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For Better? For Worse?

Economics, Exits Forcing Return of One-Trick Pony

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A few years ago, you couldn't make it through a biotech investor presentation without hearing about "multiple shots on goal." But with cash in short supply and exit strategies limited, "tightly-focused" is the new catchphrase of the day. "There's still room for different business models," said Sean McCarthy, senior principal at Pappas Ventures. "The question is: What type of biotech can be built today, and where does that next generation of companies come from?" The shift from broad pipelines to single products is one born of economic necessity, both for public and private biotechs.

On the public side, companies are increasingly cashstrapped and investors "want them to focus on getting to the next milestone," which often means cutting non-core programs, said Merriman Curhan Ford and Co. analyst Joseph Pantginis.

Yet privately held biotechs, too, are under pressure to maximize their cash runways. And as venture firms look at new funding opportunities, McCarthy said, another "inevitable question" is: Which one or two programs from the company's pipeline are the highest priority, and what would the company look like without the rest?

But money isn't the only factor forcing a shift in biotech business models; the type of exits available also play a role. McCarthy explained that the multiple-shots-on-goal model was "driven by having one eye on the public markets" – and the market was hot for strong management teams, late-stage products and broad pipelines. Today, it's all about positioning for an acquisition, and pharma wants to see multiple shots on a single target.

Biotech Supermodels

So is it even possible to build a sustainable, fully integrated pharmaceutical company (the once-touted FIPCO) anymore? More than one expert has said there will never be another Amgen Inc. or Genentech Inc. (and Genentech, as part of acquirer Roche AG, is no longer the poster-child for

independent biotech success).

David Miller, CEO of independent research firm Biotech Stock Research LLC, believes it can still happen "if you have a management team that has brought a lot of money in." He pointed to Seattle Genetics Inc. as a company that has "management expertise, a reasonable capital structure, a boatload of products, and is good at killing programs."

But Miller noted that no matter how diversified a company is, the first drug into Phase III will to a large extent determine the company's value. That's why Seattle Genetics killed multiple lead programs until it found the right one to advance, he said.

McCarthy suggested that a sustainable company could perhaps be built "on an incremental basis" – adding programs one at a time after the first succeeds.

That's the way "just about every major pharmaceutical company" was built, said Bob More, general partner with Frazier Healthcare Ventures. With the exception of Amgen, most were single-product companies that later expanded, he said.

Yet More noted that the business of discovering and developing drugs is very different from the business of selling them, and a company that is good at one will not necessarily be good at the other. "I don't know if the world needs another sales force," he said – not when pharma has more than enough reps trained and deployed.

All sales aside, what about building sustainable, pipeline-driven discovery and development focused biotechs like Isis Pharmaceuticals Inc. or Exelixis Inc.?

For that model to work, you've "got to have a real edge over and above what pharma can do," McCarthy said. He cited Brain Cells Inc.'s neurogenesis platform and Plexxikon Inc.'s lead generation platform as having "Exelixis potential," but he questioned whether or not such a model can succeed without the public markets.

All for One and One for All?

Of course, the public markets will rebound eventually, but this doesn't necessarily mean interest in funding broad pipelines will return as well.

Pantginis said diversification is "still on the checklist" of what public-company investors want, but McCarthy noted there's no telling what investor appetite will be when the markets build strength.

Meanwhile, with the exception of specialty pharma commercialization plays that need multiple products to put in their sales bags, pipeline diversification "gets you into more trouble than it gets you out of," More believes.

"Most people think that diversification is

risk mitigation – I would argue they are deceiving themselves,” More said. A lot of one-trick ponies have imploded when their single tricks failed to perform, but More says that’s just part of the game. “Why do these [failed] companies deserve to exist?” he said. It’s a sentiment echoed recently by public investors as well. In the wake of lead product failures, shareholders of companies such as Progen Pharmaceuticals Ltd., VaxGen Inc., NitroMed Inc. and Avigen Inc. have balked at spending cash reserves on subsequent initiatives. And from a risk-mitigation standpoint, venture capitalists shouldn’t be bothered by binary events because they are diversified through their portfolios, More added. Miller said another problem with broad pipelines is that it’s “difficult for companies to do multiple programs equally well.”

More agreed. “Doing things sub-optimally is the enemy of biotech,” he said, and “supporting more than one or two products takes enormous resources.” While Exelixis has done a good job juggling a broad pipeline, the company has recently started out-licensing more programs, More noted. McCarthy, too, said he sees more biotechs with multiple programs seeking to offload them, and a new way of going about this is to carve them into separate legal entities that can be acquired by pharma one at a time. In the past, such carving-out happened after the fact in the form of spin-outs, but it’s starting to happen preemptively, creating what McCarthy called a “menu-driven approach.”

Finding Talent

Not everyone is a fan of the tightly focused model. Glen Giovannetti, Ernst & Young’s leader of global technology, maintained that “as a business model, it’s very challenging” for a number of reasons, one of which is that it can be hard to attract the best talent to such risky, potentially short-term ventures.

Yet More maintained that serial entrepreneurs don’t get blamed for the failure of their companies, and are quickly able to secure another position (though their employees may be less fortunate). At the same time, a single-product focus brings out the “ingenuity” of CEOs, he contended. Without a pipeline to fall back on, CEOs are more motivated to really work through and understand a product when it encounters a hiccup instead of just switching gears.

Such dedication, however, if taken too far, can lead to what Miller terms “survival bias.” He pointed to Introgen Therapeutics Inc. as a company that pushed from Phase II into Phase III when such advancement wasn’t warranted. And then there’s the issue of serendipity. How many successes in the biotech industry are attributable to fortuitous findings that propelled a barely-there back-up product into the stratosphere? The prime example is Pfizer Inc.’s Viagra (sildenafil), the erectile-stimulating properties

of which were discovered only after patients in a failed cardiovascular study refused to return their pills. Another example is Onyx Pharmaceuticals Inc., whose Nexavar (sorafenib) might not have moved into the spotlight if its lead oncolytic virus program hadn't failed, or Millennium Pharmaceuticals Inc. (now part of Takeda Pharmaceutical Co. Ltd.), whose Velcade (bortezomib) was an afterthought in the LeukoSite acquisition. If pipelines get shelved as biotechs focus on just one or two products, will serendipity be lost? McCarthy agreed that serendipity is "one of the ironies" of the biotech world – but it's "not an investment thesis," he said.