bioentrepreneur
Brought to you by nature biotechnology

Finance/Funding

Published online: 22 September 2006, doi:10.1038/bioent912

Big pharma wants you

George S Mack[1]
George S Mack is a freelance writer based in Columbia, South Carolina.

There's another kind of venture capitalist lurking in the corridors of capital.

There's a growing source of money available for small startup life science companies. It may sound bizarre at first, but the investors behind this capital are not interested in turning a profit by selling your company to Wall Street or big pharma. They are strategic corporate venture capitalists (CVCs), who are actually big pharmas, biopharmas and medical device companies who sorely need your ideas, products and technology platforms.

It all makes perfect sense if you understand the large life science company's predicament. The issue and the problem for these companies is that they have become victims of their own massive size. They require unrealistically powerful internal R&D machines to keep their pipelines pumping out innovative new products to replenish expiring patents. What's more, the law of large numbers makes it much harder to create the double-digit percentage growth that Wall Street craves when revenues have already climbed into the $20–$50-billion range.

The bottom line is that the major life sciences companies must supplement their internal discovery and development programs with mergers, acquisitions and in-licensed technologies and products. To accomplish this, they are willing to invest in small startups right alongside traditional VCs to get to the head of the line for an advance preview of devices, drug targets and molecule screens.

Okay, let's play jeopardy

A forum of entrepreneurs and deep-pocket investors gathered in Monterey, California, back in May at the C21 BioVentures Annual Conference[1]. Seed-stage venture investor Paul Grayson of San Diego-based Sanderling Ventures played game show host to a panel of CVCs (see Table 1) in front of a group of private startup biotech entrepreneurs. Grayson made people chuckle with slides presenting a number of situations and dilemmas, some of which were bizarre and others very likely (see Table 2). A major topic was how to handle conflicts between big company CVCs and small potential portfolio companies that might actually be in a position to compete with their big investors.

"I wanted to flesh out some of these issues," Grayson says. "I was trying to set up as much discussion around conflicts of interest as I could and highlight to the audience that you can manage these even in the stickiest of situations. But you do have to manage it."

On the whole Grayson's panelists didn't see it as a big problem. "I think the conflicts are easily managed," says Graeme Martin, president and CEO of Palo Alto, California-based Takeda Research Investment, which is the corporate venture arm of Japan's largest drug company, Osaka-based Takeda Pharmaceutical. "But we are very careful about firewalling confidential information," he says. "We want to protect the company who's sharing that information with us, but it's just as important to protect Takada from intellectual property (IP) contamination." Martin says his firm uses outside consultants to analyze the technology and IP before he introduces the small investee company to Takeda.

It's much the same with Yoshitaka Yoneyama, president and CEO of Astellas Venture Management in Menlo Park, California, an arm of Tokyo-based Astellas Pharma. "Usually we do not look at the structure of chemical compounds [of potential investee companies]. We rely on the IP due diligence of outside advisors," he says. "We want to know that the IP position is strong, and that the company has the freedom to operate."

Jay Hagan of Amgen Ventures in San Diego doesn't need to see the molecules either. "Data is what speaks volumes," he says. "But more importantly, one can kind of smell when there's something good going on." CVCs will normally be asked to sign a confidential disclosure agreement (CDA) with companies they are looking to invest in. Hagan says, "If I have a CDA with a company or if I'm on the board, even as a board observer, I have a fiduciary responsibility to the company not to disclose [to Amgen]."

Hagen is in fact normally an observer and not a board member (see Table 1). Likewise, Takeda's Martin and Astellas' Yoneyama choose not to be board members. There's a general awareness that potential competitors may not be effective fiduciaries on a board because they may have to excuse themselves from certain conversations and activities surrounding proprietary information, including strategy. But in Hagen's case it has more to do with accounting treatment. He says, "We want to cost account [versus equity account] for these investments, and that requires us to stay below 20% ownership and not have a voting board seat or any significant access to their key products."

