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The Company at the Crossroads *Part 1: To Commercialize or Not?*

At a certain point, every biotech company must decide what type of company it is trying to be

Call it the awkward age: that critical period when a biotech company is no longer a start-up but is certainly not yet mature. As in late adolescence, when ill-defined dreams meet the specific demands of reality, the time comes when a company has to decide what it wants to be when it grows up.

It's not as easy as it might appear. Successfully coming through this critical period requires that the company:

- understands the strategic options and associated cost;
- knows when it is time to make a choice; and
- assesses the risks, timelines, commitments, and potential rewards of each option.

Selecting the right options requires careful thought, planning, and timing. A hasty decision can prematurely foreclose a more appropriate option. Deferred decisions can result in the business drifting in several directions at once, instead of proceeding directly toward a clear destination. In both cases the result is likely to be, at best, lost opportunity and, at worst, business failure. In our experience, it is far more profitable for up and coming innovative biotechs to take control of their destinies by making a careful strategic choice at the right time and then pursuing that option single-mindedly.



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UNDERSTANDING THE OPTIONS

For the early-stage innovative biotech company, there are essentially two strategic options for the long term: (1) to become an idea factory or (2) to

Many biotechs fail to recognize that successful business strategies usually require highly conscious choices.

become a fully integrated company. Of course, there are ways to blend these two options, but the two basic options remain.

The idea factory is designed to generate innovative therapeutic products (with a strong IP position), devices, processes, or technologies and develop them to a point where they can be outlicensed to another company. The license then produces royalty payments that provide funding for generating new ideas which continue the cycle. In a variation of the strategy, idea-generating companies, especially those that have only one novel product or platform technology, may aim to be acquired by another company.

By contrast, the fully integrated firm takes ideas and innovations from discovery and development all the way to the market. Becoming such a company requires all of the functions and elements of infrastructure to execute the enormously difficult, complex, time-consuming, and costly job of commercializing a therapeutic product: R&D, quality assurance, quality control, regulatory affairs,

clinical trials design and execution, technology scale-up, manufacturing, marketing, sales, and more. Further, the kind of executive management team required to operate a fully integrated company differs substantially from that required to run a successful idea factory.

There are, of course, other business models, such as a hybrid strategy that seeks to generate ideas, outlicense them, and use the royalties to commercialize other products. Firms that have unique platform technologies can profitably exist in this hybrid space as long as they have a strategy that limits their investment dollars to a manageable number of internal product candidates. But the idea factory and the fully integrated firm are the two proven business models that typically represent the dramatically different options biotech must eventually confront.

KNOWING WHEN TO DECIDE

Knowing when it is time to decide can be as important as the decision itself. In the beginning, the strategic decisions of many biotech companies are driven largely by two factors: by the belief of the founders in their scientific or technical expertise and by the investors who provide the early funding. Both factors are compelling and important, but they should not cloud the judgment of company decision-makers, either encouraging the postponement of hard strategic choices or propelling hasty, ill-considered decisions. In both cases, the result is likely to be an unrealistic or suboptimal strategy.

Innovative scientist-founders understandably have great faith in their ideas, which often represent exciting, if distant, novel possibilities for therapeutic breakthroughs. However, many of those ideas are initially born in talent-rich university laboratories, where considerations such as the highly regulated road to drug develop-

ment, the demands of clinical trials and manufacturing, and the sheer scale of commercial operations are usually not well understood or practiced. Innovation is often the most highly coveted and rewarded skill set in these companies, and individuals are often promoted to high levels of executive management beyond their capability to run the practical day-to-day operations necessary to advance promising therapies to clinical trials.

Having evolved from that context and with little experience of the realities of drug development, many early-stage biotech greatly underestimate the difficulty, the amount of time, and the costs of moving an idea from the pure research laboratory to a marketable product. At the same time, they often greatly overestimate the value of their idea—seeing it as potentially the most important development in its therapeutic area in decades—and they underestimate the long and arduous path to product approval. As a result, they may simply proceed on the unexamined assumption that full commercialization of the company's product or products is their goal, failing to recognize that successful business strategies usually require highly conscious choices.

Because capital is king in the very early stages of a company, it often seems unnecessary to think too deeply about ultimate strategy anyway. In fact, the earlier the stage of the company, the more likely it is that investors are making the decisions through active participation of the board of directors. And because financial angels and Series-A investors usually have very short investment horizons, most of those decisions will be based on an early exit strategy, not on longer-term prospects. But investors—especially after the Series-A round—also can have their judgment clouded.

Tantalized by possibilities of the greatest possible return on the investment, they, too, may defer making a final decision on the course the company should take. Conversely, unduly alarmed by early setbacks in research or development, they may make decisions that should in fact be deferred—and prematurely deciding the company's future can sometimes be as detrimental as putting off such decisions.

