Stelios Papadopoulos

A longtime investor, company founder, investment banker and industry observer discusses the factors shaping biotech financing.

With several decades of experience, Stelios Papadopoulos has a unique view on biotech. Here he discusses the current challenges for biotech financing.

Why is the stock market important to biotech?

Stelios Papadopoulos: In every business there are those who set the tone, and there are those who respond to those who set the tone. In biotech, by far the most important group that sets the tone is public investors—those who invest in biotech companies that trade in the stock market. The second is pharma companies. They decide what they want to acquire. They like product and they like technology, and on occasion, they like footprint—maybe a Japanese company looking for a major footprint in Boston, for example. The last group is the regulatory agencies, because they determine what it takes to get something approved. Conversely, entrepreneurs and venture capitalists [VCs] do *not* set the tone. Entrepreneurs may think they set the tone. They may think they're visionaries going around telling everybody how their technology is great. But if nobody funds it, we'll never know whether it was great or not. And VCs are the most responsive people in the world. Whatever they do is in response to what the stock market or pharma wants to buy. Once we understand this, the dynamics of the biotech sector become clear.

How have the markets changed over the years?

SP: When Fidelity launched the Fidelity Select Biotech Fund in 1986, it was a $60 million fund. That was the typical size then. But the funds have grown so that today a typical fund manager controls not $100 million, but much more than that. And there's a limit to the number of stocks any fund manager can follow. Let's say you can follow and invest in 50. That's a huge number, right? A $100 million fund means you can buy, on average, $2 million per stock. But if it's a billion-dollar fund, it's $20 million per stock. Most biotech IPOs [initial public offerings] nowadays need to be heavily discounted to attract buyers. As the valuation dips to $100 to $150 million, the typical offering is $30 to $50 million. How can you invest $20 million in such an IPO? You can't. There just isn't enough liquidity. The investment community is also much more sophisticated than it was. It's not possible anymore to attract investors simply through the next hyped IPO story.

Does the small market cap of biotechs have other consequences?

SP: We understand already that investors are migrating to bigger stocks because these have much more liquidity. In addition, investment decisions today rarely center on the speculation or expectation that a company's technology will give rise to a successful set of products or that the company will evolve into a significant enterprise. Rather, most investments center on handicapping the outcome of a particular event, typically a potential acquisition or a clinical trial. For instance, investors make bets, months before a phase 3 trial is unblinded, as to the outcome. And it becomes very much a binary game. It's investing, but it's not the sort of thing that enables companies to grow the way we did in the eighties and nineties through the steady infusion of capital.

To what extent is the biotech financing model broken?

SP: The model is broken in one place: IPOs. The problem is the stock market is not prepared to invest in early-stage companies. Twenty years ago you could find some interesting biology in a university setting, and that was enough to start companies that within the usually prescribed three to five years, after raising maybe $20 to $30 million in venture capital, would do an IPO, even if they didn't have products in the clinic. Today, that is no longer the case—the typical mantra nowadays is you need phase 2 data. So now the choice is for VCs to keep on investing until they've put in $100 million or more over five to ten years to get from first principles to phase 2 data. The VC community does not have that kind of capital or that kind of patience.

What kinds of solutions do you envisage?

SP: The objective is to save innovation from becoming extinct. You could argue that for most of the eighties and nineties, biotech was the intermediary between academia and pharma. And biotech did it by inviting risk capital from the stock market. I think in some ways the lack of interest in the stock market is leading pharma to essentially circumvent the biotech sector and go directly to the source—the academic community. So that's one way by which innovation could be salvaged. The other is the potential that government and other not-for-profit sources will choose to fill the gap, which, as I see it, is the distance between interesting biology and compelling biology. The distinction is important, because the latter clearly and directly leads to new product ideas that a VC will fund. Most academics don't appreciate this subtle distinction. For interesting biology to become compelling biology, one needs a fair amount of translational research. Develop a bunch of animal models. Confirm that the biology you've observed is conserved across multiple model systems. Maybe create some probe molecules. Not necessarily drugs, but molecules that will probe the condition and give you insight into the biology. Perhaps the recently announced National Institutes of Health initiative to form a National Center for Advancing Translational Sciences might provide much-needed capital and guidance in that area.

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