents for Dicerna's techniques come from John Rossi of the City of Hope Beckman Research Institute in Duarte, CA, and Mark Behlke, chief scientific officer of Coralville, IA-based Integrated DNA Technologies.

Like other RNAi companies, Dicerna envisions using this approach against many of the biggest diseases in the developed world—cancer, cardiovascular disease, inflammation, neurological condi-

tions, metabolic diseases like diabetes, and infections like hepatitis C.

The company will spend this year laying the groundwork for its first clinical trial of a cancer drug, with a goal of getting there “some-time in 2010,” Jenson says. As with any RNAi company, if Dicerna rushes into the clinic and falls short, it could greatly harm the field. “We want to be very careful and thorough,” Jenson says. ■

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