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Filters for preparing to meet a venture capitalist

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Venture capitalists employ several criteria when considering whether to commit funds to a biotechnology startup.

Few encounters can be as unsettling to the star academic researcher as his or her first meeting with a venture capitalist (VC). Having mastered a discipline, learned the art of winning grants, and won recognition from peers, the researcher is still probably not very well prepared to meet the very different standards of business success.

Because I have worn both lab coats and business suits in my career, I would like to offer a framework for understanding the different perspectives of both sides and some suggestions on how to bridge the gap.

Fundamentals

The fundamental fact a researcher needs to understand about venture capital and life science investments is that the filter for investment selection has grown extremely fine. Historically, this represents a significant change. In the late 1980s and early 1990s, VCs were relatively aggressive in making biotech investments. But despite a number of significant winners, VCs as a group have struggled to profit from their investments.

In many cases, an important factor in their failure to achieve satisfactory returns is the 10- to 12-year product development cycle required for many drugs. Large pharmaceutical companies have structured themselves to accommodate long waits. But the cycle has proved too long for most VCs, because they typically raise their money from pension funds and endowments that expect a 20% or better annual return on their investments *within seven years*.

Few attempts to synchronize these two very different time horizons have succeeded. At various times, VCs have put their faith in such new technological waves as genomics, proteomics, and diagnostic tools. Yet, far more often than not, the waves have crashed in financial failure. Within this context, it becomes clear why veteran life science VCs have become increasingly cautious. For example, my firm and many of our peers now place special focus on therapeutic product investments. And even within that limited category, we employ multiple additional criteria to help us decide whether to even *consider* committing funds.

Filter feeding

At Morgenthaler Ventures (Boulder, CO), we use at least five filters to screen therapeutic investments. Although these filters may appear easy to comprehend, they contain enough subtleties that they often require considerable discussion with entrepreneurs—particularly if the product proposal has come directly from the research laboratory.

Filter no. 1. Is the product one of many from a platform technology or an isolated product?

This question is usually the easiest question to answer. For example, a single compound to treat a specific bacterial disease is very different from a new method for making antibiotics based on inhibition of bacterial replication. The former is a 'one-trick pony' with all the risk placed on a single product. The latter, of course, is clearly a technology platform capable of producing many different products—thereby limiting overall

investor risk by spreading it among multiple products.

Filter no. 2. How long will it take to develop the product?

As noted above, venture capital limited partner investors cannot tolerate the 10- to 12- year development cycle common for traditional pharmaceutical products. Thus, VCs must look for technologies that enable developers to 'cheat,' and cut the development times by as much as half. They can, for example, select therapeutic areas that have short treatment times with clear-cut end points (e.g., anti-infectives, whose treatment times are frequently less than a week, and which either kill the bug/virus or don't). Cancer treatments are also attractive candidates because the US Food & Drug Administration (Rockville, MD) has frequently offered fast-track approval for them. Additionally, VCs seek products that have been in clinical development (e.g., in medical school settings) that indicate appropriate safety, and sometimes even efficacy, before making the first venture capital investment.

A researcher who believes he or she is working with a faster-track technology can communicate that fact in a variety of ways, including presenting at conferences—such as those sponsored by the Biotechnology Industry Organization (Washington, DC)—that bring scientists and investors together.

Filter no. 3. Will the drug work against the chosen target? And was the choice of target the right one to begin with?

This is one of the trickiest areas, and one where scientific and business goals often clash. Although assays and associated processes for determining whether a drug will work against a given target have been relatively well established in many therapeutic areas, knowing that the target is appropriate is much more complicated.

The basic problem is that biology is replete with redundant pathways. Inhibiting one pathway may simply activate an alternative pathway that results in the same pathology. Thus, a target can be considered 'rigorously validated' only after being specifically inhibited (or upregulated) by a drug in a human clinical trial and resulting in a clinical benefit to patients. A lot of cash is routinely spent on failed clinical trials, which are very expensive. Therefore, removing 'target risk' from the drug discovery and development process in order to decrease attrition rates is essential to attracting investment.

