

BioCentury

Ebb & Flow Focus

Lessons for an 'up' round

By Kathryn Calkins
Senior Writer

With most privately held companies doing down rounds, it's news when a company is able to pull off an up round. It's even bigger news when experienced investors bestow a post-money valuation on a Phase I company that's about double what many companies in Phase II are getting these days.

Cytokinetics Inc. did just that last week, closing on \$40 million in an oversubscribed series E round valuing the company north of \$200 million post-money. The question is why can some companies do this at a time when most can't?

According to the company's venture investors, the answer is two-fold: First, Cytokinetics is a first-mover in a focused field of biology that has broad potential product applications – a profile reminiscent of Gilead Sciences Inc. (GILD, Foster City, Calif.), which is underpinned by its antiviral expertise. Cytokinetics' chosen field, the cytoskeleton, has been ignored by most other companies. Yet there are marketed drugs, most notably paclitaxel, that validate cytoskeleton components as targets, making it less risky than some other novel areas of focus.

Second, the company has made a conscious effort over the years to benchmark its rapid progress from biology to products, giving both existing and potential investors confidence that management is executing its business plan.

The metrics

Cytokinetics' last venture round was a \$55 million series C financing in November 2000. Investors included CSFB Private Equity; Alta Partners; Lombard Odier; Mayfield Fund; Sevin

Rosen Funds; and Vulcan Ventures. The company's valuation after that round was \$100-\$150 million.

The D round was a \$14 million equity investment by GlaxoSmithKline plc at the time the companies signed their partnership in June 2001. Following the transaction, Cytokinetics was valued at about \$200 million.

Under the five-year deal, the companies are developing more than 10 mitotic kinesins discovered by Cytokinetics to treat

cancer. Mitotic kinesins are cytoskeletal enzymes that act in concert to form and operate the mitotic spindle during cell division. Inhibition of the enzymes disrupts the cell cycle and induces apoptosis.

Last year, Cytokinetics and GSK (London, U.K.) moved their lead compound, SB-715992 (CK0238273) into a Phase I trial in advanced cancer. The compound targets kinesin spindle protein (KSP).

Last week's \$40 million round was thus the first the company had done in

two-and-a-half years, and it was primarily an inside round, including CSFB, Sevin Rosen, Alta and Mayfield. New investors were HBM Bioventures, General American Investors, PRM Ventures and Mizuho Capital.

"We're the ones who are happy with the company's progress. And we feel it should be valued a step above the last round," said Farah Champs, a partner at Alta Partners.

Andreas Wicki, partner with HBM Bioventures, said that he sees comparable stories that are not priced above \$100 million, and that companies with Phase II data are coming out of funding rounds with valuations of \$100-\$120 million.

"Cytokinetics has outbid them by a factor of two at least," he said.

HBM inherited a small position in Cytokinetics through its merger with NMT New Medical Technologies in February and

'This is the model. Take an area of biology and rapidly become the best in the world at it.'

— James Sabry of Cytokinetics

BioCentury™
THE BERNSTEIN REPORT ON BIOBUSINESS

PO Box 1246
San Carlos CA 94070-1246
Voice: 650-595-5333
Fax: 650-595-5589

DAVID FLORES
President & Publisher

KAREN BERNSTEIN, Ph.D.
Chairman & Editor-in-Chief

BioCentury, The BioCentury 100, and The Clear Route are trademarks of BIOCENTURY PUBLICATIONS INC. All contents © Copyright 2003, BIOCENTURY PUBLICATIONS INC. ALL RIGHTS RESERVED. No part of this publication may be reproduced, photocopied or reproduced in any form, retransmitted, or stored in a retrieval system without prior written consent of the publisher.

The contents of this publication are gathered from sources believed to be reliable, but in any case are not warranted by the publisher for a particular use or purpose. Also, the content and opinions herein may change without notice and do not constitute investment advice.

*Lessons for an 'up' round,
from previous page*

invested slightly more than was required in the current round to keep its pro-rata percentage of the company.

The science

All the investors who spoke with BioCentury were attracted to the company's depth of knowledge in cytoskeleton biology and the speed at which it has been translated into product opportunities.

