



From Benchtop to Boardroom:

A Bird's-eye View of Bioentrepreneurship

A White Paper from
BioResource International, Inc

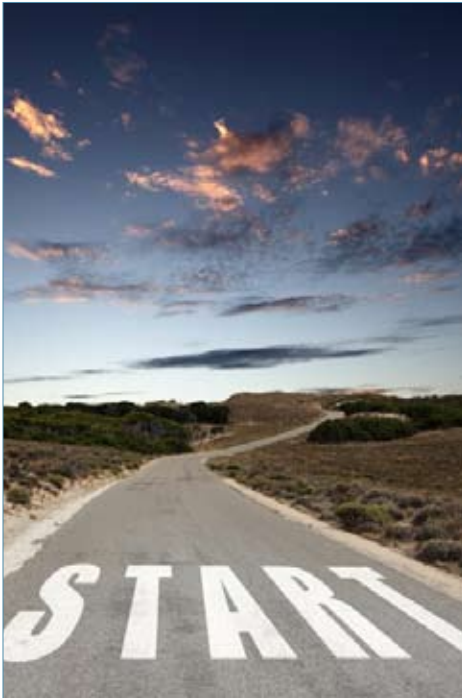
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Introduction



Are you thinking of starting a biotechnology company? Perhaps you're a scientist, a physician, or an engineer who's developed a new technology. Perhaps you're an entrepreneur with an interest in the life sciences. Or perhaps you're an executive at a life science company and would like to venture out on your own. Whatever your background, reasons, and interests are, if you're thinking about starting a biotech company, then this white paper is for you.

Biotechnology is broadly defined as the application of knowledge in the life sciences to create products or services that are beneficial to humans. It is used in a variety of industries, from enhancing the quality and efficiency of food production to producing new medicines and vaccines. Although it is just a few decades old, the biotech industry has expanded rapidly. For example, according to Ernst and Young's **Beyond Borders: Global Biotechnology Report 2012**, established biotech centers (U.S., Europe, Canada, and Australia) achieved revenues of US\$83.4 billion in 2011.

This white paper will give you an overview of issues that aspiring biotech entrepreneurs will probably encounter on their road to success--factors such as licensing, financing, personnel, partnerships, and marketing--while tying them all in with our experiences here at BRI.

What Makes a Biotech Business Unlike Any Other Business?



Simply put, biotechnology is a high risk, high reward business. Perhaps you've heard that 80% of all small businesses fail within the first five years. Yet a biotech company does not only face the same risks that all startup businesses face, but also a number of other, unique challenges.

Ever heard of the "lean start up" concept? A business approach coined by Eric Reis, author of [The Lean Start Up: How Today's Entrepreneurs Use Continuous Innovation to Create Radically Successful Businesses](#), the lean start up relies on iterative product releases to shorten product development cycles, measure progress, and gain valuable customer feedback. But while this approach has been applied successfully by numerous startups, it is not likely to apply to biotech startups.

It's relatively easy for a software company to shell out a few hundred to a few thousand dollars to hire a programmer to translate their [software as a service \(SaaS\)](#) idea into code, and then start selling their product. Then, as they get feedback (and money) from customers, they can tweak the software, release new and better versions of it over time, and consequently attract more customers and earn more profit. This is how companies like [Intuit](#) (TurboTax, Quickbooks), and [37Signals](#) (High Rise, Bootcamp), as well as entrepreneurs like Tobias Lütke, Daniel Weinand, and Scott Lake ([Shopify](#)) have done it.

Unfortunately, it's not possible to develop a new drug, biologic, or medical device prototype, market it immediately to the public, and then make small adjustments along the way based on how they're received. That would be very risky, not to mention unethical and potentially illegal! To get a drug or medical device to market, a series of incrementally bigger and more expensive trials have to be designed, approved, and conducted. All of these trials have to be funded, yet none of them will generate cash for the business. That is why it costs between \$25 million to \$100 million to develop medical diagnostics and devices, and up to \$1 billion to develop drugs, before companies can start making money off them.

High Risk, High Reward

The biotechnology industry is also one of the most highly regulated industries in business. If a company's developing a drug for instance, regulatory bodies such as [the Food and Drug Administration \(FDA\)](#) will have to approve protocols and materials for every trial before they can start recruiting volunteers. Then, once the trials are done and data have been collected and analyzed, it has to evaluate the results and approve the product.



Development, testing, and approval (not to mention licensing and fundraising) take approximately 3 to 10 years to accomplish.

Keep in mind that development, testing, and approval, not to mention licensing and fundraising, take approximately three to 10 years to accomplish. And there's a fairly good chance that anytime during this process, the company will realize that their product is not effective, or it's not safe, in which case it (and its investors) would not be able to recoup the money that's been invested.

So the only "lean" thing about starting and growing a biotech company may be the founders' salaries(!). Unlike most technology businesses, it requires significant upfront costs and years of development with little guarantee of a viable product. While there are milestones along the way to indicate whether it makes sense to continue investing time, money, and effort, a biotech entrepreneur will not know the full impact (or lack of it) of a product until many years and dollars have been committed.

