Denise Myshko

Raising Capital in a *Tight* MARKET

> "Our focus on orphan dseases has helped with venture capital and philanthropic funding."
>
> **WILLIAM BAIRD III** / PTC Therapeutics

The venture capital environment is in a transition period, slowly recovering from the conditions that have plagued the entire economy.

The global financial crisis has made it challenging for the biotechnology industry to raise capital to fund innovation. Experts say venture capital money is still available, but often the VC community is looking for lower-risk, short-term projects.

As a result, biotech companies are increasingly looking to alternative sources of capital. Experts say this is a natural reaction to normal business cycles, and when venture funding dries up companies embark on other strategies to survive.

For example, in 2008 and 2009 industry leaders say alliance deal making and applications for grants increased.

At The National Cancer Institute, applications for the SBIR grant program increased by almost 70% between 2008 and 2009.

"This increase was a direct reflection of funding drying up in the venture capital market," says Michael Weingarten, director of the NCI's SBIR program. "We became the only game in town for many companies and a lifeline for biotech companies looking to fund new innovation and new technologies in the cancer field."

(Editor's Note: Please see the digital edition to read more about how some companies pursued alternative funding options.)

The funding markets continue to be very tough, which is not a big surprise given the macro environment, says Oliver Fetzer, Ph.D., president and CEO of Cerulean Pharma.

"There continues to be a fair amount of uncertainty in terms of the direction both biotech and venture capital are going to go," he says. "Society is expecting more innovative products at potentially lower prices rather than higher prices. This creates a pricing environment that makes it tougher for biotech companies to find a clear path to profitability."

At the same time, Dr. Fetzer says, the venture capital firms are finding themselves in an environment devoid of many big success stories.

"As a consequence, it is becoming harder and harder for venture capitalists to raise meaningful funds," he says. "The whole venture capital industry is in a phase of contraction right now."

Dr. Fetzer says this creates an environment in which the venture capitalists who do have money have strong pricing power.

"It's a very aggressive and highly competitive environment; they expect to get into deals at a very low price point," he says.

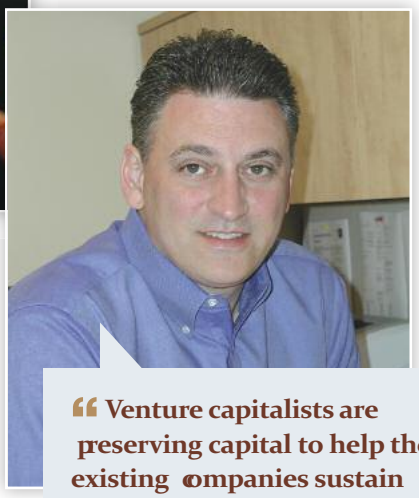
Glen Giovannetti, global biotechnology leader at Ernst & Young, says since there is less capital available, investors are raising the bar in terms of which companies they'll fund.

"This market condition is affecting the venture capital side and new listings; it's a challenging environment in which to get the deal done," he says.

Gil Bashe, executive VP at Makovsky & Company, says the amount of money pouring into innovation is the same, but the big difference is that the bar for valuation is now higher.

"There are more companies seeking fund-

> "Companies have to invest in competitive research. It's a true failure not to do so."
>
> **GIL BASHE** / Makovsky



> "Venture capitalists are preserving capital to help their existing companies sustain themselves in this period of downturn."
>
> **DAVID PERALTA** / NanoBio

ing and, therefore, funders have their pick of companies to chose from," he says. "Five years ago, the preferred exit for many of these companies was a public offer, which allowed investors to liquidate their shareholdings and pull capital out of their investments. This has changed."

David Millard, chair of the business department at Barnes & Thornburg, says the tightening of the venture capital industry is temporary.

"The venture capital industry has been shrinking and has less money available for new investments," he says. "In 2009, venture capital companies focused on their portfolio companies to make sure they had enough money to survive. This has started to ease up, and we are beginning to see some new investments."

The VC Outlook

The impact of the recession on the biotech industry has been tremendous. In a recent survey by Deloitte, 44% of those surveyed believe 20% to 40% of existing biotech companies won't exist in five years as a result of the global recession.

On the bright side, industry experts say looking forward, the life-sciences sector will continue to attract the largest share of U.S. venture capital investment given that the demand for innovative pharmaceuticals, diagnostics, and devices is expected to increase.

While the third-quarter 2010 venture capital funding for the life-sciences sector declined from a strong second quarter, the sector remained on pace to outperform 2009, according to findings from the MoneyTree Report by PricewaterhouseCoopers and the National Venture Capital Association (NVCA), based on data from Thomson Reuters.

Investment in the sector fell 25% from the second quarter in number of deals and 30% in dollars. Compared with the third quarter of 2009, the sector also showed a decline, dropping 5% in dollars and 3% in number of deals.