The cytoskeleton comprises the structures of the cell involved in dynamic cellular functions and mechanics, including cell division, intracellular transport, cell motility and the establishment and regulation of cell polarity. Drug targets include filaments — the primary structural elements of the cytoskeleton — as well as the enzymes that organize and regulate the filaments and transport molecules along them.

Steve Dow, a partner with Sevin Rosen, said Cytokinetics' scientific founders were pioneers in understanding the workings of the cytoskeleton, which gave the company a head start in a relatively new area of biology.

The company and its investors believe that this understanding will allow it to improve on existing drugs that validate the area. In cancer, for example, disrupting mitosis is a proven strategy, as microtubule binding anti-cancer drugs such as the taxanes Taxol and Taxotere, and the vinca alkaloids vincristine, vinblastine, vinorelbine and estramustine, all work by disrupting mitotic spindle function. However, because peripheral neurons also use microtubules to transport nutrients and proteins, each of these agents produces some degree of peripheral neuropathy.

In contrast, Cytokinetics' cancer program is targeting KSP, which acts as a motor that drives cellular proliferation during the M phase of the cell cycle when chromosomes pair up in the center of the cell and then split apart. The KSP inhibitors do not appear to cause peripheral neuropathy, because they are only expressed during the M phase and are not expressed in post-mitotic tissues such as peripheral neurons.

Mitotic kinesins such as KSP also are overexpressed in cancer cells compared to normal proliferating cells.

"We know that the areas we work in are validated in human diseases," either

(Cyto)skeletal pipeline

Development programs at Cytokinetics.

Product	Indication	Status	Partner
SB-715992 kinesin spindle protein (KSP) inhibitor	Cancer	Start Ph II in 2003	GlaxoSmithKline
2nd KSP inhibitor	Cancer	File IND in 2003	GlaxoSmithKline
Small molecule sarcomere activator	Acute heart failure	File IND in 2003	
Angiogenesis program	Cancer	Lead identification/optimization	
Cytokinesis program	Cancer	Discovery	
Metastasis program	Cancer	Discovery	
Mitosis program	Cancer	Discovery	GlaxoSmithKline
Mitosis program	Fungal infection	Discovery	
Small molecule	Hypertension	Discovery	
Small molecule	Asthma	Discovery	
Small molecule sarcomere activator	Chronic heart failure	Discovery	
Virulence program	Fungal infection	Discovery	

because marketed compounds in those fields target the cytoskeleton or because genetic mutations in genes encoding cytoskeletal proteins cause diseases, said James Sabry, president and CEO.

Besides cancer, the company believes it can apply its biology to therapeutic programs in cardiovascular disease, fungal infections, neurodegenerative diseases, inflammatory diseases and AIDS/HIV. For example, in cardiovascular disease, ACE inhibitors, diuretics, vasodilators such as nitroglycerin and nitroprusside and inotropic agents such as dobutamine and milrenone all activate the cardiac sarcomere — a cytoskeletal target that comprises the basic contractile unit of the heart — to treat congestive heart failure.

Sabry noted that investors want to see a platform that is likely to generate multiple products that reach the marketplace. This is best accomplished, he argued, by focusing on one area of biology and owning it. "This is the model. Take an area of biology and rapidly become the best in the world at it," Sabry said.

But investors said Cytokinetics also has the ability to move beyond its understanding of the cytoskeleton to apply its knowledge throughout its platform of high throughput screening, chemistry, informatics, pharmacology and preclinical capabilities. Indeed, said Dow, the company "had some automation and a screening process based on this knowledge of biology that allowed them to identify compounds that are

now in the clinic in an unprecedented period of time."

Cytokinetics has made its goal to pinpoint targets specific to disease conditions while also eliminating the negative effects on normal cells of drugs like paclitaxel. To this end, it uses its Cytometrix cellular phenotyping technology to inform lead compound identification.

According to Sabry, Cytometrix is "an attrition management system." It measures the effects of a compound on an entire cell's phenotype rather than measuring the output of the target of interest alone, as most high throughput screens do. By showing the phenotype that results from a cell's exposure to a compound, the system is designed to allow scientists to pick for optimization only those compounds that interact in the desired manner with the desired target and have no effect on other cellular targets.

Cytometrix thus reveals the functional effects of drugs on intact human cells, which HBM's Wicki said is a key reason for the company's success in finding and optimizing lead compounds. "They have good screens that function in a high data-throughput mode. Many companies do isolated screens that do not include the functional biology," he said.