But none of this is meant to discourage you! Do not forget what's on the right side of the "high risk = high reward" equation. Biotechnology is a high reward industry. Companies that make it to the end of the cycle are rewarded with revenues and profits that businesses selling most other products cannot hope to duplicate right off the bat. It's also immensely gratifying to be part of an industry that discovers, develops, and delivers products that directly improve the life and health of millions. Take it from us here at BRI--it's an exciting time to be a biotech entrepreneur!

How a “Perfect Storm” Ushered in the Modern Biotechnology Era

Year after year, biotechnology products take up more space in the world's collective pool of innovative output. According to Ernst and Young's [Beyond Borders: Global Biotechnology Report 2012](#), biotech companies raised an impressive \$33.4 billion in funding in 2011, and these investments continue to fuel cutting-edge advances and applications in a wide variety of fields including medicine, agriculture, and energy production.

In spite of its explosive growth, however, the biotech industry is fairly young. Compared to the approximately 160-year-old oil and gas industry, the 240-year-old automobile industry, and even the 75-year-old computer industry, the business of biotechnology clocks in at a mere 40-some years. The following are three elements that coalesced to foster the recent expansion of this unique industry.

1. Bayh-Dole Act



US Senators Birch Bayh, left, and Bob Dole, who sponsored a small amendment (P.L.96-517) to the Patent and Trademark Act in January 1980. (Keystone/Getty Images)

The term “biotechnology” was coined in 1919 by Hungarian agricultural engineer Karl Ereky in his book, [Biotechnology of Meat, Fat, and Milk Production in an Agricultural Large-scale Farm](#) (translated), where he described how he used living organisms to convert raw materials into products that are useful to humans. Certainly, one could claim that early cheese production and wine brewing techniques were examples of biotechnology. However, it wasn't until the Bayh-Dole Act was adopted in 1980 that the business of biotechnology began to come into its own and the industry began to expand.

Before the Bayh-Dole Act, less than five percent of the U.S. government's approximately 28,000 patents were licensed to commercial companies.

By allowing universities, small businesses, and nonprofit organizations to keep the rights to all of their federally funded inventions, the Bayh-Dole Act paved the way for these institutions – where most biotech discoveries take place – to license out their inventions to commercial entities.

Consequently, more universities and university researchers were motivated to find biotechnology solutions that can fulfill unmet needs. In addition, incentives to engage in technology transfer that could lead to the development of commercially successful products turned what was once a predominantly academic endeavor into something more practical. Needless to say, the Bayh-Dole Act spurred widespread commercial innovation in the biotech space.

2. Recombinant DNA Technology

Stanley Cohen and Herbert Boyer of Stanford University discovered and applied for a U.S. patent on recombinant DNA in 1974. Recombinant DNA is a technology that enables scientists to insert genes from one organism to another to create a biological molecule, clone genes, or insert foreign genes into another organism to give it new traits.

Although humans have been manipulating living things for thousands of years—from domesticating plants and animals to selectively breeding them for specific characteristics—it was only after human DNA was successfully inserted into bacteria and mammalian cell lines to produce the first human protein by cell culture that the modern biotechnology era began.

Recombinant DNA made the genetic modification of organisms possible—an application that has become very useful to the agriculture industry.

From then on, scientists could clone molecules in massive quantities. The technology became incredibly valuable as a research tool, allowing scientists, for instance, to determine the nucleotide sequence of any gene. It could also be used to create large amounts of protein to treat certain illnesses; Genentech, one of the pioneering biotechnology companies of its time, developed human insulin by culturing large quantities of bacteria that have been given the human insulin gene. Lastly, recombinant DNA made the genetic modification of organisms possible—an application that has become very useful to the agriculture industry, where the insertion of genes to plants to make them resistant to drought or herbicides is now commonly practiced.



3. Clusters of Capital

Perhaps you have noticed that biotech companies tend to cluster in certain geographic areas. In the U.S., for instance, biotech “hubs” can be found in San Francisco and San Diego, California; Raleigh, Durham, and Chapel Hill, North Carolina (also referred to as Research Triangle Park or RTP); and Boston, Massachusetts.

What exactly do these places have that foster innovation in the biotech space? Serial biotech entrepreneur Craig D. Shimasaki, in his book, [**The Business of Bioscience: What Goes into Making a Biotechnology Product**](#), cited five elements that can be found in abundance in and around these areas:

- **Venture capital willing to fund life science companies**
- **High-caliber academic and basic research institutions performing research in the life sciences**

- Entrepreneurial leaders with seasoned experience in growing and building biotechnology companies
- A talented scientific work force to support and grow biotechnology organizations
- Laboratory incubators that meet the particular needs of biotech companies

If you look at RTP, North Carolina, where BRI is located, for instance, you will notice that it has several universities and training centers with graduate programs not just in the life sciences, but also in business administration. These include Duke University in Durham, the University of North Carolina at Chapel Hill, and NC State University in Raleigh. NC State University is where BRI's Versazyme, a broad spectrum protease that helps poultry digest more protein from animal feed, was discovered.

In addition, RTP has one of the highest concentrations of people with PhDs in the nation. And not only is it home to **many venture capital and angel investor groups**, its General Assembly funds a **private, nonprofit organization** dedicated exclusively to biotechnology development. It also boasts several incubators and business accelerators, such as the **NC State Technology Incubator** and the Park Research Center, where nearly 80 startup and early stage companies are nurtured.