Despite the declines, PwC executives say funding for the life-sciences sector remains on course to pass investment levels of 2009. Compared with the first three quarters of 2009, biotechnology funding remained on track for a better 2010, already showing a 25% year-on-year rise.

During the third-quarter of 2010, biotechnology funding increased slightly to $944 million from $942 million for the same quarter in 2009. The number of deals decreased 4% from 113 during the third quarter of 2009 to 108 during the same quarter in 2010.

Forty-five U.S. venture capital funds raised almost $3 billion during the third quarter of 2010, according to Thomson Reuters and NVCA. This level marks a 40% increase by dollar, compared with the second quarter of 2010, during which 51 funds raised $2.1 billion.

Matthew Hudes, national managing principal, biotechnology, Deloitte Consulting's Life Sciences & Health Care group, also believes there is cause for optimism.

"Recent IPOs are a direct indicator of an improving market," he says. "It does appear there is an IPO window opening up in biotech and other industries as well. This is a direct correlation with venture funding."

Upcoming Conferences

- **New Paradigms to Fund, Manage & Outsource Product Development for Biotech & Small Pharma**
  January 13 - 14, 2011
  Westin Market Street Hotel, San Francisco
- **The 10th Annual Bio-IT World Conference & Expo**
  April 12, 2011
  Boston

> "Venture capitalists are shifting their focus to more mature investments."
>
> **MATTHEW HUDES**
> Deloitte Consulting

An active M&A market and a level of IPOs consistent with a slow but steady economic recovery drove the venture-backed company exit activity during the third quarter of 2010, according to Thomson Reuters and NVCA.

The acquisitions volume marked a 7% increase from the second quarter of 2010, and M&A in the first three quarters of 2010 has already almost doubled full-year 2009 transactions.

Life-sciences M&A deals had a higher disclosed value at $2.3 billion compared with $1 billion for information technology.

> “The venture capital industry is in a phase of contraction right now.”
>
> **DR. OLIVER FETZER** / Cerulean Pharma

> “There will be a bigger investment uptick in biotech when the generalist investors and mutual funds feel comfortable.”
>
> **GLEN GIOVANNETTI** / Ernst & Young

What VCs Look For

Mr. Giovannetti says investors are looking for unique and differentiated opportunities, and companies that have made progress in a very capital-efficient way are favored.

“Venture capitalists are increasingly looking at project financing opportunities for single product candidates,” he says. “They will still seek to build freestanding companies, but that funding will go to broad platform technologies that have the opportunity to produce multiple product candidates.”

Kevin Starr, managing partner at Third Rock Ventures, says his company looks to fund companies developing products that have more than a marginal impact on patients and avoid those destined for an already crowded space.

“We like areas such as rare genetic disorders, and new approaches to tackling tough disease areas like oncology and CNS,” he says.

Mr. Starr says another determining factor is the strength of the management team.

“We’ve been building companies for long enough to know that a well-varied team with complementary skills that can translate the science is going to be very important,” he says. “We try to find areas that our customers — big pharma, biotech, and device companies — are excited about. We’ve facilitated partnerships even before the companies were launched.”

Seeking Other Opportunities

Mr. Bashe says in the past investors and founders of the enterprise didn’t need to put as much of their own capital into an offering; today this has shifted.

“Once upon a time, company founders put 15% or 20% of their own capital into an offering, and the rest was funded by outside sources,” he says. “The ratio used to be based on a 20/80 rule; today it’s more like 40/60.

> “We try to find areas that our customers — big pharma, biotech, and device companies — are excited about.”
>
> **KEVIN STARR** / Third Rock Ventures

Tips for Attracting Funding

- Focus on innovation: me-too and fast followers are not going to be rewarded; companies need a differentiated product with strong data.
- Develop clarity around the vision and strategy as these relate to creating value. This should be separate from the scientific strategy.
- Study the market: what companies are the current market leaders; what are the clinical guidelines; what would it take to displace current market leaders; what would be the market reaction to a new product; how does a new product impact a market need; and what is the comparative effectiveness of the product.
- Make sure key people/management are in place; make sure a well-rounded board is in place.
- Have a good patent strategy.
- Partner with disease foundations and academic groups.
- Be relentless in the pursuit of alternative sources of funding, including foundation grants, government grants such as those at the NIH, and corporate venture capital programs.
- Study the models and portfolios of different venture capital companies.

Source: PharmaVOICE

> "The VC industry is shrinking globally, but the death of the industry is greatly exaggerated."
>
> **DAVID MILLARD** / Barnes & Thornburg

The founding partners, the innovators, friends and family, and the angel funders have to come up with a lot more of the initial cash to support a private offer."

