In the Midst Of A Shakeout, Biotech VCs Must Embrace New Partners, New Math

(A#2010900180)

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Issue:	*Start-Up* Sep. 2010
Section:	Feature Articles (Long Article)
Article Type:	Corporate Strategy/Dealmaking Trends; Corporate Strategy/Finance
Industry Segment:	Biotechnology; Pharmaceuticals; Supplies, Equipment and Devices
Subject/Market Dynamic:	Business Models; Corporate Venture Investing; Early Stage Dealmaking; Entrepreneurs; Incubators (venture); Near-Term Biotech Strategies; R&D Strategies; Start-Up Strategies; Venture Capital Deal Structures; Venture Capital Firms; Venture Capital Investment Areas
Companies:	Abbott Laboratories Inc.; Ablexis LLC; Adimab Inc.; Agios Pharmaceuticals Inc.; Alnara Pharmaceuticals Inc.; Amgen Inc.; Amgen Inc./Avidia Inc.; Avila Therapeutics Inc.; Babraham Institute; Bayer AG; Bicycle Therapeutics Ltd.; Biogen Idec Inc.; Boehringer Ingelheim GMBH; Cadence Pharmaceuticals Inc.; Calithera Biosciences Inc.; Celgene Corp.; Crescendo Biologics Ltd.; Cubist Pharmaceuticals Inc.; Cubist Pharmaceuticals Inc./Calixa Therapeutics Inc.; Eli Lilly & Co.; Envoy Corp.; Envoy Therapeutics Inc.; Grifols SA; Human Genome Sciences Inc.; Incline Therapeutics Inc.; Johnson & Johnson; Johnson & Johnson/Alza Corp.; Kymab Ltd.; Maxygen Inc.; Merck & Co. Inc.; Merck & Co. Inc./GlycoFi Inc.; Movetis NV; National Institutes of Health; National Institutes of Health/National Cancer Institute; Novartis AG; PanGenetics BV; Regeneron Pharmaceuticals Inc.; Roche/Genentech Inc.; Sanofi-Aventis; Shire PLC; Stromedix Inc.; Talecris Biotherapeutics Inc.; University of California/University of California, San Francisco; US Department of Health and Human Services; Versartis Inc.
Summary:	With funds and firms closing, a new reality awaits those who survive until the next economic upswing. Some of the elements are already in place, such as VCs' willingness to take capped returns and exits via risk-sharing contingency-based acquisitions. The emphasis on capital efficiency may change the types of companies VCs can afford to back, and corporate funds are now a vital part of biotech venture, especially in the early stages.

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Biotech Backers Are Learning to Live with Exit-by-Earn-out	*Start-Up*	Mar. 2010	2010900061
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In the Midst Of A Shakeout, Biotech VCs Must Embrace New Partners, New Math

With funds and firms closing, a new reality awaits those who survive until the next economic upswing.

by Alex Lash

Some elements of the new reality are already in place, such as a willingness to take capped returns and exits via risk-sharing, contingency-based acquisitions.

A "pay as you go" mentality that requires tranched financings means VCs are sharing the financial risk with their portfolio companies.

The emphasis on capital efficiency may change the types of companies VCs can afford to back, with a preference for late-stage single-product plays, diagnostics and health care services outfits.

Corporate funds are now a vital part of biotech venture, especially in the early stages, as Big Pharma can't afford to let innovation lag.

Whether the economy recovers or derails into recession again, it's becoming clear that the drug world, and especially the financing of crucial early-stage innovation – the industry's fuel for decades – will not emerge from the crisis in the same form. The pressures are already forging new models and altered expectations among biotech's venture investors – those that survive. The allure of venture as an alternate asset class has dimmed, and venture investors are increasingly hard pressed to find backers. This financial dearth has kick-started a shakeout with predictions that anywhere from a quarter to 40% of venture firms will not be able to raise new funds. (*See "Biotech Backers Are Learning To Live With Exit-by-Earn-Out,"* START-UP , *March 2010 [A#2010900061]*.) Those that can will need exemplary track records or convincing new models to satisfy their limited partners.