In the last few years, however, as state and local governments began to realize the economic value of the biotech industry, new biotech clusters are emerging in a variety of regions across the U.S. and around the world, as more resources to support research and development in the life sciences are allocated and distributed. So it won't be long before biotech innovation will find its way into all corners of the world as the industry continues to grow and evolve.

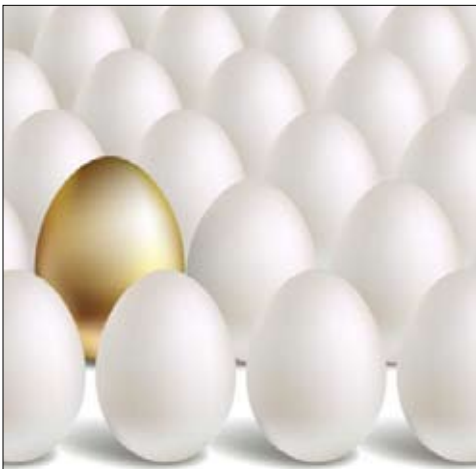


The RTP region in NC is the location of several universities and training centers with graduate programs in both life sciences and business administration, including Duke University, the University of North Carolina at Chapel Hill, and NC State University.

Five “Must-Have” Qualities of Biotech Entrepreneurs

There are many skills and attributes that successful biotech entrepreneurs possess. Many of these attributes are not unique just to biotech startups - other types of successful entrepreneurs have them too. However, a biotech company not only faces the same risks that all startup businesses face, but also a number of other, unique challenges. Because starting a biotech company is a high risk, high reward endeavor, it takes a certain entrepreneurial personality to successfully do it.

The following is a list of five qualities that we feel are important to become a successful biotech entrepreneur:



1. Vision

When you think about the future, do you imagine how things might be different? Do you like working out possible solutions to existing problems in your head, no matter how vague or improbable they may be? The most successful biotech entrepreneurs tend to have unusual foresight; they can imagine innovative solutions to problems, even if they have yet to figure out how to manufacture or implement those solutions.

But foresight isn't enough. Successful biotech entrepreneurs also need to have the driving desire and discipline to follow through on their vision. This trait keeps the fire lit over the course of many years, which is typically how long it takes to develop a new technology or therapy. It keeps them from giving up even as they encounter obstacle after obstacle on their path to success. Persistence in implementing your vision is absolutely necessary, because take it from us here at BRI - there will be many challenges along the way!

2. Self Awareness

Even the most gifted individuals do not possess all of the skills necessary to run a biotech company. No one can be the company's go-to scientist, business strategist, negotiator, human resources manager, project manager, legal consultant, financial consultant, marketing consultant, or systems administrator.

Having blind spots with regard to your strengths and weaknesses can lead to too little or too much delegation, micromanagement, and miscommunication of directives and intentions.

This may sound like common sense, but just because you are the world's leading expert in a specific biotech field doesn't make you the world's leading expert in all the aspects of leading and managing a biotech business. Having blind spots with regard to your strengths and weaknesses can lead to too little or too much delegation, micromanagement, and miscommunication of directives and intentions. Successful entrepreneurs constantly look for ways to get honest feedback from mentors, colleagues, and employees, and they work with other team members who can compensate for their weaknesses.

3. Cross-cultural Communication

Successful biotech entrepreneurs can communicate what they do to non-experts in a clear manner, as well as quickly grasp new information. If you have a scientific background, take the time to understand the marketing, financial, and business issues that are

relevant to your goals. Conversely, if you have a business background, you need to be well-versed enough in the technical and scientific issues to ask relevant questions and acquire the information you need.

Being "bilingual" in this sense is crucial because biotech entrepreneurs often wear different hats and need to be adroit in shifting between the scientific and business worlds. Scientists tend to be very logical and detailed-oriented. They are trained to be skeptical when analyzing data, which helps ensure the soundness of research. Business people, on the other hand, are more interested in taking and managing risks that will help move the company forward. Thus, having the ability to "speak" both business and science is a key skill of the successful biotech entrepreneur.

4. Non-linear Thinking

Running a business is a heuristic endeavor. In his book, *Drive: The Surprising Truth about What Motivates Us*, Daniel Pink distinguishes between algorithmic and heuristic tasks. Pink writes:

"An algorithmic task is one in which you follow a set of established instructions down a single pathway to one conclusion. That is, there's an algorithm for solving it. A heuristic task is the opposite. Precisely because no algorithm exists for it, you have to experiment with possibilities and devise a novel solution. Working as a grocery checkout clerk is mostly algorithmic. You pretty much do the same thing over and over in a certain way. Creating an ad campaign is mostly heuristic. You have to come up with something new."

NEWS FLASH: businesses are started and run by humans (not robots), and problems involving humans are typically solved through the nonlinear thinking that fuels heuristic tasks. Successful biotech entrepreneurs are able to jump forward, backward, and from side-to-side through the steps of any project while keeping their eyes focused on the goal. The seemingly paradoxical dynamic of being focused while remaining flexible is the hallmark of many successful biotech entrepreneurs.

