Product Development

Plucking from pharma

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While most industry watchers are betting on which biotech products will be grabbed by big pharma, such deals can flow in the other direction, as well. In recent days, three private biotech companies have taken over compounds that big pharma found problematic. All three think they can find dosing regimens and indications to solve shortcomings that the big companies didn't want to deal with. Miikana Therapeutics Inc. is taking on a cancer compound from Roche, while Sunesis Pharmaceuticals Inc. and Elixir Pharmaceuticals Inc. are taking on cancer and metabolic compounds, respectively, from Bristol-Myers Squibb Co.

Changing the dose

For Miikana, which has been a preclinical company out trying to raise $20-$30 million in a series B round, the deal with Roche now gives the biotech a Phase II cancer compound to talk about.

Under last week's deal with Roche (SWX:ROCZ, Basel, Switzerland), Miikana received exclusive worldwide rights to MKC-1, an oral small molecule cell cycle inhibitor that has an undisclosed mechanism of action. The compound has completed Phase II trials as monotherapy in third-line metastatic breast cancer and non-small cell lung cancer (NSCLC).

Although ROCZ's Phase II results showed limited efficacy, Miikana believes the compound was dosed at subtherapeutic levels.

In the 35-patient breast cancer study, there were two partial responses, for a response rate of 5%. There also were two minor responses. In the NSCLC trial in 34 patients, there were one partial response and two minor responses.

The problem, said Miikana co-founder Gail Eckhardt, was that MKC-1 was dosed at only 95 mg/m^2 in the Phase II studies. Following Phase I trials, the recommended Phase II dose — defined as the dose at which no more than 30% of patients had dose-limiting toxicities — was 125 mg/m^2. Eckhardt, who is Miikana's clinical oncology advisor, said ROCZ was cautious with the dose because adverse events were seen at an even higher dose in Phase I studies.

Miikana President and COO Dinesh Patel told BioCentury that MKC-1 is metabolized by the liver, but ROCZ's trials included patients with "severe, impaired liver function. We concluded that in all adverse event cases, patients had severely impaired liver function, and this resulted in high exposure to the compound."

Miikana (Fremont, Calif.) plans to start Phase II studies in breast cancer and NSCLC in the fourth quarter of this year and first quarter of next year, respectively. "The question is whether we'll get the expected response rate at 125 mg/m^2," said Eckhardt. "We think we have a good chance, and we're looking for a 10-15% partial response rate."

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Patel said the planned trials will exclude patients with severely impaired liver function and will have more monitoring than previous trials.

Behind MKC-1, the company's preclinical cancer compounds include MKC-1313, an HDAC inhibitor, and MKC-1260, an Aurora kinase inhibitor.

For ROCZ, the decision to out-license MKC-1 was one of resource allocation, according to Patel.

Miikana paid an undisclosed amount up front, plus equity, and ROCZ is eligible for milestones and royalties.

Changing the regimen

If Miikana's deal should help with its venture round, the BMY deal might be the push that Sunesis needs to get its IPO moving. The company filed to go public in December. By obtaining worldwide rights to BMS-387032, now SNS-032, Sunesis has embellished its story with a second clinical stage cancer product.

The key will be getting around problems that BMY found in Phase I trials of the cyclin-dependent kinase (CDK) inhibitor.

"The challenge for in-licensors is to find something where the value was not apparent to the people running the original program," said CEO Daniel Swisher. "It seems like BMS suspended development of SNS-032 in favor of other programs. BMS only completed one of several Phase I studies before abruptly" shelving the compound.

BMY (New York, N.Y.) has another early stage kinase inhibitor for cancer in development, dasatinib (BMS-354825) BCR-Abl inhibitor. Last year, the company reported data from a Phase I trial in late-stage chronic myelogenous leukemia (CML) *(see BioCentury, Dec. 13, 2004)*.

In its S-1 filing, Sunesis said BMY saw statistically significant increases in QTc prolongation in patients receiving 24-hour infusions of SNS-032. QTc prolongation is associated with torsade de pointes-type arrhythmia, a potentially fatal ventricular tachycardia.

Also, after a one-hour infusion regimen that included higher peak drug levels than the 24-hour infusions, "pronounced, rapidly reversible decreases in white blood cells were observed between 24 and 48 hours."

The S-1 added that "BMS did not complete two of these planned Phase I clinical trials, and we cannot be certain that BMS did not abandon these trials due to safety concerns."

Sunesis (South San Francisco, Calif.) hopes to get around the safety issues by testing a different dose and administration schedule in a Phase I trial slated to start in the second half. "Our protocol is going to involve daily three-hour infusions for five days in a row every three weeks. We plan to do a dose-escalation trial to find the maximum tolerated dose and test whether the compound is active," Swisher said.

"We think more frequent dosing is called for because in the

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