The new reality has even experienced VCs scratching their heads. "We're increasingly skeptical of the traditional biopharma investment model," says Quaker BioVentures founding partner Brenda Gavin. "If the definition of insanity is doing the same thing over and over again and expecting different results, then we are all insane. Hope is *not* a strategy."

By "hope" Gavin means the possibility of a "white-knight" pharma company providing an exit through acquisition, practically the only exit available these days with IPOs both rare and illiquid. But even though these white knights are hungry for pipeline-filling drugs, they are loathe to take on early-stage risk for costly up-front sums as they try and assuage the demands of Wall Street and investors for regular earnings growth. (*See "Reacting to the Crisis: Biotech Venture Capital's Plan B,"* START-UP , *December 2008 [A#2008900248]*.)

VCs who survive must therefore do so by adaptation. "People might say, 'There's always ebb and flow,' but we need new models and ways of doing things," says Corey Goodman, PhD, a veteran of academia, biotech and briefly Big Pharma, who is now helping to start an investment fund in San Francisco. "It's not as if we'll wait for another 12 months and life will be as nice as it was before."

Unlike high-tech, where disruptive technologies like the Web or applications like Twitter can turn societal practices and business models on their heads, the drug business can only make iterative changes. The core of the business – bringing safe, effective drugs to market – requires many years, many dollars, and many smart, well-compensated people. Anecdotally, VCs talk of a shift to health care sectors with shorter development timelines than biopharma: diagnostics, devices, software and services.

It might not just be anecdote. Investment in the first-half of 2010 in the three non-biopharma health care sectors was $1.8 billion, the same amount invested in traditional biotech medicines. If the trend continues, it would be the first full year since 2000 that VCs put at least one dollar into non-biopharma investment for every dollar they put into biopharma. In the 1990s, biopharma investments actually lagged the other three health-care sectors combined. It's too early to say we're returning to that era, but with all the talk of VCs looking for shorter investment cycles, it's a trend worth watching.

Another sign of the search for faster returns is the shift away from financing early-stage preclinical programs to later-stage clinical assets, as VCs look for companies with products already in development that need $20 or $30 million – not $100 to $150 million – to reach a milestone that attracts a Big Pharma buyer. It's a strategy that requires a keen eye and good contacts, and it's no panacea: it can simply mean trading earlier technical risk for later regulatory risk. But there are success stories. For all the handwringing over the current IPO market, one of the few firms not only to go public with a robust valuation but also to attract a buyer was Belgian firm **Movetis NV**. Its backers took a basket of gastrointestinal compounds from **Johnson & Johnson** in late 2006 and brought the lead constipation drug to market in Europe in three years, with a $147 million IPO along the way. [W#200720090] [W#200930657] Nine months after approval, Movetis sold to **Shire PLC** for $566 million. [W#201010095] (*See "Shire Emphasizes The GI Space In Its Bid For Movetis ,"* "The Pink Sheet", *August 9, 2010 [A#00720320012].*)

Other creative examples to overhaul the standard venture model are coming to the fore. Some are becoming industry standard practice, such as "pay as you go" risk-sharing in venture rounds and acquisitions. Others are still experiments, such as the separation of platform firms from the products they spin out.

One model that's been popular for a decade – funding a biotech with a lead compound to late-stage proof-of-concept before a bigger development partner takes over – is in trouble, no matter how lean (or "virtual") the biotech's overhead, according to some observers. "I worry the most for single-compound companies," says John Hession, an attorney at Cooley Godward Kronish LLP in Boston who advises start-ups and investors on venture rounds. "The old binary solution of taking a compound through Phase II is much harder to finance."

Putting it another way, Quaker's Gavin rhetorically asks, "How do VCs fund all of these companies to Phase III, which seems to be the stage that Big Pharma is comfortable with?"