5. Constant Learning

You probably don't buy as many music CDs as you used to; people's ability to download digital music has severely crippled the music CD business, just as CDs previously took over the market for audio cassettes. The business landscape is always changing. Newer technologies and methodologies are constantly being developed, and one of them could eventually render your product obsolete. Your customers' needs could change. State and federal governments could adopt regulations that do not favor your business.

Furthermore, if your business reaches any level of success and/or if you hire more people, the culture within your company will shift.

The environments within and outside your company are ever changing, so the skills you'll need to navigate them must evolve as well. To be successful in your entrepreneurial endeavors, you have to constantly learn and evolve yourself.

This "learning" can take many forms, from attending meetings and lectures, to reading relevant business books, to joining and participating in the activities of professional organizations (local organizations such as [CED](#) and [EO](#) have been instrumental in my learning and professional development as CEO of BRI). Also, I can't say enough about having good mentors who can guide you along the way.

So do you have what it takes to be a biotech entrepreneur? Don't worry if not all of these 5 qualities resonate with you. Just as there are various types of leaders, there are many types of entrepreneurs. As I see it, biotech entrepreneurship is a "full-contact marathon," – full contact in that it requires commitment of heart, mind and spirit, and marathon because it demands discipline and perseverance. The sooner you realize that, the sooner you will be on your way to biotech startup success!



Ready, Set, Go: Getting Your Biotechnology Start-up “Started Up!”



We have since provided you with an overview of the “perfect storm” that ushered in the modern biotechnology era, the risks associated with starting a biotech company, and the qualities that a biotech entrepreneur must have to successfully manage those risks. If after reading this far, the lure of biotech fortunes and being your own boss still is compelling you to take the risk and start a biotech company, here are just a few things to consider before you make the leap:

Is there a large enough market opportunity?

Your idea may be novel, useful, and scientifically sound, but if it’s applicable to only a few hundred people, then you’d find it very difficult, if not impossible, to capture the interest of biotech investors. Most biotech investors look for market opportunities that are north of \$100 million.

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Is there a significant need or “pain” in the marketplace?

Biotech investors want products that address significant needs in the market, not “me-too” products. In order for your idea to become widely applicable, it should meet a need more effectively than current offerings.

Is there scientific and technological merit?

The time it takes to develop a marketable biotech product—several years to over a decade—makes it very difficult for potential investors to value a biotech startup. As such, they rely heavily on subject matter experts and the quality of research published in peer-reviewed journals.

How far can you take your idea?

Are you looking to develop a single product or a platform technology that can support multiple products? Recombinant DNA technology, for instance, is a platform technology that has since supported the development of numerous products, including human insulin, hepatitis B vaccine, and herbicide-resistant crops. Companies with platform technologies with multiple applications will have more “shots on goal” and thus be more attractive to investors.

Is this the right time to license the technology?

Technology Transfer Offices typically like to license-out a technology when you've reached a trigger point, like some form of investment, an experienced entrepreneur joining the company or a partnering event.

Obtaining a License



Now that you've done a thorough evaluation of the market opportunity, scientific merit, and potential for long-term growth of your biotech start-up, the next order of business is to get control of the technology, usually in the form of a license agreement with the institution that owns the patents or technology. Biotech companies live and die by their patents. Investors will not risk their money on your idea if you do not have a legally defensible monopoly on the market, so a key milestone is first securing a license for the technology you're planning to develop.

As discussed earlier, the biotech industry began to expand in the early 1980s after the Bayh-Dole Act allowed universities and nonprofit organizations to own the rights to all of their federally funded inventions. So if you want to commercialize one such invention, even if you're the one who invented it, you'll first have to secure a license from the organization that owns the intellectual property.

As a case study, Versazyme, a natural feed enzyme that increases the digestibility of protein in feed, was discovered by BRI co-founder Dr. Jason Shih while developing a thermophilic poultry waste digester at North Carolina State University. Dr. Shih was a researcher and professor at NC State University's Department of Poultry Science at the time, so when we decided to form a company and commercialize the enzyme, we negotiated with NC State to transfer all intellectual property relevant to the discovery – six patents in all – exclusively to BRI.

As more academic institutions realize the value in commercializing inventions and discoveries developed by their own faculty and staff, many have established a Technology Transfer Office to help in licensing that technology out to private for-profit enterprises. The tireless staff in these offices provide guidance in planning a patent strategy; implementing such strategies; and negotiating and executing non-disclosure agreements, material transfer agreements, and license agreements with startups and established companies.

However, there are differences in the sophistication and efficiency of the licensing process from one institution to another, so we encourage you to contact the transfer or licensing office of the institution that you're interested in to learn more about their licensing philosophy. A good resource for information and networking in this space is the [Licensing Executives Society](#).

4 Factors To Keep In Mind During Licensing Negotiations

We have already established that one of the crucial first steps for biotech companies starting out is to obtain full control of the technology that they're planning to commercialize, and that control typically comes in the form of licensing agreements with institutions that own the patents or technology. Here are 4 factors that you should keep in mind when negotiating your license agreements:

1. Consider the type of industry and technology application.

The terms of a license can vary greatly depending on the type of technology you're interested in. Royalties for therapeutics and biologics are generally higher than those for diagnostic and medical devices.

