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# Will it Rain RNAi Companies? Dicerna Co-Founder John Rossi Says New IP Opens Avenues

Malorye Allison, 11/6/07

If all goes as planned, Cambridge-based RNAi pioneer Alnylam (NASDAQ: ALNY) will be celebrating Thanksgiving with a new competitor in its backyard, in the form of Dicerna Pharmaceuticals, a brand-new startup fueled by about \$13 million from Oxford Biosciences. Dicerna capitalizes on a new approach to making gene-silencing medicines that sprang from the laboratory of a co-founder, John Rossi, at City of Hope in Duarte, CA.

If Rossi gets his wish, even more little RNAi companies will soon follow.

“There’s always a need for more companies, so you can treat more diseases,” Rossi says. But before, “Nobody else could make [RNAi-based drugs] unless you wanted to get a license from Alnylam.”

Though some people argue that Alnylam has oversold its position, many observers agree with Rossi that the Cambridge firm’s patent portfolio gives it a big competitive advantage in the RNAi therapeutics arena. But because Dicerna is built around a new approach to RNAi,

Rossi says, “we’ve just formed a company whose choices are wide open.” Dicerna hasn’t yet selected which diseases it will target, and its IP is still at the application stage, but according to Rossi the company will provide licenses to others as well as developing its own therapeutics.

It’s not too surprising that Rossi is the catalyst of this new endeavor. Though he keeps a lower profile than some of RNAi’s other big names, he is one of the most widely respected and prolific pioneers of research into applying the technique—in which short strands of RNA are used to turn genes off—to treat diseases. His lab is working at the field’s cutting edge, doing some of the earliest human trials (in HIV patients). That work involves tinkering with the molecules themselves: Changing their chemical makeup even slightly can make them more powerful or less likely to cause side effects.

It was through such tinkering that Rossi made a surprising discovery.

Previously, like most other experts, Rossi believed that the specific length of Alnylam’s RNAs was ideal



for gene silencing. But while trying to get better results in his experiments, “We noticed that if [the strands] were a bit longer we got more potent knockdown,” Rossi says. It was good news that the longer strands actually worked. The fact that they seem to work better than the short ones is even more exciting—more powerful knockdown should mean that less drug is needed.

Dicerna cofounder Mark Behlke, a vice president at Coralville, IA-based biotech supplier Integrated DNA Technologies (IDT), heard Rossi give a talk about this approach and the two soon became collaborators. They ended up

developing these new “dicer substrate siRNAs” jointly. Dicer is the natural cellular machinery that chops these longer RNA strands up and turns them into silencing tools. City of Hope and IDT own the patents on the technology, which Dicerna has now licensed.

With two of its founders out of state, how did Dicerna wind up in Boston? For one thing, the company’s VC backers, its CEO, and a third co-founder—Doug Fambrough, a partner at Oxford who will be chairman of the board—are here. What’s more, says Rossi, “Boston is a rich environment for drawing upon highly trained personnel and provides a rich intellectual environment for employees, such as seminars, collaborations and other business related activities.”

Dicerna is scheduled to be for-

mally launched in November. That news broke ahead of when the startup wished it would on the In Vivo blog last week. “The financing has not been finalized, but we’re anticipating \$13 million, and we’re not looking for additional financing at this time,” says Fambrough. [11-14-07 Update: Dicerna announced today it has closed the financing and that Skyline Ventures is co-lead investor with Oxford Bioscience Partners on the \$13 million deal.]

Rossi feels efforts at commercializing RNAi have lagged recently. (The first drug based on the technology has yet to be approved). He says that since Merck gobbled up Alnylam rival Sirna, “We don’t know what is going on there.” Another player, CytRx, recently spun out its RNAi therapeutics program into a new subsidiary called RXi, but has not yet announced any

product candidates. “Alnylam is really the only company doing very much right now,” he says.

Rossi is heartened that more new companies are forming, however. “I’ve heard of a couple, but they are not public yet,” he says. With Dicerna now adding to the IP mix, things could get even more interesting.

Though he points to challenges ahead, such as choosing the right disease targets and overcoming the drug-delivery hurdles facing all RNAi efforts, Rossi is confident that things will indeed get interesting. “These drugs are going to move faster than others,” Rossi says. “The discovery [of RNAi] was only made 9 years ago, and now there are already clinical trials. How long did it take to get the first monoclonal antibodies that far?” ■