The New Math Of The Venture World: Pay As You Go

The recent complicated financing of start-up **Incline Therapeutics Inc.** is a great example of the new realities VCs face. The firm is built around an iontophoretic pain patch that J&J unit Alza Corp. briefly had on the market until a malfunction forced its withdrawal. [W#201020297] It's a late-stage asset that probably needs fine-tuning, not a long arduous clinical roadmap. With Alza being wound down, the folks at pain specialist **Cadence Pharmaceuticals Inc.** saw a chance to revive the patch, but Cadence didn't have the wherewithal to buy it. Instead, its shareholders, led by Frazier Healthcare Ventures, formed Incline in a deal that demonstrates both ends of "pay as you go." First, Incline receives a tranche of $22 million, and a second tranche could bring $21 million more. [W#201030292] On the acquisition end, Cadence is the only buyer, with a two-step option process with fees that not only provide Incline with working capital but ratchet up Incline's price tag the longer Cadence waits. Once Cadence pulls the trigger – the price could reach as high as $228 million – Incline is still eligible for a $57 million milestone at the time of the pain patch's FDA approval. [W#201020298] (*See "Cadence, VCs Relieve J&J's Pain, Map Out A Clever Exit In The Process,"* START-UP *, July 2010 [A#2010900175].*)

It's not just Incline. "Pay as you go" is becoming de rigueur up and down the pipeline, as the monumental risk of drug R&D is being shared more aggressively. At one end, venture rounds are almost always tranched, with the recipient forced to prove its merits to get the next slice. At the other end, most acquisitions of private

biotechs now feature a structured or earn-out component. "The tranching of deals and the structured exit are a sea change over the past five years," James Garvey of SV Life Sciences told *"The Pink Sheet"* in June when SV announced its new $523 million fund. (*See "Sidestepping the 'Washout,' SV Life Sciences Closes $523 Million Fund,"* "The Pink Sheet" DAILY *, June 29, 2010 [A#14100629057].*)

No one interviewed for this story sees venture-round tranching going away. In fact, some recipients of venture capital see the development in a positive light. "Everyone's getting tranched, as far as I know," says **Stromedix Inc.** CEO Michael Gilman, PhD, whose Cambridge, MA company has raised $30 million in venture cash over two rounds as it develops drugs against fibrotic organ failure. [W#200730910] [W#200830205] "Once people get used to it they accept it. Sometimes giving someone a pile of money can make them a little sloppy."

But with every round of funding now tied to milestones, the parties must get used to longer negotiations. "It really adds complexity," says Dan Janney of Alta Partners in San Francisco, whose firm has been regularly tranching its investments since 2000. He notes that some projects are more amenable to tranching than others. It's relatively straightforward, for instance, to put together a milestone-driven deal with a biopharma company that has a single product already in development, where progress is measured by success in clinical trials. But for earlier-stage, "greenfield" work, as Janney puts it, or companies that aren't compound-centric, tranches based on strict milestones can be tricky business. "The game can change rapidly, and you don't want to constrain an entrepreneurial team," he says.

Living With Earn-Outs

After forcing risk-sharing upon their portfolio companies, venture capitalists face the same music when it comes time to exit. In 2009, nine of the 11 acquisitions of private biopharmaceutical companies with publicly available data included earn-outs. The average up-front tripled the investors' total cash in; the average total earn-out doubled the up-front. In other words, if the investors wanted anything close to a 5x return or more, they'd have to wait for a lot, if not all, of the contingent events to happen. The biggest gap between up-front and milestones came in antibiotic developer **Cubist Pharmaceuticals Inc.**'s takeout of **Calixa Therapeutics Inc.**, in a deal that gave Calixa just $92 million up front and more than $300 million in milestones. [W#200910151] (*See "Cubist Hopes for A Blockbuster Antibiotic With In Acquisition of Calixa,"* "The Pink Sheet" DAILY *, December 14, 2009 [A#14091214001].*)

What are the odds of the earn-outs actually coming to fruition? Are they just another form of pie-in-the-sky bio-bucks? There are little data and no consensus, but the trend continues. As of mid-August there were 13 acquisitions of privately held biotechs this year (not including the $3.4 billion sale to **Grifols SA** of private-equity-backed **Talecris Biotherapeutics Inc.**, once the plasma unit of **Bayer AG** that spun out with backing from two private-equity firms.) [W#200410272] [W#201010068] Of the 13, at least seven were structured with earn-outs. (*See Exhibit 1.*)

Exhibit 1

Two Years Running, Biotech VCs Have To Earn Their Return

There have been 13 acquisitions of privately held biopharma firms in 2010 as of August 23. (We are not including the nearly $4 billion takeout of private-equity-backed Talecris, the former plasma unit of Bayer AG.) At least seven have included post-acquisition earn-outs, and in five of the seven the total earn-outs were larger than the up-front payment. In two more – J&J/Respivert and Sandoz/Oriel – no details were available but might have included earn-outs.

