

# “The Pink Sheet” DAILY

## PRESCRIPTION PHARMACEUTICALS AND BIOTECHNOLOGY

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### Venture-Backed Dicerna Cuts First Pharma Deal as Prelude to 'B' Round

As it looks for a new investor to lead its second round of funding, RNA interference startup Dicerna Pharmaceuticals has signed its first big-pharma customer. Japan's Kyowa Hakko Kirin will pay \$4 million upfront and as much as \$120 million in milestones to develop therapeutics around an undisclosed solid-tumor cancer target using Dicerna's technology.

The deal is the first of the new year in the nascent RNAi field after a relatively quiet 2009 ('The Pink Sheet' DAILY, Dec. 22, 2009). Dicerna was founded in 2007 around work licensed from the City of Hope research center near Los Angeles. The firm is looking to build a patent portfolio around its Dicer substrate technology, which uses strands of engineered oligonucleotides that are longer than those patented by more established companies.

Dicerna says it is part of a “next generation” of RNAi companies that are finding ways around the intellectual property positions of firms such as Alnylam Pharmaceuticals.

Dicerna, of Watertown, Mass. also says its drugs have shown more potency and longer staying power in preclinical tests, a major concern with RNAi-based drugs. They have yet to prove themselves in clinic, but Kyowa Hakko Kirin is interested enough to make a small bet.

Dicerna officials declined to elaborate upon the initial solid-tumor target but said the alliance can be expanded to up to 10 more targets and beyond oncology, with the financial structure for each target “roughly the same magnitude” as the first, said Chief Business Officer Martin Williams.

Dicerna's molecules, dubbed DsiRNA, are designed to interact early on with the chain of cellular events that lead to the “gene silencing” of RNA interference—essentially the hijacking of messenger RNA so that the protein they encode is never expressed. DsiRNA interact with the Dicer enzyme which, as its name suggests, chops invasive genetic material into pieces.

The trick is to get Dicer to produce just the right pieces that interfere with the cell's messenger RNA. Part of the intellectual property Dicerna hopes to patent are the tricks to manipulate and orient the DsiRNA so that Dicer turns them into “one cleavage product,” CEO Jim Jenson told “The Pink Sheet.” Dicerna's first patents could be issued this year, he added, noting the company has filed more than 50 applications.

Shorter RNAi-related molecules (the difference is just a few base pairs of nucleotides) bypass Dicer in the RNA interference process.

Dicerna has the option to co-promote and equally share profits from the first drug that emerges from the collaboration. It doesn't need to achieve milestones in the first program to trigger Kyowa's options on other targets, Williams said: “There's no gating event that precludes us from moving to other targets.”

## **The next round stays in-house**

Meanwhile, Dicerna is looking for additional investment. "We're actively marketing a B round to move our own programs forward within the next couple of months," Jenson said. "We're looking for one additional investor."

Abingworth, Oxford Biosciences and Skyline Ventures invested \$21 million across two tranches of Dicerna's A round in 2007 and 2008. All three have signed on for the B round, Jenson said.

Jenson said the B round cash will go toward Dicerna's in-house development, directed at a solid-tumor target that is "clinically validated," but needs new drugs because of toxicology or resistance problems. "We'll consider several delivery options," he continued.

Delivery has been a vexing problem for the first generation of RNAi therapy companies. The fragile molecules break down quickly in the body. The most advanced clinical candidates are aimed mainly into the lung or the eye—targets that don't require systemic delivery. Dicerna officials said their molecules might also solve delivery problems, with the extra structure of the molecule serving as a "handle" to which aptamers, antibodies and peptides can be attached to help shepherd the drug into the targeted cell. Dicerna last summer began a collaboration with Archemix to create aptamer-DsiRNA conjugates.

But the initial focus with Kyowa, despite the Japanese firm's pioneering role in monoclonal antibodies, will be on more conventional modes of RNAi therapy delivery. "The state of the art today is lipid nanoparticles," said Dicerna's Williams. "That's the first thing we'll try."

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