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Igenica eyes tech partnerships

Mark Goldsmith
Third Rock Ventures

Q&A

Mary Haak-Frendscho
Igenica

VCs invest $33M as drug trial nears

Igenica Inc. is taking an old-school approach to running a biotech company while positioning itself to take advantage of one of the industry's hottest areas.

How convinced are investors? Third Rock Ventures, the Column Group and 5AM Ventures are among those that extended Igenica's $33 million Series C round by ponying up another $14 million recently.

The money will help Igenica start a Phase I trial with its lead drug, IGN-523, targeting acute myelogenous leukemia. The drug is a so-called "naked antibody," a Y-shaped molecule that isn't piggy-backed onto another molecule.

At the same time, Igenica has evolved into antibody-drug conjugates, a space that has exploded, particularly after the Food and Drug Administration a year ago approved Genentech Inc.'s Kadcyla against breast cancer.

Antibody-drug conjugates hit cancer cells with a one-two punch, coupling a highly targeted antibody with a toxic payload of chemotherapy. Instead of the chemo drug scattering and damaging healthy cells surrounding a tumor, ADCs are better able to pinpoint cancer and minimize side effects.

Igenica invented a technology

— which it calls SNAP — that stabilizes the native antibody, which could accelerate an ADC's development because it uses standard manufacturing techniques.

Igenica can partner the technology with other companies, using the cash from those collaborations to develop its own ADCs or antibodies alone.

I spoke separately with Igenica CEO **Mary Haak-Frendscho** and **Mark Goldsmith** of Third Rock about Igenica's technology and its plans. I've combined here some of their responses, edited for clarity and space.

Is this built for partnerships or to develop ADCs on your own?

HAAK-FRENDSCHO: We built this company to be fully enabled: target discovery, antibody discovery and now our own ADC program.

We're in discussions with several companies and have established an evaluation collaboration that they can use for their programs. This is a great unmet need, to have access to ADC technology but to also have a homogeneous technology to really empower (other companies') antibody programs.

Were ADCs in the original plans for Igenica?

HAAK-FRENDSCHO: It was not on the radar screen for Igenica, but there were companies working in this space. ADC technology was a good three decades in development, but it was less than three years ago that it was convincingly clinically validated.

Igenica and our former CEO, Mike Rothe, said, "Let's start dipping our toe in the ADC pool" and he brought in chemists. When I joined last year, I made a commitment to increase our focus on that area, so over the past year we have focused our drug discovery and we're looking to select two clinical candidates this year for ADC programs.

ADC ABCs

There are more than 30 antibody-drug conjugates in clinical development for cancer, including at least five from Genentech Inc. Among the other Bay Area companies in the space are Five Prime Therapeutics Inc. and CytomX Therapeutics Inc. of South San Francisco. In the Bay Area, only Genentech has ADCs in clinical trials.

Here is a look at Genentech's ADCs:

Antibody drug coagulate	Payload	Disease	Status
RG-7596	MMAE	Diffuse large B-cell lymphoma, non-Hodgkin lymphoma	Phase II
RG-7593	MMAE	Diffuse large B-cell lymphoma, non-Hodgkin lymphoma	Phase II
RG-7458	MMAE	Ovarian cancer	Phase I
RG-7636	MMAE	Melanoma	Phase I
RG-7450	MMAE	Prostate cancer	Phase I

MMAE is monomethyl auristatin E.

SOURCE: Igenica October 2013 report at ADC World Forum.

GOLDSMITH: We saw Igenica as an integrated set of capabilities from the outset. We didn't invest (in 2012) on one single parameter. We were most impressed with several technologies that together created a kind of end-to-end to therapeutic antibody discovery.

We didn't know exactly how it would play out. When Mary joined, she had a similar view of it as a priority. She and the new chief scientific officer (Thi-Sau Migone) committed resources and the science progressed, and now it is a core part of the company.

And you've also got a drug going into Phase I.

HAAK-FRENDSCHO: One of the cool things about this drug is it targets CD98 (a protein that is important in amino acid transport). That's up-regulated on virtually every patient sample we've tested in AML. Rather than treating a subset, it has the potential to treat the majority of AML patients.

This target is not just expressed on the tumor cells, but the tumor stem cells as well.

We're looking to enroll our first patient this quarter.

The Phase I design is that we should have not only a safety indication, but by the end of the year we're looking for proof of activity. If all goes well, that will trigger us to file another IND in (the skin cancer) squamous cell carcinoma, where an overwhelming majority of patients express the target.

When could you file an investigative new drug application on an ADC program?

HAAK-FRENDSCHO: Our own program will probably be 2016. Those are a little longer timelines than naked antibodies or small molecules.

Do you see Igenica competing against Seattle Genetics or ImmunoGen or other drug developers?

GOLDSMITH: I think it's all of the above. They're all competitors and they're all potential collaborators. There are not many companies that can discover novel antigens and discover antibodies against those antigens and conjugate those with toxins.

You might find partners who want access to one of those but not the complete value creation equation in the platform. Igenica is engaging partners around ADCs and more broadly around the other technologies. ■