The preponderance of risk-sharing continues last year's trend, in which nine of 11 purchases of venture-backed biotechs forced risk upon the investors. Contingent payouts in M&A aren't a new concept, but until 2009 they added very little to the upside of an acquisition. Last year, however, average total deal value of the 11 deals was more than twice the average up front.

UP-FRONT TOTAL ($ MILLIONS)	TOTAL MILESTONES ($ MILLIONS)	DEAL DATE	DEAL HEADLINE	POTENTIAL DEAL VALUE ($ MILLIONS)
22	93	Aug. 2010	BioMarin buys ZyStor	115.00
10 (stock)	at least 7.6 (stock)	July 2010	Evotec acquires DeveloGen	17.60
180	200	July 2010	Lilly buys Alnara	380.00
"majority" of 120	n/a	June 2010	Gilead Sciences acquires CGI Pharmaceuticals	120.00
75	485	June 2010	Sanofi buys TargeGen	560.00
n/a	n/a	June 2010	J&J buys RespiVert	100.00 (est)
10.31 (stock)	0.00	May 2010	BioTime acquires ES Cell	10.31
14.33	0.00	Apr. 2010	VaxGen buys diaDexus in reverse merger	14.33
46 (stock)	0.00	Apr. 2010	MDRNA acquires Cequent	46.00
n/a	n/a	Apr. 2010	Sandoz acquires Oriel Therapeutics	n/a
18	79	Feb. 2010	BioMarin shops for LEAD Therapeutics	97.00
7.56	0.00	Feb. 2010	DiaMedica finalizes deal for Sanomune	7.56
18	19	Jan. 2010	Vivalis acquires Humalys SAS	37.00

SOURCE: Elsevier's *Strategic Transactions*; Company reports

The Few, The Proud, The Early-Stage

Even more dire is the state of promising research, with products years, even decades away. Who will fund RNAi drugs, stem-cell therapies, and synthetic biology – the endless amount of new biomedical ideas that come from labs around the world? Fewer and fewer venture capitalists are willing to do so, though some still say they can make early-stage investing work well.

Perhaps the most discussed biotech venture effort in 2010 is Third Rock Ventures' second fund, which the Boston firm is currently raising on the back of its 2007 first fund of $378 million. According to SEC filings from early April, the goal for Third Rock II is $400 million. There have been no progress reports since, and the firm's partners and representatives refused to talk about fundraising, citing "quiet period" rules. Plenty of others are talking about Third Rock's early-stage strategy, however. The firm, which was founded by former Millennium Pharmaceuticals Inc. executives, including CEO Mark Levin and Chief Operating Officer Kevin Starr, is as likely to dream up its own companies and put its partners in key operating roles, as it is to jump into deals brought in from the outside. That's not unique, but Third Rock is notable for its leaps into "big science," as it looks for its portfolio companies to be the flagships in their respective areas.

"It's a very different kind of partner you're seeing: experienced executives in biotech, now making decisions and building companies from scratch," says Pearl Freier, a Boston recruiter who often works with VCs to find executives for their portfolio companies. "That's the model for the future, with people who can take the company and figure out an exit in a much shorter timeframe."

The jury has yet to weigh in on Third Rock's model. The firm has just one exit, the recent sale of **Alnara Pharmaceuticals Inc.** to **Eli Lilly & Co.** for $180 million up front and $200 million more in potential earn-outs. [W#201010082] It also helped steer **Agios Pharmaceuticals Inc.** into a long-term R&D relationship with **Celgene Corp.**, a move that echoes the multi-year partnership deal between monoclonal antibody developer **Regeneron Pharmaceuticals Inc.** and **Sanofi-Aventis**. [W#201020172] [W#200720829] The arrangement provides security for the biotech but arguably limits its potential acquirers to a pool of one, if and when that time comes – a notion that Third Rock's investors dispute. (*See "Celgene Teams Up With Agios In Long-Term Cancer Metabolism Pact,"* START-UP , *May 2010 [A#2010900124].*)

When asked about Third Rock's overall strategy, Starr declined to say much except that "We have found it particularly helpful to initially fill key leadership roles to provide hands-on strategy and experience to successfully launch companies with the best vision, science, operations, people and culture."