By contrast, the most exciting current science (e.g., identification of a new cell signaling factor—news that would qualify for the cover of a prestigious journal such as *Cell*) is rarely something that provides a validated target or new drugs against an already validated target. The researcher may have found an important new target, but modulation of the target may have no role in disease modification. However, making such an analysis in the face of a scientific acclaim can cause significant interplays between a VC and the scientist's ego.

Filter no. 4. Does the new company have experienced management?

This is another area of cultural disconnect. Scientists typically think that getting the idea is the hardest part, and have little appreciation for what it takes to translate the idea into a commercial platform and develop products from it. Although frequently mundane, the drug discovery and development process is lengthy, time consuming, and complicated, and requires management and other expertise seldom found in a university faculty. Furthermore, venture fund-raising and managing activities in a focused and cost-effective manner is not generally part of the skill set of university researchers. Scientists able to recognize this fact early on are best able to see their idea through to commercialization.

Often, the best way to attract institutional venture capital to academic research is to work closely with a university's technology transfer office. It should be able to pair researchers with experienced managers, who, in turn, can help create a business plan and the rudiments of a management team able to work with VCs.

In addition, founding scientists need to recognize that their most important contribution to the fledgling company may be as an advisor. Ask yourself: "Do I want to continue as an academic following the scientific truth wherever it leads? Or do I want to constrain myself to the rigid demands of meeting corporate milestones?" Either choice entails a radically different lifestyle. Often academics find themselves far better suited to chairing or serving on the company's scientific advisory board.

An example that illustrates this point can be found in the relationship between Ribozyme Pharmaceuticals (RPI; Boulder, CO), where I served as CEO, and its scientific founder, Tom Cech, who won a Nobel Prize for the discovery of ribozymes. Tom proved quite sophisticated about the difference between academic and corporate life and knew from the beginning that he wanted to make his contribution as chair of the scientific advisory board and as consultant to the company. He never worked as an employee of the company nor served on the board of directors.

The resulting partnership between Tom and the company worked very effectively over many years. While the company focused on developing commercial technology platforms and products, Tom offered advice on scientific questions relative to the ribozyme technology (e.g., mechanism of action) and also ended up providing several high-quality graduate

students and postdocs who became full-time company employees. Everybody won.

Filter no. 5. Is the deal financeable? In other words, will it attract a syndicate of first class, knowledgeable co-investors with staying power?

This is a screen that many researchers also tend to underestimate. Even apparently sound commercial propositions may prove insufficiently attractive to enough quality investors. Sometimes, the hindrance will be a conflict of interest with another investment. Sometimes, the hindrance will simply be that the idea does not fit the rather capricious standards of VC fashion.

Academics can control such problems in part by making sure that they work with VC partners who enjoy the respect of their peers and have demonstrated that they can form VC syndicates for companies that they champion. Having quality VC syndicates, even if they take longer to create than anticipated, are much more important than raising funds earlier by a syndicate that cannot support the company in the future. Academics will be wise to resist impatience while their initial VC partners go through the syndicate-building process.

Above all, budding bioentrepreneurs should recognize that building an 'A'-team of VC backers is essential for any deal to succeed. Especially in startup deals, it is important to recognize that the first investment is unlikely to be the last. As a result, financial syndicates need to have at least two characteristics to be effective. The first of these is 'deep pockets,' which means that the investors should be willing to set aside significant funds (usually equal to, or greater than, the initial investment) for future investment in the company. In addition, the investors should to be able to add value from their seats on the board of directors.

One of the criteria I set before accepting the CEO position at RPI was that the VC syndicate (and board) should be 'AAA' quality. Fortunately, this turned out to be the case. Some of RPI's investors had advanced scientific degrees, some had experience with drug development, and others offered deep general management experience and important industry contacts. Their collective contribution was essential to the growth of the company.

Conclusions

Even if a researcher's technology passes through each of the filters I have noted above, he or she should not expect anything close to instant success. The process leading to initial investment will remain long and uncertain, requiring multiple layers of due diligence and multiple meetings with potential investors to overcome uncertainty and skepticism.

Yet the satisfactions, both mental and financial, can be substantial. Every academic researcher I have known, no matter how ambitious for recognition, has also felt a deep desire that his or her work might contribute to overall societal good. I can think of no better route than translating research into a company whose products succeed with physicians and, especially, their patients.