But Lilly Ventures typically does take a board position. Ed Torres of Lily Venture explains, "We take our responsibilities as a director very seriously and understand that at all times we must act in the best interest of the portfolio company. If a potential conflict presents itself, we disclose it to the board and to senior management and then determine the most appropriate course of action."

Pay to play, or else

One sore point with CVCs is the increasingly common 'pay to play' provisions that many lead VCs put into their syndicate deals. It amounts to assembling a group of investors and assuming that in future fund-raising rounds everyone will participate at their original prorated share. This makes a lot of sense for VCs who anticipate that it could take a decade-long commitment and many rounds of financing to bring a company to a profitable liquidation. If an investor doesn't want to continue that commitment, pay-to-play terms could cause him to be stripped of certain rights and liquidation preferences.

"We don't like it, and where we have a choice we try to avoid it," says Martin. He empathizes and understands the importance of those types of agreements. "But the reality is that the strategic focus of our company could change at right angles to our original investment thesis." And if that happens, he says, "It quite honestly becomes extremely difficult for Takeda to consider further investment into that entity. Our interest is the strategic focus of our [parent pharma] company, and therefore it's difficult for us to invest once that strategic focus is lost."

Amgen's Hagan is not crazy about pay to play, but he understands that it is a reality in today's VC deals. However, he poses a hypothetical but highly realistic scenario: what if his parent firm Amgen licenses technology from a portfolio company and begins providing $10 or $15 million per year in revenue to it? "If we were successful in helping to facilitate a large partnership like that between a portfolio investment and Amgen, I think we'd probably look for a little relief [from pay-to-play penalties]. At that point our strategic mission is done," he says, "and the company arguably is much better off with the partnership."

Strategic success comes in different forms

The process of strategic investing can be successful without even making

an investment. Astellas Pharma (API) has not yet established any solid alliance relationships with any of its venture group's portfolio companies. However, "during the screening process," says Yoshi Yoneyama, "we often see potential immediate in-licensing opportunities for API when products are already in late preclinical or early clinical stages." Yoneyama has recently introduced such a prospect to his company's business development group, and in April of this year API licensed ILY101 from Santa Clara, California-based Ilypsa. The drug is now in phase 2 clinical trials for hyperphosphatemia in chronic kidney disease patients on dialysis. Interestingly, CVC firm Johnson & Johnson Development Corporation is one of Ilypsa's investors.

Like his peers, Takeda's Martin starts every deal negotiation focused only on the strategic goals of his company's agenda. "The intention is either to license some of the key assets out of those companies, or if the fit is good enough, acquisition," Martin says. Indeed last year after its due diligence examination, Takeda Pharmaceutical and San Diego-based biotech firm Syrrx agreed on a merger. Martin says his venture arm was considering Syrrx initially as an investment opportunity and later as a collaboration partner. But, "In the course of these discussions, it morphed into an acquisition," he says. In January Takeda announced that its SYR-322 drug, a product developed by Syrrx, had entered into global phase 3 clinical trials for type II diabetes. "For us, it was a superb acquisition," says Martin. "And a great exit for the investors."

Lilly's Torres finds that being exposed to companies in their early stages allows Lilly personnel to engage in networks with companies as they explore new scientific horizons or new business models earlier then they might do so on their own. "Also, by being an active investor and helping the portfolio company be successful, more novel molecules or technologies will be available downstream for the pharmaceutical industry to partner with," he says.

Growing, but not on a logarithmic scale, yet

CVC investment in life sciences companies has grown but not much over the last few years (see Figure 1). Yet, with far fewer initial public offerings (IPOs) than in previous years, signs point to an upturn in mergers and acquisitions (M&A) as exit strategies for small companies. Indeed, the month of July saw not a single biotech, pharma or medical device company come to the public markets in an IPO. M&As can still be very profitable liquidity events for venture capital investors. "The complexities of a public market today and the lack of a reliable public exit probably mean you're going to see an increase in M&A activity," according to Sanderling's Grayson. Amgen's Hagan says, "We're seeing a lot more activity and new firms [CVCs] coming in, and I think you'll see more and more acquisitions of early stage companies.