Rates can also differ depending on how far along a product is on the development pipeline, whether the license you seek is exclusive or nonexclusive, how competitive the market is for the product, and how important the patent will be to you (patents for core technologies will typically command higher royalties).

The following table lists general ranges for some financial terms that may be found in a licensing agreement. Note that the trend in most biotechnology licenses is a small up-front fee, high milestone payments, and mid-high royalties.

	THERAPEUTIC/BIOLOGIC	DIAGNOSTIC/MEDICAL DEVICE
Typical up front license fee	\$25,000 - \$1,000,000	\$25,000 - \$50,000
Potential milestone payments	Varies from \$25,000 to multiple millions based upon the stages and technology	Varies from none to millions depending upon the technology
Estimated royalties	5% - 12%	0.5% - 7%
Estimated minimum annual royalties	\$50,000 - \$1,000,000 or more depending upon the technology	\$20,000 - \$100,000 or more depending upon the technology

Source: Shimasaki, C.D. (2009). The business of bioscience: What goes into making a biotechnology product. New York: Springer Science + Business Media.

Other terms that may be considered are maintenance fees, sublicense fees, and the assumption of ongoing patent expenses.

2. Have a plan.

Those who fail to plan will plan to fail. It's important to put some thought into a good business plan that showcases your expertise, potential, and initiative before coming to the table to negotiate. Licensing institutions have a vested interest to transfer the technology to those entities with a decent chance of success in commercializing the technology.

That said, they won't expect a full-fledged executive team and immediate investment commitments, but there needs to be some road map for how your company will reach its milestones and be successful.

3. Don't go at it alone.

Licensing negotiations is a team sport. Don't attempt to negotiate a license agreement by yourself! Work with a legal team that is proficient in contract law and ideally has some partners who understand the risks and challenges that bio-tech startup organizations face.

4. Don't burn bridges.

Whatever happens, do your best to maintain amicable working relationships with licensing institutions. License negotiations can take up to a year with several meetings and back-and-forth communications. You may need the institution's help even after you've come to terms, such as when future business partnerships or terms of financing require that you renegotiate certain aspects of the license.

While it all may seem quite daunting for the uninitiated, take comfort that there is a method in all this madness, as well as several individuals and organizations that can guide you.

Licensing institutions won't expect a full-fledged executive team and immediate investment commitments, but there needs to be some road map for how your company will reach its milestones and be successful.



How to Choose the Right Legal Team for Your Biotech Start-up



President Harry Truman once said: “If you want to go fast, go alone, if you want to go far, go with others.” The same can be applied to start-ups. If you want to build a sustainable, scalable, and successful biotech enterprise, you need to work with others who can compensate for your weaknesses. (If you believe you have no weaknesses, then this whitepaper has nothing to offer you!)

Take legal expertise, for instance. You need access to legal expertise to make decisions on everything from the best corporate structure for your business, to the impact of contractual terms, to best practices in intellectual property protection, to the implications of tax law. However, you likely do not possess the depth and breadth of legal skills necessary to do all this. Nobody can be their company's go-to

scientist, business strategist, and legal consultant at the same time. Luckily, in most business-friendly regions, there are several law firms that can help start-ups on an as-needed basis. Some might even waive or discount their initial fees.

So how do you go about finding the right attorneys to help your biotech start-up? Consider these 4 steps:

Ask other biotech entrepreneurs.

Don't just rely on advertisements and company websites. If you know other entrepreneurs who've successfully grown their own biotech companies, ask for the names of attorneys they've used, who among those attorneys they'd recommend, and why. If appropriate, ask for anecdotes that illustrate an attorney's competence and value. The more specific your peers are in describing their attorneys' contributions to their businesses, the more informed your decision will be.

Consider legal specialties.

Corporate law firms who specialize in or have a dedicated practice group in the life sciences are more likely to understand and appreciate the challenges and risks that biotech start-ups face. You can find many of them practicing in biotech clusters such as San Francisco and San Diego, California; Research Triangle, North Carolina; and

Boston, Massachusetts. These lawyers can also offer you the added benefit of contacts in the venture capital and biotech industries, which might be helpful in future efforts to raise capital and/or find business partners.

Go local.

You may not have this option if you operate in an area with very few biotech start-ups. But if you do, and all things are equal, choose a local attorney over one that is out of town. Even though technology has drastically changed how we communicate, the ability to have face-to-face meetings with your legal team when you need to without having to hop on a plane will save you much in time and expenses.

Remember, your legal team will be spending many hours over the years advising you. You need to be sure you're comfortable working with them.

Start small- to medium-sized.

Unless they have smaller practice groups within their firm that specialize in the life sciences, very large law firms are more likely to assign less experienced associates or junior staff to your business. As a start-up with a wide range of needs, it's better to work directly with a partner or a senior member of a small- to medium-sized law firm who can draw on years of experience for advice, than with a junior attorney fresh out of law school, even if that attorney works at a prestigious firm.

