How to start a biotech company

Adriana Tajonar
California Institute of Quantitative Biosciences (QB3), San Francisco, CA 94158-2330

ABSTRACT **The spirit of life science entrepreneurship is alive and well, with outstanding innovation hubs arising throughout the country and the world. Of note, many of these hubs flourish in close proximity to research universities. If universities are the engine for discovery, then startups are the vehicle for innovation. The creativity and drive of young researchers has the potential to explore novel or underserved applications and revolutionize industries.**

Monitoring Editor
Doug Kellogg
University of California, Santa Cruz

Received: Aug 1, 2014
Revised: Sep 4, 2014
Accepted: Sep 9, 2014

INTRODUCTION

With the current exuberant energy surrounding biotech entrepreneurship, it is hard to believe that the industry is close to 50 years old. Much has changed since Herb Boyer, a professor at the University of California, San Francisco (UCSF), and Bob Swanson, a young entrepreneur and aspiring venture capitalist, started Genentech in 1976, giving rise to the entire biotechnology industry. Back then, spinning out a company was limited to faculty members or experienced biotechnology professionals. Today, the democratization of life science entrepreneurship is allowing graduate students and postdocs to apply their scientific expertise toward the commercialization of newly developed technologies. Much like the path of a PhD project, the life of a science startup is not straightforward, but there are some common milestones from birth to growth and success (Figure 1).

THE BIRTH OF A STARTUP

In 2009, Dan Widmaier was a fifth-year graduate student at UCSF in the area of synthetic biology. His research was centered on engineering *Salmonella* to produce and secrete spider silk. Spider silk protein has incredible tensile strength, being stronger than steel and tougher than the body armor and tire material Kevlar. Despite these properties, the silk extraction process has remained incredibly labor-intensive for hundreds of years, limiting its use mostly to luxury textiles. Dan saw an opportunity to use synthetic biology to streamline the production and extraction of spider silk. He convinced his lab-mate and collaborator Ethan Mirsky and microfluidics expert David Breslauer, then a graduate student at the University of California, Berkeley, to join him in creating a new company, and Refactored Materials was born in 2009. The team successfully applied for small business grants from the National Science Foundation and Department of Defense with their proposal for producing spider silk from engineered microbes for ballistic armor and medical device applications. The company started their operations out of a single bench in an incubator space at UCSF called the QB3 Garage. Since then, Refactored Materials has successfully raised two venture rounds and is going after the textile market, a much larger market than originally anticipated that has seen little innovation since Lycra in the 1950s. In a few years, expect your athletic clothes to be more breathable, your socks to be softer, and your silk garments to be more durable, all thanks to three grad students with a vision to change the world, one spider dissection at a time.

TURNING RESEARCH INTO AN AGENT OF CHANGE

There is no question that having a meaningful impact on society is a powerful driver for scientists. It is not surprising that so many of the discoveries that have improved our society by increasing efficiency, adding capabilities, and bettering health have come from basic research done in universities. Universities, however, are not equipped to fully translate technologies out of the academic lab into the market, and a separate vehicle is needed to truly fulfill the promise of societal impact. Certain efficiencies in the industry environment are rare in academia. This has been the case since Genentech's inception and remains true today, a reminder for young scientists and future entrepreneurs that industry is the conduit for translational applications.

Startups are the vehicle needed for this translation for three key reasons. First, startups can address key technical risks and arrive at go/no-go decision points with relatively low amounts of capital and close to no overhead. Of importance, thinly capitalized startups are

DOI:10.1091/mbc.E14-06-1162

Address correspondence to: Adriana Tajonar (adriana.tajonar@qb3.org).

Abbreviations used: CEO, chief executive officer; IP, intellectual property; LLC, limited liability corporation; NDA, nondisclosure agreement; QB3, California Institute of Quantitative Biosciences; SBIR, Small Business Innovation Research; STTR, Science and Technology Transfer Research; UCSF, University of California, San Francisco; VC, venture capital, venture capitalists.

