



January 29, 2009

Dicerna Expects Industry Deal in '09, Takes Aim at Undruggable Targets

LEVERAGING A STRATEGY of pursuing targets undruggable by technologies other than RNAi, Dicerna Pharmaceuticals has set its sights on inking at least one industry alliance in 2009, a company official told RNAi News this week.

While "nothing is done until it's done in this business ... [discussions] are progressing very well in a very serious manner," and Dicerna plans to have consummated its first industry partnership before the end of the year, CEO Jim Jenson said. He added that the company intends to primarily strike deals on a target-by-target basis.

According to Jenson, the maturity of Dicerna's partnership talks is in part related to big pharma's "very strong appetite for RNAi" because of the technology's potential to hit targets not amenable to small molecules and biologics such as antibodies. And when it comes to Dicerna's top disease area of interest, oncology, there is no shortage of such targets, he said.

"There are granddaddy oncogenes that the academic and pharmaceutical communities have wanted to be able to hit but have not been able to do so," he said. "We are targeting several [of these], which we have not yet publicly identified but would be readily recognized by potential partners."

Jenson's comments come just days after Dicerna Chairman and Co-Founder Douglas Fambrough, who is

also a general partner at one-time Sirna Therapeutics investor Oxford Bioscience Partners, suggested that smaller RNAi drug shops should focus on undruggable targets in order to compete with larger, better-financed rivals in the space.

Speaking at the Center for Business Intelligence's Executing on the Promise of RNAi conference in Cambridge, Mass., last week, Fambrough noted that many of the first RNAi drug programs focused on well-validated, and often well-addressed, targets as part of a bid to prove the gene-silencing technology's potential without adding the additional layer of complexity that goes along with novel targets.

Indeed, the first two RNAi drugs to enter the clinic, Opko Health's bevasiranib (formerly Acuity Pharmaceuticals' Cand5) and Sirna's Sirna-027, were wet age-related macular degeneration drugs designed to silence vascular endothelial growth factor and VEGF receptor-1, respectively (see *RNAi News*, 11/12/2004 and 11/26/2004). Alnylam Pharmaceuticals' first clinical candidate was also a VEGF-targeting drug for AMD, ALN-VEG01, but the company officially shelved the program in late 2005 (see *RNAi News*, 9/23/2005).

But with RNAi drugs now in the clinic and a handful already licensed out to big pharma partners, the field has moved past the need to prove itself, and those developing drugs based on the technology should focus on so-called undruggable targets to realize the most value out of their pipelines, he said.

In addition, smaller companies lacking the scientific resources or broad intellectual property estates of a company such as Alnylam may be better suited to woo partners if they are developing a drug against a target that has thus far stymied small molecules or antibodies, Fambrough added.



www.genomeweb.com
The GenomeWeb Intelligence Network



January 29, 2009

Dicerna ...

continued from page 1

On the sidelines of the CBI meeting, Art Krieg, CSO of Pfizer's Research Technology Center, which oversees the company's therapeutic RNAi activities, voiced similar sentiments.

"A lot of the companies leading in the RNAi field have chosen targets for early development that I would consider more proof-of-concept targets where the target has been validated but is addressable by other technologies," he told RNAi News. "Our perspective, as big pharma, is that we do not have interest in going after those kinds of targets for our RNAi program."

Krieg agreed that the RNAi field has largely moved beyond this stage and that Pfizer has "accepted ... that RNAi works and that you can knock down targets in vivo using this technology if you get it into the right tissue, out of the endosome, and so forth."

But at the same time, it makes little business sense to use RNAi "for the kinds of targets you can go after easily using other technologies," he said. And when it comes to partnering, "we're not interested in ... an RNAi compound against a target that we think we can hit [using a] technol-

ogy [with less] risk — at least not at prices that might be attractive" to a licensor.

Aside from Dicerna, at least one other RNAi drug firm has decided to take this route: Intradigm.

As reported by RNAi News earlier this month, Intradigm dropped its lead cancer therapeutic candidate ICS-283, which the company had previously said would enter phase I testing this year, in order to focus on undruggable targets (see *RNAi News*, 1/8/2009).

ICS-283 targets VEGF, a well-validated target for anti-angiogenic cancer therapies. However, Intradigm recently made the decision that the agent was not commercially promising enough, CEO Phil Haworth told RNAi News at the time.

"The real value of siRNA and our delivery technology is to develop drugs that treat diseases whose targets are not accessible through antibodies or small molecules," he said. "VEGF's value was that it was validated through antibodies and small molecules," but as a result it lacks the "real benefit of an siRNA approach."

— Doug Macron