Another early-stage newbie with buzz is the Column Group of San Francisco. Its first fund was $259 million, and it has invested in seven biotechs. It's currently trying to raise a second fund of $350 million. A more veteran early-stage firm with recent success is 5AM Ventures, which closed its third fund in December. The fund's $200 million mark is 33% higher than 5AM's second fund, but even with the extra cash the firm will be "less aggressive" in taking deals forward by itself, founder Andrew Schwab said in December. At that time the new fund had one investment, protein-discovery firm **Envoy Therapeutics Inc.** [W#200930541] It has since added a second, helping with the Incline spin-out described earlier.

Even with a few dedicated early-stage stalwarts, platform companies might find it harder to attract investors who need to see tangible, attainable milestones mapped out. "The bar goes up in terms of the impact and value of your platform," says Katrine Bosley, CEO of **Avila Therapeutics Inc.**, a Waltham, MA covalent-bond platform firm that started before the downturn in 2007 and has attracted more than $50 million in venture cash and debt. "We think our opportunity is huge, but could we start it today? I don't know."

Some Say The Party Is The Platform

That's led a number of firms, including antibody manufacturing players **Adimab Inc.** and **Ablexis LLC**, to make what a few years ago would have been a heretical decision: stick to the platform and forgo dreams of graduation into drug development. The platform-only approach has its skeptics. At Elsevier Business Intelligence's annual *BIO-Windhover Pharmaceutical Strategic Outlook* earlier this year, Versant Ventures managing director Brian Atwood said, "It doesn't matter if you go back to Genentech or up to Human Genome Sciences today, the event that creates huge value is a really interesting therapeutic compound that you own and that you develop on your own account."

Adimab CEO Tillman Gerngross, PhD, on the same panel with Atwood, said his investors were willing to bet the start-up would find a way to return their money while sticking to a more capitally efficient discovery-only model. Part of his confidence is based on his previous success: his sale of yeast-based antibody platform **GlycoFi Inc.** to **Merck & Co. Inc.** for $400 million in 2006. [W#200610072] (*See "Adimab Inks Merck, Roche Deals and Banks on the Value of Discovery,"* START-UP , *June 2009 [A#2009900142].*)

Gerngross has mused about creating spin-offs that turn Adimab technology into products. But one entrepreneur is actually testing the model. Willem "Pim" Stemmer, PhD, the inventor of DNA shuffling and a veteran in protein engineering, had cash from his $290 million sale of **Avidia Inc.** to **Amgen Inc.**, plus money from the less-successful sale of assets from Avidia's parent company **Maxygen Inc.** [W#200610161] Stemmer rolled the proceeds tax-free into a new, self-funded start-up **Amunix Inc.** It's a platform company with a half-life extension technology called XTEN that Stemmer says improves upon traditional pegylation. Stemmer's model is to spin out compounds into new companies that attract venture backers. VC-backed firms often waste money in the transition from one to the other, Stemmer says, and he's "disappointed" that more VCs don't recognize the benefits of a structure that cleanly separates research from development.

Stemmer's first attempt is **Versartis Inc.**, which licensed three XTEN compounds from Amunix, including a me-better version of the type 2 diabetes drug *Byetta* (exanetide). Versartis started Phase I trials this summer. For $11 million, Index Ventures received 50% ownership and board control. [W#200930241] "VCs usually hold all the power," says Stemmer. "In this case, because Versartis needs [Amunix] to do work on the molecules, there's a more balanced arrangement of power." In part that's because Amunix also holds the IP. Without a claim to the technology, Index asked for options on three more compounds at $5 million each to bulk up Versartis for an eventual acquisition. Stemmer thinks a buyout can happen by the end of 2011, with at least one more round of funding between now and then.