When private funding isn't an option, companies are pursing the grant path. Like Cerulean, NanoBio and PTC Therapeutics are two companies that have been aggressive in pursuing strategic grants and partnerships, including grants through the IRS's Therapeutic Discovery Project program. Part of the healthcare reform law included a provision to provide tax credits and grants to small firms for projects that show potential to produce new therapies, reduce long-term healthcare costs, or significantly advance the goal of curing cancer within the next 30 years.

The credit or grant covers up to 50% of the cost of qualifying biomedical research, up to a maximum credit of $5 million per firm, and $1 billion overall, and is only available to firms with fewer than 250 employees for investments made in 2009 and 2010. Companies can opt to receive a grant instead of a tax credit, so start-ups that are not yet profitable can benefit as well.

NanoBio received five grants from the IRS program, each for $244,479, says David Peralta, VP, chief operating and chief financial officer at NanoBio. To date, more than $115 million has been invested in the company's NanoStat technology platform through research grants, partnerships, and equity investments, including $45 million in private equity financing from Perseus.

PTC received 12 grants for a total award of $2.5 million, says William Baird III, chief financial officer, PTC Therapeutics.

"This is just one piece of a much broader strategy that we've embarked on over the last five or six years; we are also pursuing nondilutive grant funding from both government agencies as well as philanthropy or disease advocacy groups that sponsor research," Mr. Baird says. "Through this multipronged strategy, we've raised more $100 million. On the corporate side, we've now done six major collaborations, and we've brought in about $20.5 million in cash funding from those deals."

Mr. Baird says the company remains relentless in the pursuit of grant opportunities.

"We've received $10 million in grant awards in 2010 alone, and we have about $50 million in pending grants," he says. "Our focus on orphan diseases and diseases of high medical need has helped us secure venture capital, philanthropic funding, as well as corporate collaborations." PV

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Alternative Funding Options

Despite a tough funding environment, money is available to companies that have a compelling story to tell.

Although experts characterize the funding environment as difficult, companies have been successful by aggressively pursuing — and securing — venture capital funding.

For example, in the last year and half, Cerulean has participated in two rounds of financing. In November 2010, the company closed a $24 million Series C financing led by Lilly Ventures to advance its nanopharmaceutical clinical development candidate, CRLX101, into a Phase II trial in non-small cell lung cancer. And in July 2009, Cerulean closed a $10 million Series B-1 financing to advance the clinical development of CRLX101 (formerly IT-101).

"There is no substitute for really strong data," says Oliver Fetzer, Ph.D., president and CEO of Cerulean. "In our case, the data for our CRLX101 program have been getting better and better. Without the really strong data, it's very tough to get people motivated to put their money to work."

Companies have to be able to articulate their story very well, he says.

"Executives have to have conversations that go beyond the technology itself," Dr. Fetzer says. "The more they can paint a picture beyond the exciting technology and address how it meets a market need or how it addresses a more severe payer environment, the more attractive the opportunity will be to potential investors."

Even still, Dr. Fetzer says companies should seek out collaborations with larger pharma companies and look for funding from other opportunities as a way to build value into the company before seeking venture capital funding.

One avenue is through grants from government agencies, such at the National Institutes of Health, as well as through disease foundations.

Grants a Funding Source

NanoBio is one such company pursuing this strategy. Recently, the company has received several grants: a $6 million grant from the Bill & Melinda Gates Foundation to support the development of an intranasal vaccine for respiratory syncytial virus (RSV); and a $1.5 million grant from the Department of Defense to study, with the University of Michigan Medical School and NanoBio as a subcontractor, the use of nanoemulsion-based therapies for protection against burn and wound infections.

"We have been pretty aggressive in our efforts to secure strategic grants," says David Peralta, VP, chief operating and chief financial officer at NanoBio. "We'll continue to pursue this strategy, and we have a number of opportunities that are pending; this has been a No.1 opportunity for us. A second opportunity is nondilutive funding in the form of partnerships related to a number of our applications that we know we can't take forward on our own. We have a handful of opportunities pending with these partnerships as well."

The company has a licensing agreement with GlaxoSmithKline for its lead program, the over-the-counter use of NB-001, an advance in the treatment of cold sores. Developed by NanoBio, NB-001 provides significant antimicrobial activity against the virus that causes cold sores, herpes labialis.

PTC Therapeutics is another company that is pursuing this model as well.

"A good example is our partnership with the Parent Project Muscular Dystrophy foundation and the University of Pennsylvania," says William Baird III, chief financial officer, PTC Therapeutics. "Parent Project Muscular Dystrophy is focused on Duchenne muscular dystrophy, one of the disease areas in which we're working. We have a drug, ataluren, that could help about 13% of the patients with Duchenne muscular dystrophy, patients who have a genetic mutation known as a nonsense mutation."

Through early funding from the Parent Project Muscular Dystrophy, PTC was able to identify several promising therapeutics targets that might treat Duchenne by either increasing or decreasing target proteins.

