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## Dicerna, Kyowa \$1.4B Pact Called Largest Target-Based RNAi Deal

By Donna Young  
Washington Editor

In its first major deal, Dicerna Pharmaceuticals Inc. is partnering with Japanese biopharmaceutical firm Kyowa Hakko Kirin Co. Ltd. to discover, develop and commercialize drug delivery systems and siRNA medications using Dicerna's Dicer Substrate Technology for undisclosed oncology targets.

The deal potentially could garner Dicerna more than \$14 billion and is the largest target-based RNAi deal ever closed, said Martin Williams, senior vice president and chief business officer, who called the \$4 million up-front cash payment from KHK "quite healthy for a single target."

Williams noted that Silence Therapeutics plc and AstraZeneca plc, both of London, inked a \$400 million deal in July 2007 to develop drugs against respiratory disease targets. Days after that deal was announced, Swiss drug giant Roche AG formed a partnership with Cambridge, Mass.-based Alnylam Pharmaceuticals Inc. for RNAi therapeutics, but that collaboration was a nonexclusive licensing platform deal and not target-based, he noted. (See *BioWorld Today*, July 9, 2007, and July 10, 2007.)

Under its partnership with KHK, Dicerna stands to gain up to \$120 million in research funding and development and commercial milestones for the exclusive rights to one oncology target, with the firms having the option to expand the collaboration for up to 10 targets under similar terms, Williams told *BioWorld Today*.

Williams said there was no timeline for that option to kick in, stating that "Those additional targets could come online anytime from now on." The \$14 billion Dicerna expects to bank, is "assuming all of the targets are pursued," he noted. Dicerna also is entitled to sales royalties on any products coming out of the collaboration, he added.

The partnership also includes a 50-50 co-promotional and profit-sharing option for the initial target in the U.S., Williams said. The firms have not yet disclosed whether the profit-split and co-promotional option will be available for any additional targets if the deal is expanded, he added.

While the companies have yet to disclose the types of cancer targets they will be pursuing, Williams divulged that the deal is for solid tumors.

Dicerna's patented Dicer Substrate technology is a "sec-

ond-generation approach" to small interfering RNA, explained CEO James Jenson.

"They enter the pathway at a different point, upstream in the pathway where a microRNA would enter, and they are longer molecules as well," he said.

While siRNAs are generally 21 nucleotide base pairs, Dicerna's molecules are 25 or longer, Williams said.

"The biological properties have really turned out to be quite extraordinary," Jenson said. "They are extremely potent. They are much more potent than the first generation smaller 21mers that enter the pathway downstream. It's now standard for us to get multiple single-digit picomolar Dicer substrates against the target of choice and to be able to do so in a matter of a couple of months. So the potency is quite extraordinary."

Jenson said Dicerna's molecules also last longer in the body. "They have a longer duration of action, we think because of use by the full RNA pathway," he said.

The combination of properties of "extraordinary" potency, duration of action and ability to manipulate the molecule for delivery purposes is what distinguishes Dicerna's technology from other siRNAi molecules, Jenson added. He noted that the deal with KHK also includes collaborating on the delivery systems for the siRNAi drugs coming out of the partnership.

Dicerna is working on two approaches: a lipid-based nanoparticle system, and a second approach Jenson described as an integrated drug delivery system, which he said was a "double-punch molecule with a payload and a targeting moiety attached that would be injected as a molecule in saline, and it should have the biodistribution not unlike any other biologic."

KHK, he noted, is working on its own liposome particle delivery system.

"Our approach is to have multiple options available that allow us to tailor the appropriate delivery system to the indication of the disease we are going after," Williams said. "The key is flexibility and choice."

Dicerna, which had been in talks with KHK "on and off for quite some time, for a year or so," chose the Japanese drugmaker because of its commitment to the RNAi space,

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Williams said, noting the company's June 2008 deal with Alnylam for an RNAi product to treat respiratory syncytial virus. (See *BioWorld Today*, June 20, 2008.)

"They have a great deal of expertise there and a lot of knowledge," he said. "So for us, this is just a really great fit in terms of a partner who really bought into the technology and really shared the vision of creating RNAi drugs out of our technology."

The firms also have a "very strong cultural connection" and a "shared entrepreneurial philosophy," Williams added.

Dicerna also has an in-house RNAi clinical drug development program under way for a yet-to-be disclosed cancer target, Jenson noted. "Our approach for our in-house program has been to pick a clinically validated therapeutic

target that needs a new drug, either because of reasons of toxicity or drug-resistance, and that also gives us access to biomarkers," he said, adding that the firm is aggressively moving that program forward.

Dicerna plans within the next two months to initiate a Series B financing round with its current investors Oxford Bioscience Partners, Skyline Ventures and Abingworth. The company is "looking for an additional investor to join the team," he added.

"We see ourselves as a second doorway in the RNAi space, not just because of the biological and chemical properties of the molecule, but also a second doorway in regard to intellectual property," Jenson said, noting that the firm has more than 50 patent applications of its technology in prosecution. "So we are being very aggressive in this area," he said. ■