Index Ventures has also backed another version of the model. It funded **PanGenetics BV** in 2005 and structured the firm as two separate companies so the assets could be sold on their own merits. [W#200830103] It looks like PanGenetics will end up with a 50% success rate. It sold PG110, an anti-nerve growth factor painkiller in Phase I, to **Abbott Laboratories Inc.** last year for $170 million upfront, giving investors an exit. [W#200920489] None of the cash went toward PanGenetics' second main asset PG102, a Phase I anti-CD40 antibody for psoriatic arthritis. (*See "PanGenetics' NGF Antibody Sale Illustrates Index's Asset-Focused Strategy,"* START-UP , *December 2009 [A#2009900281].*) The firm announced September 2 it would no longer fund PG102 or other assets. With operations winding down, CEO Kevin Johnson is returning to Index to try his hand at more asset-focused investments that draw upon his PanGenetics experience. "We didn't get everything right on the first run," Johnson says.

The Rise Of The Corporates

It's not quite cats and mice playing in peace, but the preponderance of corporate venture groups investing side-by-side with traditional VCs is something few would have predicted 10, even five years ago. Everyone should get used to it. Pharma needs products, so if VCs won't – or can't – fund the early-stage substrate, Big Pharma had better do it, lest their thin pipelines grow even thinner. Right now, with plenty of cash in their coffers and Wall Street hounding CFOs to keep their balance sheets clean, venture deals make more financial sense to the big firms than a bunch of small acquisitions or power-shifting licensing deals. Venture also gives pharma a window into new technologies, products, and management teams much earlier and for less money than a typical business development deal.

Many firms have had internal investment groups for years, even decades. But the frequency with which they're getting involved, especially in early rounds, is a profound shift. Last year, 22% of all biopharma venture rounds had at least one corporate participant. In 2010 so far, four of 20 (20%) of Series A biopharma rounds and 12 of 32 (38%) of Series B rounds have had at least one corporate investor. Corporate presence also correlates to larger deal averages – about $2 million, or 14% more, for Series A and $8 million, nearly 50% more, for Series B. (*See Exhibit 2.*)

Exhibit 2

When Corporate VCs Join Early Rounds, Biotechs Get More Money

As of late August 2010, there have been 52 early-stage venture fundings of biopharmaceutical companies this year. More than 30% have included a corporate venture fund, with participation particularly high in Series B rounds. Rounds including CVC are bigger (and in case of B raises, significantly so).

January Through August 25, 2010	Number Of Financings	Total Dollars Raised ($ millions)	Percentage Of Financings With Disclosed CVC Participation (number of financings)	Avgerage Amount Raised In Non-CVC Financings ($ millions)	Average Amount Raised In Rounds With CVC Participation ($ millions)
Series A	20	288	20% (4)	14	16
Series B	32	650	38% (12)	17	25

SOURCE: Elsevier's *Strategic Transactions* , Company reports

"I think the strategics have to fill the gap," says Cooley's Hession. "They need new interesting things for their portfolio." In the last year a number of new corporate venture groups have cropped up, including **Boehringer Ingelheim GMBH**'s $134 million fund, J&J's Red Script Ventures, Merck Serono Ventures, and Abbott Labs' device-focused fund. Sanofi-Aventis CEO Chris Viehbacher talked late last year about forming a VC fund, too, but nothing concrete has yet emerged.

Shire, which has grown on a no-R, just-D business model aligned around a few specialty markets, is the latest to come to the corporate venture party. Its board has handed $50 million to its business development team to invest in 10 to 15 companies. Executives say they're looking ahead 10 years, and the new fund will give them not only a sneak peak at nascent work but allow them to nurture programs and technology that might otherwise go underfunded (or get funded by rivals). "We don't want to lose every penny we put in, but it's more about access to technology and knowledge," says Shire Senior Vice President of Business Development Gwen Melincoff, who is running the fund. "If we end up acquiring or licensing a few products from a couple of companies we invest in, that's success."

Shire won't lead an investment, and for deal flow it will rely on the business-development team to bring in ideas, not a venture capital partner. "A venture fund can do due diligence, get more deal flow, but on the downside, having the general partner aligned with your particular business might not always happen, and you always have to ask whether the management fees are a good use of your money," says Melincoff.

