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# Wall $treet BioBeat

## How to Improve Series B-Round Valuations

### Leveraging Drug Development Expertise Early On Can Build Momentum

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How can biotech entrepreneurs and venture capitalists best meet the challenges of a Series B financing? One answer, surprisingly often overlooked, is the creative use of drug development domain expertise that gets products into the clinic quickly and creates the environment for a momentum-building "up" B round.

Many Series B rounds, of course, are just the opposite: down. According to data collected for North America by VentureSource, the average reported pre-money valuations for many biotech companies going into Series B are often less than the post-money valuation of the companies after their Series A. And that's just the companies willing to reveal such information.

My estimate, and that of my partners, is that, taking into account all biotech startups in North America, probably 60% of Series B financings are down rounds.

The challenges with Series B are easily understandable. The company may have already made good progress during its one to two years of Series A financingincluding selection of a management team, completion of key animal experiments, and determination of early safety data.

But investors still don't know whether the proposed technological solution will affect human biology the same as it affects animal biology. Nor do they know whether the biological effect will translate into efficacy in a disease setting.

To answer those questions the company must complete final animal studies and Phase I safety trials and then establish proof of principle in at least small numbers of patients. All thatplus a financial cushion that lets the company seek subsequent funding from a position of strengthis what makes Series B rounds expensive, anywhere from $25 to $40 million.

Such economics naturally translates into a bias toward lower valuations for Series B.

**How B-Round Valuations Matter**

One might legitimately ask whether, in such circumstances, a down Series B round actually matters. It is, after all, just one of several financing events on the way to an eventual exit via IPO or acquisitionthe only valuation that counts in the end. Many biotech companies do, in fact, emerge from down B Rounds unfazed and go on to achieve ultimate success.

My answer, however, is that B round valuations can matter and should be seriously addressed when possible. First, down valuations naturally influence perceptions and emotions between partners. The management teams, who have invested time and ego in the company at no demonstrable return, may become upset with their venture capital backers and cynical about the fund-raising process.

Similarly, limited partner investors in venture capital funds may regard a down B round as the sign of a bad investment. In both cases, mutual trust has been known to suffer. No matter how understandable the problem, it is always better to avoid it than to have to explain it!

Second, and more substantively, attaining an upward valuation in Series B can become part of a process that propels a startup to greater progress and an earlier liquidity event. It's a high bar, but it is often more possible to surmount than many people believe.

Here, starting with the most obvious, are strategies that have proven successful:

Own clearly superior technology and have a management team with substantial industry experience. Only a few companies, of course, qualify.

Build an A Round syndicate of experienced, deep-pocketed venture capitalists. My rule of thumb is that it takes about three such VC firms with the capacity to absorb half the B Round and, thus, to support the valuation.

Find a corporate venture capital partner to lead the B Round. Although such VCs are, technically, separate from their parent corporations, they are more likely to place a higher value on research and product areas that complement those of their parents.

Make creative use of drug development domain expertise.

#### Leveraging Drug Development Short Cuts

Domain expertise, to me, refers to drug development experience that is obtained after working with dozens of potential pharmaceutical products in many product pipelines aimed at specific disease states. It's seeing what can go right and what can go wrong over a period of many years. It's also knowing how to design "killer" experiments that either stop organizationally popular projects in their tracks or validate them, qualifying them for accelerated treatment.

Above all, it's learning where the short cuts are to getting products into the clinic and achieving early proof of principle for the company and investors.

Generally speaking, drug development domain expertise leads to taking on projects with clear-cut clinical endpointsinfectious diseases, for example, where one can be certain that a bacteria or virus is really dead. It tends to avoid projects with lengthy, expensive trials such as those involving metabolic or central nervous system diseases.

More narrowly, it may mean targeting specific indications when possiblee.g., pancreatic cancer rather than breast cancerwhere trials are relatively shorter.

In my experience, such domain expertise is even today a frequently neglected art in biotech. This is surprising, given the painful lessons of the 1980s and 1990s when biotech investors learned that too much emphasis on research tools related to drug discovery often meant a nearly endless outflow of investment dollars, few or no products, and increased (not decreased) costs of drug discovery. Such science can be very seductive, especially to those trained mainly in basic science.

In the 2000s many entrepreneurs and investors are placing more emphasis on drug development, but much still needs to be done. At least one third of the biotech investment opportunities that cross my desk are open invitations to long-term tool development or hopelessly complicated clinical trials.

One U.S. HIV project we saw, for example, offered intriguing science, but would have required many years of hard-to-monitor clinical tests with thousands of enrollees in Africa!

Instead, biotech success is more likely to come when companies employ innovative drug development strategies to establish early proof of principle. Smart biotech entrepreneurs and investors know they have relatively few chances at grabbing the gold ring and do their utmost to take advantage of them.

**A Recent Example**

Let me give you a recent illustration of how drug development domain expertise has worked in practicewith positive impacts on one company's big early financing round.

GlobeImmune is developing yeast-based immunotherapies targeted at a range of intracellular infectious diseases, as well as cancers. It is the kind of broad technology that might, in other circumstances, have seduced company management to show efficacy in as many animal models as possible. Instead management asked the question: Which disease offers the earliest possibility of clinical proof of principle? The decision was complex.

Three diseases offered the best possibilitiesinfectious HIV, hepatitis C, and cancer. All three offered large potential markets, but very different drug development pathways.

HIV required extensive and expensive monkey-model animal trials, complicated regulatory requirements, coordination with federal agencies, and competition. Moreover, the failures of previous HIV immunotherapy trials had created a certain aura of cynicism among investors that might have been difficult to overcome. Such barriers might have slowed studies by months and, perhaps, years.

Development of hepatitis C therapy faced fewer constraints, but offered no obvious animal model. Cancer, on the other hand, lent itself to a well-established animal model. Subsequent safety trials take place in patients with the disease, and clear biological markers offer an opportunity to measure the drug's biological activity in patients early on.

GlobeImmune thus chose cancer as its first target. That choice has meant that even at the beginning stages of safety trials on very ill Stage IV cancer patients (who have failed all available therapy), GlobeImmune has been able to demonstrate clear biological activity.

This, along with other data, brought in new investors at a stepped up Series B valuation this August (in the face of considerable skepticism about cancer immunotherapy companies, where the failure rate has been high).

Manythough still too fewother examples come to mind, as well.

How should young companies identify and nurture drug development domain expertise? The answer is to make it a key criterion for early selection of staff, venture capitalists, and scientific and clinical advisory boardsand then making their input central to product development decision-making.

If done properly, the company will greatly increase its chances of higher valuations even in their high-risk, early rounds and, ultimately, a successful, profitable exit.

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