

START-UP



Windhover's Review of Emerging Medical Ventures

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Orthopedics

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Patience Pays Off for Cytokinetics

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**Patience Pays Off
for Cytokinetics**

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○ **Business:**

Drug discovery & cellular bioinformatics

○ **Founded:**

May 1998

○ **Founders:**

- James Sabry, MD, PhD
- Larry Goldstein, PhD
- James Spudich, PhD
- Ron Vale, PhD

Cytokinetics Inc.'s recently signed research collaboration with **Glaxo-SmithKline PLC** provides some third-party validation for the three-year-old start-up's cytoskeleton-based technology platform. (See "Cytokinetics: A Platform Case Study for the Next Decade," *START-UP*, June 2000.)

The deal, which centers on the discovery and development of small-molecule therapeutics that target mitotic kinesins for applications in the treatment of cancer and other diseases, provides Cytokinetics with nearly \$50 million in committed funding during the minimum five-year research term: \$14 million in up-front cash, a \$14 million equity investment, and at least \$20 million in research funding. Cytokinetics also stands to earn from \$30-50 million in pre-commercialization milestones on each of the more than 10 mitotic kinesin targets that are the subject of the collaboration, as well as

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royalties on any marketed products. The company also has a buy-in right on any drug candidates: a product-by-product option to co-fund certain development activities, thereby increasing the royalties it is otherwise entitled to. Cytokinetics also enjoys a co-promotion option for North America, with GSK agreeing to reimburse it for the costs associated with fielding a sales force.

Robert C. Blum, VP, business development, said that a number of the drug companies with which Cytokinetics spoke before reaching an agreement with GSK were not prepared to relinquish those sorts of rights to a biotech partner. They “were willing to reward us very handsomely for what we had produced to date, but did not acknowledge what we wanted to become. That’s where GSK and a couple of other companies distinguished themselves from the field.”

But finding the right partner apparently took some doing. As far back as May 2000, Blum told *START-UP* that he was in “advanced discussions with a number of pharmaceutical companies” regarding the mitotic kinesin program. A series \$55 million series C financing in November of last year gave Blum and his colleagues more time to work with and thus the ability to drive a harder bargain.

That Cytokinetics was ultimately able to command such value for its mitotic kinesin targets reflects the extent to which they have been validated as small-molecule targets. Several current cancer therapies provide proof of concept for exploiting the cytoskeleton, which plays a major role in cell division, or mitosis. Paclitaxel (*Taxol*), vincristine, and estramustine each attack cancer by targeting tubulin, a cytoskeletal protein and a major player in cell division. But because tubulin is implicated in a variety of important cellular activities in addition to cell division, interfering with its activities in cancer cells inevitably results in serious side effects.

Mitotic kinesins, on the other hand, appear to be expressed only when a cell is undergoing division; they also seem to be up-regulated in cancers, according to Blum, offering the possibility of a cleaner side-effect profile for drugs that target them. Cytokinetics has already identified hits for each of the targets involved in the GSK deal, as well as a few lead anticancer candidates, according to Blum, including one that has shown antitumor activity in *in vivo* tumor models.

And Blum says that as the collaboration progresses, and projects may revert to Cytokinetics—granted GSK’s rejects are worth pursuing—the company will build its development and commercialization infrastructure accordingly. He adds that, to the extent possible, those capabilities will be developed on an as-needed basis and in accordance with the maturing of the company’s other discovery programs. Although Cytokinetics’ management harbors ambitions to move downstream, Blum says they’re “not currently looking for in-licensing opportunities that will have us quickly leapfrogging into development and marketing before our own internal efforts directed at the cytoskeleton have had an opportunity to bear fruit.”

So far, Cytokinetics has done some of its own preclinical work, relying on outsourcing when necessary. It has also brought in about 20 medicinal chemists and is looking for more—a significant challenge, acknowledges Blum, given the severe shortage of well-trained chemists and the many biotechnology and pharmaceutical companies courting talent.

Cytokinetics’ preclinical work also includes a program in congestive heart failure that Blum hopes to partner in an alliance that may borrow some architectural features of the deal cut with GSK. Until then, says Blum, the company’s \$75 million in cash (it’s raised a total of \$80 million in VC-backed funding) should enable it to fund that program, as well as research in antifungals for the next several years.

Cytokinetics' leadership is also projecting business development transactions from its activities related to cellular bioinformatics—which will initially have the company profiling compounds provided by drug companies, and may later generate other opportunities for collaborations.

But as the combinatorial chemistry start-ups learned the hard way during the mid- and late-1990s, generating value through a technology platform that offers only a partial solution to the drug discovery puzzle is no simple task. Database companies are increasingly out of favor: it's simply difficult to get drug companies to pay enough money for a subscription to make the process of data collection worthwhile—and only data that's difficult to collect can even purport to command a high price. And so far, Cytokinetics has no significant deals to show for its bioinformatics efforts. But in the very near future, reports Blum, the company will announce a series of development agreements that will provide at least partial validation for Cytokinetics' automated cellular technologies. Still, it's clear in the conversation, and from the structure of the GSK deal, that Cytokinetics wants its valuation firmly based on a proprietary drug-discovery model.



Comments?

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