Execution

Sabry knows that investors are less interested in the parts of the company's

Lessons for an 'up' round,
from previous page

discovery platform than in its output. "From the beginning, we've had a clear vision as a product company," he said. Robert Blum, CFO and senior vice president of finance and corporate development, added that being a product company in 1998 was out of vogue among the genomics startups. "But we have executed in line with expectations," he said.

Thus the company expects to have three compounds in the clinic by year end. SB-715992 will enter multiple Phase II trials in several cancer indications, and the company will file INDs for another cancer compound and for a compound in cardiovascular disease. All were discovered and developed by Cytokinetics within five years.

"They were able to show they could execute in a quick timeframe," Dow said. This, coupled with the company's deep biological knowledge, "conspired to create an attractive investment opportunity," he said.

Champsy noted that there is a small group of companies with a novel compound that has potential in a broad range of cancers, translating to significant market potential. "There is value to something like that," she said.

Champsy cited Telik Inc. as an example. TELK (Palo Alto, Calif.) has built a market cap of \$453 million on the back of its TLK286, which in a Phase III trial to treat ovarian cancer and Phase II trials to treat non-small cell lung cancer and colorectal cancer. The small molecule targets glutathione-S-transferase PI-1 enzyme (GST PI-1).

According to Wicki, Cytokinetics will see more interest from mezzanine or cross-over investors if its Phase II trials prove successful. HBM, which has not invested heavily in the current round, will consider a significant investment following the release of data, he said.

Partnering

The GSK deal is the biotech company's only drug development partnership. But by Dow's reckoning, it "is in the top 10% of biotech deals done," even though the transaction was completed when the Cytokinetics technology was at the target validation stage.

The company's IP in cytoskeletal biology was an important driver for the deal, Champsy noted. At this point, Cytokinetics has 51 issued U.S. patents and 10 notices of allowance as well as exclusive licenses to four other issued U.S. patents.

Without the GSK piece, Cytokinetics' valuation "would be below \$100 million, no doubt," said Wicki. "You like to see a

'They were able to show they could execute in a quick timeframe.'

— Steve Dow of Sevin Rosen

deal-making capability at the company, and of course, you like to see the figures. Under this deal, if the compound delivers, it will be phenomenal."

GSK committed \$50 million, including upfront payments and the \$14 million in equity. For each target, Cytokinetics can receive \$30-\$50 million in milestones. While GSK has marketing rights, Cytokinetics has options to co-develop

and co-promote products in North America. Also, under certain conditions, targets and lead compounds can revert to the biotech company.

The level of resources committed by GSK as well as the deal structure have allowed Cytokinetics to develop clinical capabilities as its lead product moves downstream. The company has added an early stage clinical capability since 2001, and the current financing will help Cytokinetics round out its clinical development and pre-commercialization groups as well as put it in a favorable position to opt in on its lead cancer programs, said Blum.

Blum noted that the company is in early discussions to partner its cardiovascular program. He said that such a partnership would need to be structured so that it leverages the company's new clinical development capability and helps Cytokinetics continue to move downstream.

"We've demonstrated we can do this rapidly in more than one program area, with each having clinical validation. So, it's really a different story we're telling now. It's a clinical stage story," Blum said.

Building relationships

Blum noted that the current financing benefited from the time Cytokinetics has invested in building relationships with investors who were not prepared to come in at earlier stages of the company's development. These included mezzanine investors the company had courted. "Many companies don't nurture those relationships, so they have to introduce the company when the time comes," he said.

"Our strategy has been to make sure future investors know about us today," Sabry said. "The industry is plagued by a lack of execution. The problem is productivity, but it requires multiple visits over multiple years for an investor to see our productivity."

Wicki agreed. "They got in front of us," he said. "Seeing groups like HBM gets the stock in their universe. You can pull on these contacts later." From a VC perspective, he added, "it is much easier if you've seen a company over three or four or five years. You can see they have executed, which builds trust."

The search for intelligent life

We know you have many choices for headlines. But finding real intelligence is a lot harder. That's why top managers and investors in the life sciences community depend on *BioCentury, the Bernstein Report on BioBusiness®* for its leading perspective on the strategic issues essential to the formation, development and sustainability of life science ventures in 2004 and beyond.

'It's the BioCentury'™