

Strong at the Broken Places: Models for Industry's Future

By Trista Morrison

There's a lot of talk these days about how the biotech industry's business models are broken.

The venture capital business model doesn't support innovation, complain both struggling start-ups and investors trying to pull together syndicates. Yet despite attempts at de-risking, many venture capitalists aren't hitting their target returns. Dennis Purcell, senior managing director at Aisling Capital, predicted the Series A-Series B-Series C-IPO model will not last.

Meanwhile scientists are complaining that the discovery model is broken. At a recent conference, Marc Tessier-Lavigne, executive vice president of research and chief scientific officer for Roche AG's Genentech subsidiary, bemoaned the "dramatic decline in productivity despite a dramatic ramp-up of R&D spending."

And almost everyone agrees the current drug development model, with its \$900 million average price tag, is not sustainable. "I actually believe that what had been the model is going to drive us to extinction," said serial entrepreneur Cory Goodman.

None of these complaints are particularly new.

Back in 2005, *BioWorld Today* Columnist Cynthia Robbins-Roth wrote about the "broken model of biotech venture funding" and the need for an academic/start-up "hybrid" model, among other issues. Yet she noted that biotech groups like PharmSTART, Bioaccelerate, Cato Bioventures and others were testing new business models to address those problems. (See *BioWorld Today*, Aug. 3, 2005.)

And today, as financial difficulties throw a spotlight on the shortcomings of traditional business models once again, plenty of biotechs continue to seek innovative solutions.

Xcovery: Sustainable Platform Financing

Sheridan Snyder, founder of Genzyme Corp. has an idea for biotech funding that doesn't involve venture capital.

Snyder's latest start-up, Xcovery Inc., is churning out a pipeline of improved kinase inhibitors discovered by Chris Liang, director of medicinal chemistry at The Scripps Research Institute and co-inventor of Sutent (sunitinib, Pfizer Inc.). While many platform technology companies tap into venture funding until they can be acquired by big pharma, Snyder has no such exit plans for Xcovery.

"Are we ever going to sell that platform? Not if I can help it," Snyder maintained.

Snyder has thus far provided Xcovery's funding out of pocket, but the firm needs bigger-dollar backers to start clinical trials. Snyder's plan is to funnel the first eight compounds into a limited liability company (LLC) and obtain \$5 million from limited partners. He anticipates that will be sufficient to drive the lead molecule to Phase I and attract a partner, and the partnership funding will support subsequent development and out-licensing of the next few compounds.

But Xcovery will not pour excess licensing revenue into discovery work. Instead, that money will be paid out to the limited partners along the way. And when all of the compounds have been licensed, the investors can either walk away or re-invest in a new LLC incorporating the next handful of product candidates generated by the platform.

As biotechs play an increasing role in serving as the discovery engine for pharma, Snyder predicted that the LLC model could provide a "viable alternative" for platform companies.

BioVista: Artificial Intelligence for Discovery

What happens when you combine the vision of Anadys Pharmaceuticals Inc. and Cellzome Inc. cofounder Aris Persidis with that of his brother, artificial intelligence expert Andreas Persidis?

You get BioVista Inc., a start-up with a drug profiling platform that goes way beyond data mining to identify new uses for existing compounds.

Andreas explained that BioVista is not "reshuffling existing information, but creating new things." The brothers endowed their data management platform with an awareness of concepts like drugs, diseases, side effects, organs, genes, biological pathways and more. They then applied the technology to 8,000 diseases, 12,000 adverse events and 15,000 drugs from the world's formularies, using every scientific publication, conference presentation, FDA report and patent filing available.

The results have attracted biotech and pharma partners for eight ongoing projects involving discovery, repositioning, adverse event profiling, patient stratification and other services. BioVista also has generated an internal pipeline comprising more than 30 repurposed generic compounds, the lead two of which are in preclinical studies for multiple sclerosis. They, too, have generated partnership interest.

"Our strength is a prolific discovery capability," Andreas Persidis said, adding that BioVista is the first company to "promote the art and science of repositioning systematically."

Calvert: Bridging the Translation Gap

The Calvert Research Institute, a sister company of contract research organization Calvert Laboratories, is tackling two common biotech business model complaints: the "valley of death" between federal funding and investor funding and the need for more products rather than more companies.

Calvert Research uses the cash flow from its CRO services business to license early-stage research from academia. The group then uses its CRO capabilities to advance the projects through preclinical development and hands them off to big pharma or big biotech.

"Our goal is to be sort of the middle-man player," explained Vice President Andy Burch.

Investments in companies like AcSentient Inc. (acquired by ISTA Pharmaceuticals Inc.) and Pinnacle Pharmaceuticals (acquired by New River Pharmaceuticals Inc., now part of Shire plc) have resulted in exits for the firm. But Burch said Calvert was disappointed to find that many biotech start-ups had "essentially wasted" their first \$3 million or so on infrastructure, when Calvert could have completed the whole preclinical project for less. So the firm turned its focus to academia, signing deals with Auburn University, Tulane University and others.

"Ninety percent of what we work on does not need to be a company by itself," Burch said. And when Calvert's work is through, the firm plans to take an up-front payment and move on rather than seeking royalties.

"We more or less clean it up so maybe big pharma will be interested," Burch said, "then we step aside."

Flexion: Faster, Cheaper Development

Michael Clayman and Neil Bodick, the team behind Eli Lilly and Co.'s much-lauded drug development unit Chorus, have parlayed their successful business model into a new venture, Flexion Therapeutics.

The premise is that while achieving clinical proof of concept usually takes three to four years and \$15 million to \$40 million, Flexion can do it in one to 2.5 years and \$3 million to \$5 million.

What's their secret? Clayman says his team is "focused entirely on the so-called killer experiment." They only collect data needed to advance to an indisputable efficacy study, often not just placebo-controlled but comparator-controlled as well. If the drug succeeds, formulation work and other skipped studies will have to be completed, but at that point the drug has a much higher chance of success and warrants the investment.

Flexion is applying this method to molecules sitting on the shelf at big pharma. "Some of these molecules are separated from greatness by a single clinical dataset," Clayman said.

He explained that Flexion might license three such molecules: one of which is of interest to the pharma and two that are not. For the molecule of interest, the pharma has no obligation until it sees the proof-of-concept data, at which point it can pay a success fee, milestones and royalties to have it back. For the other two molecules, Flexion will offer the pharma a small fee, milestones and royalties for development and marketing rights.

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