When you find attorneys who meet most or all of these criteria, be sure to spend a significant amount of time meeting and talking with them before making a decision (most of them have budgets for "client development" and won't charge for initial meetings). Ask them to explain a few relevant terms and cases that you don't fully understand.

Remember, your legal team will be spending many hours over the years advising you. You need to be sure you're comfortable working with them. Also, they need to be able to distill their knowledge and experience into advice that's relevant to your business. Ask yourself: Are they good communicators? Are they good educators? Are they patient with your follow up questions?

While you're not bound indefinitely to just one law firm for all stages of your biotech enterprise, whom you choose for legal counsel will be one of the most important and impactful decisions you can make as a start-up entrepreneur. Choose wisely, and your legal team will become one of your most trusted advisors as you grow your business.

6 Components of a Strong Biotech Business Plan

One of the things that make the biotech industry unique is the significant amounts of money that businesses will need to develop a product. While internet or software companies can commercialize a product through bootstrapping or after just one round of seed funding, a biotech firm will typically need three, four, or even more rounds of fundraising. On average, it costs between \$25 million to \$100 million to develop new medical diagnostics and devices, and more than \$1 billion to take new drugs from the laboratory through regulatory approval to sales.

Raising money will arguably be the single most time-consuming activity you will engage in as a biotech entrepreneur.

There's no way around it: raising money will arguably be the single most time-consuming activity you will engage in as a biotech entrepreneur. And to be successful, you'll need to start with a strong business plan. Based on our experience, here are 6 key components to include in a biotech business plan:

1. Market Opportunity

You will need to describe what problem your product will solve, how painful that problem is (cancer is a much more painful problem than hiccups), and how many people have it (biotech investors will generally only invest in market opportunities north of \$100 million). You should also show that there's currently no solution available, or if there is, that it's either ineffective or significantly inferior to yours. Don't be intimidated if you're dealing with the latter; the presence of competitors is actually a good indicator of market opportunity.

2. Intellectual Property

As previously mentioned, patents give your company a legally defensible monopoly on the market. You will need to present your patent portfolio and whether the patents are issued or pending, U.S. or global. With no product in sight for approximately three to 10 years, intellectual property is one of only a few assets upon which a biotech start-up company's valuation is based.



3. Market Strategy

Once you've demonstrated that there's a significant market need, you'll need to discuss your strategy for capturing that market and your time frame for implementing it. You'll also explain why you think your strategy will work based on your understanding of customers (e.g., their needs, purchasing habits, etc.); how your product will be priced and why your price points make sense; and how it will be sold and distributed. This section will probably also need to discuss some of the potential partners in your space, as biotech companies often hand off late stage development to larger companies with deeper pockets.

4. Financial Projections

In this section, you'll describe how much money you intend to raise and how it will be used to achieve product development milestones. You'll also estimate your gross margins, net income, expenses, cash flow, and balance sheet on a pro-forma basis for the next several years. Broad categories such as "Administrative" and "Marketing Support" would suffice; investors understand that it's impossible to make detailed projections too far into the future. Support a positive outlook with evidence.

5. Management Team

Here, discuss the qualifications of your management team and explain how they can help your company achieve its goals. For the purposes of funding, focus on business leadership and scientific/technical expertise. Is your CEO a serial entrepreneur with a track record for founding and growing biotech companies? Is your Chief Scientific Officer widely published in prestigious journals? Highlight those qualities. If you don't have a complete executive team, don't worry; most start-ups can't immediately afford to hire the expertise they need. However, be sure to discuss how you plan to obtain that expertise, such as by initially relying on consultants.

6. Executive Summary

Here is the plain truth: investors rarely have time to read through an entire business plan. With possibly hundreds of startups vying for their attention, many will just commit to reading the Executive Summary. Then if – and only if – they find it compelling enough, they'll ask for the plan itself. Thus, the Executive Summary is not an introduction to the business plan; think of it rather as like a resume, a standalone document that succinctly highlights key attributes, and whose goal is to entice investors to follow up and learn more.

Your business plan is intended to be a living document. Update it whenever significant changes occur in your technology, business model, marketing strategy, or management team composition. Lastly, since you're completely swamped with all the commitments associated with starting a biotech company, you may be tempted to outsource the writing of your business plan to a third party. My advice is to avoid doing that. Hire consultants to help you edit and bounce around ideas, but the plan should be a document that you write yourself. The discipline of thinking through and writing a comprehensive business plan is almost as important as the end product itself.

Raising Capital: The Good, the Bad, and Ugly

Fundraising for your biotech start-up can be tricky because you want to secure just the right amount of money. Raise too much during the early development stages, and you risk diluting ownership equity. Raise too little, and you risk running out of cash before you reach a major commercial milestone. This dilemma is further complicated by the fact that it's actually quite difficult to figure out just how much capital you'll need to grow your start-up because life science research is often unpredictable.

One way to reduce risk and optimize the process is to use what is known as the "stair-stepping" method. It entails raising only enough money, with some cushion, that would enable you to reach the next milestone – and then repeating the process for each milestone until you're done. That way, each time your company achieves a higher level of growth, it will enjoy a significant increase in valuation, thus minimizing the dilution at each stage of growth, and making it more feasible to secure the next round of funding.