This early-stage research was compelling enough that the NIH made a five-year, $13 million grant commitment to PTC in 2007.

"This grant award would not have happened had it not been for the early-stage support from PPMD," Mr. Baird says.

PTC has pursued a tiered grant approach.

"A great example of this strategy is our collaboration with the Spinal Muscular Atrophy Foundation," he says. "In 2006, the foundation gave us a grant of $1.6 million, which covered a year's worth of research. We had very specific research goals that we established with them. Upon hitting those goals, they made another commitment of $1.6 million. At that point, we moved to the chemistry optimization stage and the SMA Foundation made a very big commitment to us with $8.6 million."

More recently, in September 2010, PTC Therapeutics was awarded a grant of about $1.6 million from the FDA's Office of Orphan Products Development to support an ongoing Phase III study of ataluren in patients with nonsense mutation cystic fibrosis (nmCF).

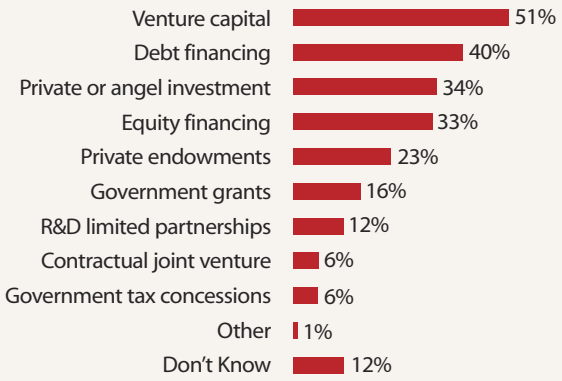
In June 2010, PTC received a $5.4 million

Seeding Drug Discovery (SDD) Award from The Wellcome Trust to support the development of drugs that target Bmi-1, a protein that has been linked to drug resistant cancers. The Wellcome Trust launched the SDD funding initiative in 2005 to facilitate early-stage small-molecule drug discovery in areas of unmet medical need.

In December 2009, PTC received a $1 million Challenge Grant award from the National Heart, Lung, and Blood Institute. The Challenge Grants, a program under the American Recovery and Reinvestment Act, that is designed to stimulate new areas of research. The two-year grant will support an ongoing Phase IIa clinical trial of ataluren in hemophilia A and B because of a nonsense mutation.

Recession's Impact on Biotech

Which areas of biotech financing do you believe have been hit hardest?
(Respondents selected up to three)



Source: Deloitte. For more information, visit deloitte.com.

New Programs at the NCI

The National Cancer Institute, the U.S. government's principal agency for cancer research and training, has also expanded its grant program. A new initiative at the NCI is the Bridge Award, which is designed to support the next stage of development for previously funded SBIR projects in the areas of cancer therapies, diagnostics, and cancer imaging technologies. SBIR companies can apply for up to $3 million in additional funds following the completion of their Phase II projects.

NCI has awarded $9.9 million in Phase II Bridge Awards to help small businesses develop and commercialize innovative cancer technologies. The four companies to receive the FY 2010 Bridge Awards are 20/20 GeneSystems, Advanced Cell Diagnostics, AmberGen, and Praevium Research.

"We're incentivizing investors — venture capitalists, big pharma, and other investors — to invest with us," says Michael Weingarten, director of The National Cancer Institute's SBIR program. "We are doing this by giving competitive preference to companies that are able to raise matching funds from third-party investors. We've funded 10 projects over the last two years using this bridge award, and we're finding that this approach is helping companies raise outside capital from the VC community. For every dollar the NCI invests, our Bridge awardees have been able to raise 2.3 dollars in third-party funds."

Mr. Weingarten says investors like the program because NCI is sharing the risk for developing these technologies into products.

"Every company we fund has to go through peer review at the NIH; review panels made up of both academic and industry leaders vet projects before we will provide any funding," he says. "By the time a company receives a Bridge Award, it has actually gone through the peer review process several times. We want to make sure we are funding strong projects that can succeed and be brought to market."

Mr. Weingarten says the NCI also has started to hold annual investor forums.

"On an ongoing basis we have about 400 active projects," he says. "We showcase our strongest companies to the investment community and to big pharmaceutical companies. The goal is to help these companies raise additional funding as their SBIRs are being completed. We want to help them make the right connections with investors who can provide the next stage of funding after us and ultimately help develop promising products and technologies to benefit cancer patients."

The SBIR is a set-aside program, meaning that 2.8% of the agency's budget is put aside to fund small businesses in a range of topic areas. For the NCI, that comes to $110 million annually; across the NIH as a whole it's a $650 million program.

Phase I SBIR grants are typically a six-to-12 month project with funding averaging about $150,000.

According to the agency, if the company is successful and can show feasibility of its technology, it can then apply for a Phase II SBIR award of about $1 million for a two-to-three year project. PV

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