Takeda's Martin agrees. "It's almost to the point where I think there are certain segments of the startup industry that really construct their business plan around acquisition as an exit," he says. However, once a trend like this develops, valuations of portfolio companies tend to increase based on precedents that have been set. "Then the whole thing starts to get a little bit too expensive for pharma to want to entertain," he says. "I think you'll see these cycles occur."

There are also startups that might be referred to as 'virtual companies' with perhaps two scientific founders, few if any other employees, but with a very important molecule. Martin says there are some VC and CVC firms that are attempting to specialize in identifying assets of this kind of company and getting the IP licensed by big pharma. "We're seeing that more and more," he says.

Understanding the differences

Before engaging with investors, entrepreneurs need to understand the distinction between the traditional VC whose main interest is return on investment and CVCs whose interests are strategic (see Table 3). "For us, the financial return is not so important," says Yoshi Yoneyama of Astellas. "If it comes it's fine, and we can use that new money for a new investment. But our primary objective is to promote potential alliances between companies and our headquarters who wants to see our activities support the R&D pipeline." Another difference is that CVCs normally don't take the lead in venture syndicates (see Table 1). There's an apparent reliance on the lead VC's due diligence and setting of the terms. Pharmas just don't want to get themselves embroiled in any extra liability issues.

In the traditional venture capital model, a small company might well get the interest of a decision maker in a VC firm who wants to invest in the startup's technology. After he makes that decision, he must find other investors who want to come in on the deal and be part of the syndicate. Sometimes it doesn't happen, and the startup founders have their hopes dashed. But raising money is something CVCs don't have to do. Nevertheless, the parent company could find itself in a cash crunch, which could limit the amount of investment capital available. Moreover, the individuals in the CVC firm could change, and the new people could bring in a different investment philosophy, even though the parent company's strategy is the same. "That is probably the biggest challenge," says Paul Grayson. "Someone new may have no interest in working with the current portfolio investments."

Venture or vulture

Some entrepreneurs have used terms like 'vulture capital' to portray what they believe to be inequitable terms and conditions arising from investment by venture firms. But in the case of the CVC there's the slightly different sentiment that the strategic investor is in the deal to plunder, seize and lock up all of the small company's valuable assets. "That's a misconception," says Graeme Martin. Although his firm has successfully negotiated for rights of first negotiation to parts of a pipeline in companies, he says they understand very well that it would not bode well if the name of Takeda became all dominating to the extent that other potential pharma businesses may be put off from working with that company.

"These days I think we are much more savvy than we have been in the past. We are looking for complementarity and synergy," he says. "But of course we are also looking for strategic returns from that interaction."

Figure 1: CVC investment in life sciences

Source: PricewaterhouseCoopers/National Venture Capital Association MoneyTree Report based on data from Thomson Financial