So where can you go to raise capital? Consider the following sources of funding for biotech companies, each with different interests, values, and limitations (roughly listed in order of the most likely to least likely funding source):

Personal Money

I don't necessarily recommend this because a biotech start-up is inherently a risky venture, but I know of many successfully entrepreneurs (including BRI's founders) who've used credit cards, home equity loans, and even second mortgages to help fund their start-ups. It's fairly common for entrepreneurs to invest in their own companies. It doesn't have to be a large amount – in fact, staking most or all of your net worth can be considered financial naiveté by investors. On the other hand, investing a reasonable amount can demonstrate commitment (i.e., "skin in the game").

Friends and Family

These people will generally invest in your company because they believe in you, and not because they have an understanding of the technology or market opportunity. Most also won't grasp the extraordinarily high risks

faced by an early stage biotech company. You wouldn't want people you care about to risk their life savings. If you're going to take money from this group, make sure they're **qualified investors**, meaning that they have an individual or joint (with their spouse) net worth of \$1 million or an annual income exceeding more than \$200,000 (individual) or \$300,000 (joint).

Angel Investors

These are high net-worth individuals, working either alone or in groups, who invest in companies during the seed or early development stages. Unlike friends and family, they're more likely to invest because they understand the industry and/or market need. They rarely advertise their activities, however, so the best way to find them is by getting referrals from local universities and research institutions, business networking groups, and fellow biotech entrepreneurs. Angel investors generally prefer to work with local businesses.

SBIR Grants

The goal of the **Small Business Innovative Research (SBIR) grant** is to help companies move technologies and concepts from the research and development stage to the commercialization stage. The grant application process is highly competitive, but if you win, the money is significant: up to \$150,000 or more over six months for Phase 1, and up to \$1 million or more over two years for Phase 2. And because winning peer-reviewed grants adds tremendous credibility to your research, they're looked upon favorably by investors. SBIR grants are offered through federal agencies such as the **U.S. Department of Agriculture**, the National Institutes of Health, and the **National Science Foundation**.

Venture Capital Firms

Few biotech companies can bring a product to market without venture capital (VC) support. In later stages of product development, you're going to need much more than the typical \$25,000 to \$250,000 of angel investment. Venture capital firms are professional, institutional managers of risk capital and typically invest anywhere between \$1-20 million. They also bring in valuable industry expertise and connections that can increase your likelihood of success. You can search for VC firms in the United States on the **National Venture Capital Association website**. Look for firms that have a successful track record in the biotech space.

BRI tapped into all of the sources listed above to fund our start-up venture, but each company has a different path to fundraising. Some rely solely on SBIR grants and angel money, while others go directly toward the venture capital route. However way you decide to raise money, you can avoid raising too much or too little by always having a clear idea of what the money will be used for. How much you need until the next milestone will depend upon your product, technology, and/or business model. Lastly, always raise a bit more than the anticipated need, because getting to the next milestone will almost always take longer and cost more than you think it will.

Why Your Biotech Startup Needs a Partner (or Two, or Three)

There are lots of risks and uncertainties in doing a biotech startup, but at least one thing is certain – you are not likely to do it alone. For your startup to be successful, at some point you will need to develop, test, manufacture, or market your new technology or therapeutic. And because of the tremendous amount of resources to transition from bench top to bedside (or in BRI's case, barnyard), a biotech startup will almost always be well advised to form strategic partnerships to be commercially viable in the long term.



So when putting together your business plan, think about the various steps in your “value chain” (e.g. prototyping, pilot scale manufacturing, commercial scale-up, marketing, etc.), then brainstorm the types of partnerships you'll need to complete each of them. Most successful biotech companies form several different types of alliances simultaneously to diversify risk and leverage the strengths of different partners.

Partnerships Can Supercharge Growth

BRI is an example of how partnerships can help accelerate business growth. When BRI co-founder Dr. Jason Shih discovered, isolated, purified the unique strain of bacteria that produced a novel enzyme that forms the basis of Versazyme® and Valkerase®, he knew he could only scale up the production to a certain level. Luckily, we found two companies willing to perform large-scale enzyme fermentation for us and were able to bypass the risk and cost of building our own fermentation facility. While we have since built out some limited manufacturing capacity in-house, these early supplier partnerships enabled us to invest our precious capital in other key areas of the company.

Partnerships and strategic alliances are especially crucial if you plan to expand your business overseas. In addition to being cost-effective, local partners can help you navigate the considerable cultural and regulatory differences between your home country and the country you're attempting to penetrate.

At BRI we've always taken more of a global view, and so in 2008, we were fortunate to partner with Novus International, an animal health and nutrition company that operates in over 90 countries, for the global distribution of Versazyme and Valkerase. As a result of the partnership driving sales growth in the global markets, BRI has grown

tremendously, such that in 2012, Inc. magazine included BRI in their Inc. 500 list of America's fastest growing companies.

You'll Have to Kiss a Lot of Frogs

So how exactly do you find strategic partners for your startup? Not unlike other aspects of business, the answer is to "network, network, network." You can participate in conferences that provide structured opportunities for companies to discuss potential partnerships, such as the BIO International Convention, the JP Morgan Healthcare Conference, and other industry specific conferences. If you're working with angel investors and venture capital firms, they can be a deep resource for introductions to potential partners.