Despite those misgivings, corporate-VC alliances are evident in several flavors. Drug companies are giving cash to independent VCs to do their investing through dedicated funds. MPM Capital has arranged side-by-side funds with **Novartis AG** and **Biogen Idec Inc.** Former MPM managing director Kurt von Emster and Corey Goodman's new firm VenBio will soon announce a Big Pharma as its lead investor. Pharmas are the customers – the ultimate buyers of biotechs and their assets – so why not work closely with them to know what they want, says Goodman. "There won't be a lot of companies going public. The best way to set up a fund is to be completely independent but work with potential buyers." According to Goodman, VenBio will be a "strategic fund" but won't insist that its portfolio companies grant obligatory options to sell assets, or the entire company, as some pharma-affiliated funds require.

Other Sources Can Help...Around The Edges

As we've seen with corporate venture, other sources of new funding help fill the gap left behind by a shrinking pool of traditional VCs. At best, each will represent a sliver of cash compared with traditional venture, but they could provide VCs, left with smaller funds and fewer staff to source and manage deals, an extra pair of eyes for scouting and extra cash to leverage.

A few disease foundations have set up funding "venture philanthropy" mechanisms that stretch their non-profit dollars beyond basic research into translational projects. The National Multiple Sclerosis Society's Fast Forward investment arm made its first $500,000 award in May. It plans four such awards a year from a $15 million pool it manages on behalf of Merck Serono, which participates in the funding decisions.

The government is dipping a toe into this area, too. The **National Institutes of Health**'s **National Cancer Institute** has a pilot program that effectively acts as an extension to the SBIR, or small-business grant program. The Phase II Bridge program provides up to $3 million over three years to start-ups that can also rope in matching private funds. It has six awardees so far, two drug companies, one diagnostic firm, and three in the imaging space. Now the government wants to apply the public-private investment concept to a proposed "countermeasure" fund to invest in start-ups working on vaccines, antibiotics, and diagnostics to fight all kinds of infection-causing microbes. The proposal calls for the feds to put in $200 million and look to leverage private capital. It comes as part of a broader **US Department of Health and Human Services** review and would need Congressional authorization.

Incubators have captured some attention, too, and if they start to prove effective in nurturing new ideas into more commercially viable projects, we should see venture dollars, both from traditional and non-traditional sources, allied with the incubators. (*See "Corporate Biotech Incubators,"* START-UP *, December 2009 [A#2009900277].*) One example to watch is at the **University of California, San Francisco**, which has built at its Mission Bay biotech campus an incubator that often serves as the next step for ideas that come from the school's world-class research community. The most recent addition to the campus' entrepreneurially friendly network is Mission Bay Capital LLC (MBC), a tiny $7.5 million fund with a commitment to fund ideas from UCSF and nearby UC campuses. Its pro-bono managing partners are the two men, Regis Kelly, PhD, and Douglas Crawford, PhD, who are also top brass at the UCSF-affiliated California Institute for Quantitative Biosciences (QB3). The firm will return 20% of its profit to fuel subsequent funds and set up a QB3 endowment.

MBC has already made two investments: as the lead investor in **Redwood Bioscience Inc.**, working on an aldehyde tagging platform to create antibody-drug conjugates or antibodies with small-molecule payloads; and as a small part of a syndicate in **Calithera Biosciences Inc.**, which pulled in a startling $40 million in Series A cash in July for its work on small-molecule caspase activators licensed from the UCSF lab of former Genentech Inc. protein engineer James Wells, PhD. [W#201030295]

UCSF is trying to build a 21st-century entrepreneurial ecosystem in which the lines between venture, philanthropy and industry are increasingly tangled. The **Babraham Institute** in Cambridge, UK is another. Three notable protein-engineering firms have recently set up shop there, all with different funding models: **Kymab Ltd.** with a £20 million Series A round from the Wellcome Trust; **Bicycle Therapeutics Ltd.** with two traditional and two corporate VCs on board; and **Crescendo Biologics Ltd.**, which garnered a small A round led by Sofinnova Ventures. [W#200930586] [W#200930537]

But government money, disease foundations, and incubators can only do so much when money for new companies is drying up. It's not unanimous, but a growing chorus says that for early-stage innovation to flourish, Big Pharma must be instrumental. "It's important to work with foundations, to incubate as cost-efficiently as possible," says 5AM's Schwab. "But we believe the most bang for our buck will be from pharma. We're increasingly mutually dependent upon each other."