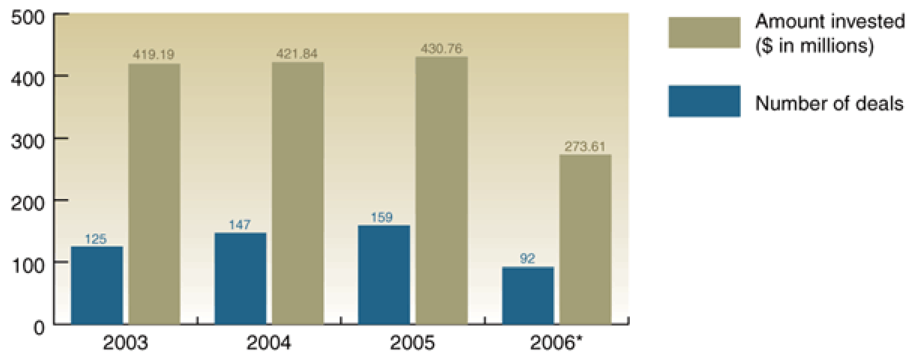

Table 1: Corporate VC firms and strategies

Company	Size of fund	Strategic focus of fund	Stage focus of fund	Syndication rules	Board
Amgen Ventures (San Diego)	$100 M/four years	Human therapeutics	Seed, Series A, Series B	Coinvest with other VCs	Observer
Astellas Venture Management (Menlo Park, California)	$60 M/evergreen[a]	Therapeutics and technology platform for drug discovery	Seed to mezzanine	Coinvest with other VCs	Observer
Eli Lilly (Indianapolis, Indiana)	$175/evergreen	80% biotech, remainder healthcare IT, medtech	Series A to mezzanine	Invest only in syndicates, will lead, co-lead and follow	Board
Johnson and Johnson (Mountain View, California)	~$100 M/year funded off balance sheet investments	Medical devices to biologics, regenerative medicine to small molecules	Seed to mezzanine, clinical stage priority	Lead, co-lead, follow	Board
Pfizer Strategic Investment Group (New York)	Balance sheet investments	'Commercial enablers' diagnostics, systems biology, modeling, healthcare IT and services	Any	None	Observer
Takeda Research (Palo Alto, California)	$10–20 M/year off balance sheet investments	Target, product, enabling technology	Concept, seed through mid-stage	Mostly coinvest, will seed with convertible loan	Observer

[a]Evergreen: gradual injection of capital into a new or existing enterprise.

Source: Paul Grayson, Sanderling Ventures, San Diego

Table 2: Dos and don'ts of venture investing

Situation	Do	Don't
When it's time for due diligence	Visit the company or set up a teleconference	Invite the company to your headquarters to display your dominance
When conducting your IP review	Evaluate the company's freedom to operate. Identify the company's long-term strategic advantage	Develop your strategy to engineer around the company's patents and trade secrets
When setting the terms of the investment	Use financial analysis, including competition, risk adjusted net present value modeling	Let the other VC's do it. Let your legal department do that “language stuff”
When sitting in on board meetings and you hear of possible competition from a big pharma	Discuss it with the board to see if there's an opportunity for your company to engage	Go call your buddies to get them on the case

Adapted from Grayson, P., “Pharma's Perspective on Venture Investing”

Table 3: Corporate venture capital (CVC) versus traditional venture capital (VC)

	CVC	VC
Structure	An arm of big pharma, big biopharma or big medtech	Institutional investor (fund)
Goals	To find new technology, platforms and products, but goals can change	To liquidate investment for profit; generally committed to investment
Access to capital	Big pharma has deep pockets and therefore CVC does not have to find investors and raise money	Must reach out and find investors. May not be successful in some instances
Position in syndicate	Does not lead in syndicates and relies on VC for terms and real management of funds	Will lead syndicate, structure deals and will lend hands-on support and infrastructure facilities to portfolio companies
Board of director status	Observer (generally)	Director
Pay to play	Hates it	Likes it
Due diligence	Hires outside consultants, but will include scientists from parent pharma firm after CDA is signed	Assumes own responsibility for understanding a potential portfolio company's technology

References

- Pharma's perspective on venture investing. 8th Annual C21 BioVentures, Monterey, California, May 23–25, 2006. Chair: Paul Grayson, Sanderling Ventures. Panelists: Roy Cosan, Johnson & Johnson Development Corporation; Jay Hagan, Amgen Ventures; Graeme Martin, Takeda Research Investment; Ilya Oshman, Pfizer Strategic Investments Group; Ed Torres, Lilly Ventures; Yoshitaka Yoneyama, Astellas Venture Management.

SPRINGER NATURE

© 2019 Nature is part of Springer Nature. All Rights Reserved.

partner of AGORA, HINARI, OARE, INASP, ORCID, CrossRef, COUNTER and COPE