As you can see, you'll have to kiss a lot of frogs to find your prince. As a startup, you'll likely be seeking alliances with larger companies that want to expand their business (e.g., add a product line, enter a new market, etc.)

Expect multiple discussions, meetings, and follow-ups, typically with their business development units, as both parties assess whether there is a good fit. One key success factor is finding an internal champion within the company you'd like to partner with who can help keep the discussions on track and moving forward.

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While it's extremely rare for a biotech startup to commercialize a product without forming strategic partnerships, be sure to choose wisely, as the wrong partner could impede growth and/or destroy value. Alliances fail when businesses don't have a clear understanding of each other's goals, needs, and contributions. So make sure your partnership's objectives are clearly defined and communicated, keep building trust between the key players, and manage the progress of your partnership in a way that is positive and mutually beneficial.

Company Life Stages and Happy Endings

This whitepaper has provided an overview of issues that aspiring biotech entrepreneurs will likely encounter on their road to success – covering, among other things, licensing, business planning, financing, personnel, and strategic partnerships.

As you start and grow your startup company, we hope that being aware of the different life stages a company typically goes through can help you not only manage your business successfully, but help set you up for a successful exit or growth plan.

If you've read Stephen Covey's bestselling book, *The Seven Habits of Highly Effective People*, then you're familiar with Habit 2: Begin with the End in Mind. Each stage provides an exit or a beginning of a new opportunity. Are you looking to be acquired by a large pharmaceutical organization after achieving a certain product development milestone? Would you like to merge with a larger firm? Or are you aspiring to create the lasting legacy of a sustainable business? The type of "ending" you have in mind should inform your goals and focus your actions.



Expect to transition through the following continuum as your business grows:

Startups do not have clearly defined roles. Everyone weighs in on a decision and pitches in during a crisis.

Start-up Phase

We like to compare the dynamics of a startup to a team of first graders trying to play a game of soccer. If you've ever seen little kids play soccer, you'll know that they typically ignore their assigned positions. Everyone rushes to the ball, and whoever gets to the ball first kicks it away and the scrum then chases after where the ball goes to next, until either the ball gets out of bounds or ends up in the goal.

It's the same with a startup. You don't have clearly defined roles. Everyone weighs in on a decision and pitches in during a crisis. Most members on the team are generalists

and comfortable playing "out of position" as needed. During BRI's early years, Giles Shih, BRI CEO, had to be a jack-of-all-trades and wearer of many hats because that's what the company demanded.

Growth Phase

Your players are starting to kick the ball around. There are more of them on your team, and they have a better idea of what position they're supposed to play and what their and their teammates' responsibilities are. You've also assigned some of them to carry some portion of the leadership role that was once entirely yours. As a result, you're operating more efficiently.

Dr. Shih knew BRI had transitioned from startup to growth phase when he could take a week-long business trip without getting a panicked phone call asking me to handle a crisis or weigh in on a decision that had to be made. However, he continued to communicate frequently and interact personally with his team. Good communication skills are a "must-have" for biotech entrepreneurs but especially during this phase, when adding more layers to your organizational structure can strain existing communication channels.

Scale Phase

You've won your first few games and are feeling good about the prospects for the season. You've developed at least one marketable product, and it's time to build and grow a market for it. So you expand your capabilities, train more leaders at new levels of the organization, add more staff, and further clarify roles. You work to maintain your team's creativity and flexibility while streamlining company processes.

You also look for strategic alliances. Scaling a business is something that a biotech company rarely achieves by itself. BRI was able to expand to Asia by working with companies that could perform large-scale enzyme fermentation (and thus avoid the risk and cost of building our own fermentation facility), as well as with Novus International for the global distribution of Valkerase and Versazyme.

Sustainable Phase

You're playing at the elite level! Only the most successfully resourced and managed companies reach this phase. By this time, you have fully developed capabilities; you typically own multiple businesses that fall under the umbrella of your organization, and they produce, manufacture, and market your portfolio of diversified products.

Significantly lower costs, combined with a strong and growing market share, earn healthy profits for your investors. But you're not complacent. You keep

Once your company reaches the elite level, it typically has multiple businesses that fall under its umbrella that produce, manufacture, and market your company's portfolio of diversified products.

researching, innovating, and looking for new markets to penetrate. Your company's not as nimble as it used to be, but you feel it's a fair trade given that you're a respected key player in the industry. By this time, some of your employees may also leave to found biotech startups of their own, thus starting the process all over again.

While you can exit at any stage, being operationally efficient within the stage you are at is critical. That way, you can leave on your own terms, at a price that's reasonable to you. Of course, there are also instances when your point of exit could be dictated for you, such as changing external circumstances or investors' expectations. With startup funding at an all-time low, we understand why many would-be biotech entrepreneurs would find it difficult to make it through the various life stages described above. But it can be done. While BRI is far from the poster child for successful biotech startups, it's a good example that the model does work.

After many long days and nights, and working through various crises and challenges, BRI can say that we are finally turning the corner from Growth phase to Scale phase. And in this high risk, high reward business, we're here to tell you that oftentimes if you believe it, you can achieve it!



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