How do you know when it's time to decide? What information is necessary to make serious additional investments in the company and its ideas? There is no hard and fast rule, but there are a number of factors that point to the window of opportunity.

First, there is the subjective feeling that comes after you have survived the early rounds of funding, when, as a decision-maker, you realize that you no longer have to think almost exclusively about capital. You've made it into subsequent rounds of funding with investors who may have longer investment horizons and your product is showing real promise.

Second, there are some objective milestones that you should have achieved. These include:

- a platform technology or drug candidate with good prospects of success;
- well-established and defensible intellectual property coverage;
- comprehensive characterization of the product, including stability;
- thorough and positive preclinical and toxicology results;
- a robust, reproducible, and cost-effective production process;
- indications of the product's manufacturability;
- reasonable assurance that the product is innovative;
- a positive assessment of the reimbursement landscape for the projected therapy; and
- early and encouraging meetings with the FDA.

Third, regardless of which strategy is chosen, many companies wish to reach the point of having Phase 1 and Phase 2 clinical trial data to support claims of clinical safety and efficacy, respectively. If so, the company will need to be prepared to:

- compile the appropriate documentation to support investigational new drug (IND) filings;
- effectively interact with the FDA;
- decide what to do internally versus contract out;
- produce clinical trial materials;
- design and execute clinical trials; and
- be prepared to address consequences and show comparability as required.

ASSESSING RISKS, REWARDS, AND REQUIREMENTS

Because the differences in risks and rewards between the idea factory and the fully integrated firm are so vast, it is essential to make a well-timed, unambiguous decision that will guide implementation of the strategy and sharply focus the efforts of the company on the ultimate goal. Those efforts include getting the type of management team in place that is appropriate for the strategy. For the idea factory, that usually means a small team that is adept at research, early development, alliances, and out-licensing. For the fully integrated firm, it means strong executive leadership in critical commercial areas like manufacturing, marketing, and sales. (For a discussion of how business processes and infrastructure should be created and measured for each strategic alternative, see *BioPharm International's* March 2008 Compliance Notes column, "How to Avoid Becoming a Biotech Zombie—Part 3".)

The risks for the idea factory are far lower than the risks for the fully integrated firm. The products that the idea factory produces need only show some therapeutic

promise. They do not have to be herded all the way through regulatory approval and use in humans.

Not surprisingly, lower risk means lower rewards. Nevertheless, for the idea factory that can generate a continual stream of ideas and then turn them over to another company for commercialization, those rewards can be reasonably consistent and substantial. Moreover, with big pharmaceutical companies facing thin pipelines and patent expirations, the market for ideas is strong.

The fully integrated company stands to reap even more substantial rewards, but the risks are concomitantly far greater than the risks for the idea factory. The fully integrated firm must make enormous investments in human and infrastructure resources. Further, for every drug that doesn't make it to full commercialization or that fails to win sufficient market share, those investments are wasted. And the odds of successful commercialization are long. For example, it is estimated that an IND has a 10–15% chance of reaching the market, and an alarming number of new drugs (50% by FDA estimates) are failing trials in late stages. The fully integrated company must therefore have enough promising products in the laboratory and the clinic as a hedge against products that fail.

Deciding between these two risk profiles is not a simple matter. Certainly, different companies, their boards, and their executives will have different appetites for risk, often depending on who among those stakeholders is ultimately making the decision. But regardless of who makes the decision, it should be made at a much greater level of granularity than a simple macrochoice between low risk or low return and high risk or high return.

With an understanding of the differing requirements for the two business models, you can clearly

and comprehensively define your risks, both external and internal: competitor actions, patent protection, gaps in core competencies and management, product development, regulatory hurdles, and other risks that could delay reaching the ultimate goal under each model. You can then consider what potential effect these risks are likely to have on cash flow and model the cash flow under different scenarios.

Unfortunately, many organizations treat risk and uncertainty in a highly unsystematic fashion. They may have a general, qualitative discussion of potential setbacks and pitfalls, but they fail to try to quantitatively calculate the chances that particular problems will occur. Instead, they simply increase the discount rate to compensate for a vaguely conceived notion of risk. But this fails to account for the specific risks of a chosen strategy. Those specific risks must be quantified in terms of their contribution to uncertainty in cash flow. Although most biotech companies lack the ability to conduct this kind of probabilistic analysis, it is nevertheless worthwhile to seek assistance with it to understand the total risk exposure of any given business plan. Then it is possible to make a fully informed decision about which business model to pursue.

Regardless of which path you choose, you will then face another crucial set of decisions that turn on risks and rewards—whether to build or buy such capabilities as:

- clinical or commercial drug supply;
- quality control laboratory testing capability for drug release and stability testing;
- internal versus CRO clinical study capabilities; and
- sales force.

It is this build-or-buy analysis that is the subject of the next article in this series. ♦



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