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Aveo Pieces Together a Plan to Rival Big Boys of Cancer Drug World

Luke Timmerman, 6/29/09

Great biotechnology stories have three essential ingredients—science, medicine, and business. Aveo Pharmaceuticals CEO Tuan Ha-Ngoc told me last week that he thinks about these same elements in his quest to build a sustainable company. Few companies ever put together all the pieces, though, and it's too early to say if Cambridge, MA-based Aveo is one of them.

Until a few weeks ago, Aveo was probably best known for the first piece of the puzzle, the science. It has what it calls a more accurate method for mimicking cancer in mouse experimental models, compared with the traditional “xenograft” approach.

Then, in late May, Aveo made headlines on the medical side, when researchers presented promising results for its lead experimental drug for kidney cancer. The first drug to come from Aveo's experimental platform, tivozanib (or AV-951) is an oral pill designed to block three specific types of molecules that allow the formation of new blood vessels; tumors rely on new vessels for nourishment as they grow. The study showed the drug

could slow the spread of malignancy with minimal side effects. If the data can be confirmed in a larger trial to start later this year, Aveo's drug could be in a position to compete with Pfizer's sunitinib (Sutent) and Bayer and Onyx Pharmaceuticals' sorafenib (Nexavar), which combined pulled in \$1.5 billion last year.

But even if things go right, Aveo won't have its moneymaking drug on the market until 2012 at the earliest. So if you're Ha-Ngoc, how do you keep the business moving forward for years when venture capital is hard to come by? You keep 100 percent ownership of your crown jewels in North America, find partners to commercialize them elsewhere, all structure the deals so they pay for your R&D engine. Then plow the profits back into R&D and do it again.

“To build a sustainable company, you can't be a single-product company or a single-indication company,” Ha-Ngoc says. “We want to be a full-fledged company.”

The Aveo story began in 2002. The company spun out of the lab of



Ronald DePinho and Lynda Chin at the Dana-Farber Cancer Institute in Boston. They started with the premise that since cancer has been cured many times in mice, and never in humans, maybe the existing mouse models for the disease could use some improvement. The conventional “xenograft” approach involves taking human cancer cells, growing them in the foreign environment of a lab dish, then injecting them into a mouse with a suppressed immune system—which all adds variables and creates an artificial environment, Ha-Ngoc says.

The Aveo model, on the other hand, involves splicing cancer-causing genes into a mouse embryo. The DNA encoding those genes is rigged so they're turned off when the mouse is born and can be switched on later in life by simply feeding the mouse a specific molecule, such as an antibiotic. This allows the mouse to develop normally, and can avoid the kinds of mutations that can arise in the lab dish, skewing traditional models, Ha-Ngoc says.

The Aveo approach was compelling enough to Merck that the pharma giant signed a partnership with Aveo to identify new drug targets in 2003. Two years later, Merck expanded the partnership to encompass testing potential drug compounds against those targets, Ha-Ngoc says. By 2007, Eli Lilly, OSI Pharmaceuticals, and Schering-Plough had also formed deals to use the Aveo technology. This year, Biogen Idec joined the pack. All these deals have added up to provide \$140 million in financing for Aveo, on top of the \$90 million the company has raised in venture capital.

Aveo is now in “active discussions” to find a partner on its most valuable asset—tivozanib for kidney cancer. Aveo’s goal is to hold onto 100 percent of the rights to this in North America, something few biotech companies ever get to do with cancer drugs.

What surprised me more is how ambitious Aveo is in its clinical development plan for this drug, even before it has found a partner. Aveo is working on a trial design that will enroll “several hundred” patients with kidney cancer, randomly assigned to get its drug or an “active comparator,” which means a drug that might work, instead the more traditional route of putting the new drug up against a straw man

like a placebo or a drug like interferon, which doesn’t work. The main goal will be to provide a clear answer on whether the Aveo drug can slow down the spread of kidney tumors, with a secondary goal will be to see whether it can help people live longer.

Besides that big trial, which is expected to start enrolling patients before the end of this year, Aveo is already lining up ways to differentiate its drug from Pfizer and Bayer’s competitors. Those drugs block the same molecule that Aveo’s drug targets, a receptor called VEGF, but they also hit other receptors involved in rapid cell growth and proliferation. By hitting multiple targets, these drugs cause “overlapping toxicities” and can’t be given in combination with drugs like Wyeth’s temsirolimus (Torisel), Ha-Ngoc says. By being very specific (Aveo’s drug blocks three forms of VEGF but no other targets), and because of its mild side effect profile, the Aveo drug should be useful in more combinations than the Pfizer and Bayer drugs, he says. Aveo expects to publish the company’s first data to support this idea in the second half of the year, Ha-Ngoc says.

Usually venture-backed biotechs don’t have more than one serious late-stage drug candidate to talk

about, but like Ha-Ngoc says, he’s not looking to build a one-drug company. Aveo’s second candidate, AV-299, is an antibody drug that’s designed to block hepatocyte growth factor, a cell-growth protein that’s involved in malignancies. Aveo, which is developing this with Schering-Plough, has completed an early-stage safety study of the drug and is now gearing up to start two mid-stage trials of 200 patients each.

On my way out the door, Ha-Ngoc showed me Aveo’s “Wall of Fame,” which bears individual color photos of all 136 of the company’s employees, in order of which year they joined the firm. There were a lot of photos pasted on 2008, and not as many in 2009, but he says he wants that list to keep growing.

“We want to create an organization that discovers and develops drugs in a different way, that takes out the guesswork,” Ha-Ngoc says. “Hopefully five years from now we’ll be recognized as a company that has commercialized an important new drug, and that has a pipeline that can reproduce it in a sustained way.” ■

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