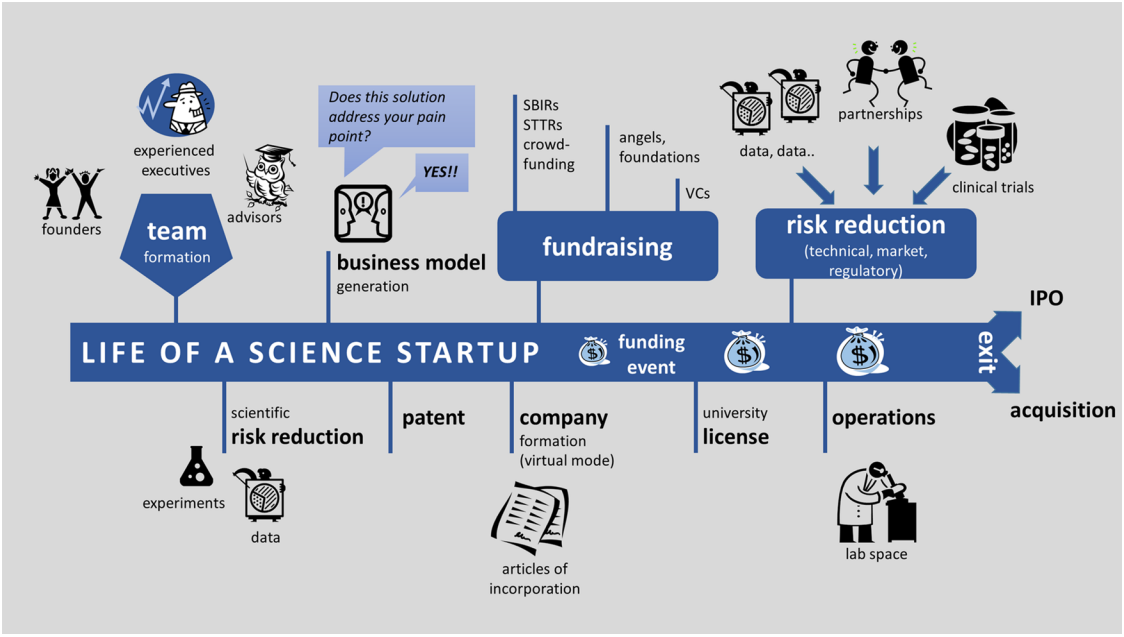

FIGURE 1: Life of a science startup.

incentivized to listen to their investors and advisors and act swiftly, a feat that is easily said but more rarely achieved in the academy. If the startup wishes to survive, the achievement of milestones is not optional. Thus every experiment is tailored at answering go/no-go questions. Data must be not only publication worthy, but, more important, worth millions of investors' dollars and years of work. Second, founders must constantly assess risk, and a thorough study is essential to select the best market for a technology with several potential applications. The selective pressures for an early stage startup are extremely high when all the contributors to a viable business model are considered. These pressures enable a competitive marketplace for the best ideas. In such a marketplace, the startup structure allows for the ability to "pivot"—to remain nimble as the business model evolves. Startup founders can ensure that the technology has a viable market and create a validated plan to get there. Third, startups allow the correct alignment of incentives for their founders in terms of real-world impact and financial return. Students and postdocs are at a point in their careers at which they can dedicate the time to build this opportunity, something that faculty founders usually cannot do. Science startups often involve the original inventors behind the innovation—postdocs or graduate students who can easily address key proof-of-concept questions and develop the original technology. In most cases, it was at the hands of these young scientists that the invention materialized, so the sense of ownership is strong, and they remain very passionate and motivated to see their work address a real-world need (and reap the benefits of their effort).

ADVICE POINTS

At QB3, the California Institute of Quantitative Biosciences, we have helped more than 200 teams of scientists start companies through the Startup in a Box Program. Of these teams, 65 have successfully raised funds within the first 18 months of coming to QB3 for help. Two-thirds of the teams come directly from academia, with postdocs or graduate students at the helm. Following are some lessons for the life science entrepreneur-to-be.

Identify the unmet need that your technology addresses

The best way to articulate your solution and the value of your approach is to clearly state the problem you are solving. It is important to solve a problem you are passionate about, but there must be a large enough market for this technology; in other words, make sure that there are enough people who care about this problem enough to pay for your solution. Going after a small or niche market is acceptable, too, but your sources of capital will be fewer, and you will need to clearly articulate how your company can even recover its costs. When looking for your market, "don't be a hammer in search of a nail"; that is, be objective when identifying a need instead of trying to make your special interest into a market that might never exist.

Build a high-quality, well-rounded team

No startup was ever created by a single person. When starting a company, find one or more cofounder(s) with complementary skill sets. For example, if you are a cancer biologist and your idea is to develop new cancer therapeutics, find someone with pharmacology or drug development experience. If you have a clinical background and want to develop a medical device, find an engineer. In the case of Refactored Materials, Dan had the chemistry know-how, Ethan brought in the electrical engineering and operational expertise, and David was able to spin fibers thanks to his microfluidics background. Having a cofounder has multiple benefits, from expanding the company's skillset, to having a sounding board and accountability partner, to showing investors that you can work with others.

Having a well-rounded team with the best people you can recruit is a key asset for a startup. Faculty cofounders commonly remain involved as advisors or board members. If your team is made up of academics, it can be extremely helpful to find an experienced entrepreneur or executive with startup experience. A youthful team is great, but an experienced person will help anchor the team and give you credibility in front of investors. The same goes for qualified mentors and advisors: everyone in your team should be passionate about the company's vision and mission.

Understand incentives, and use them to drive your company to success

Once you have put your all-star team together, make sure the people involved are incentivized to do their best work for the company. At the very early stage, you will not have the funding needed to steal your colleagues away from a salary in industry, consulting, or any salary for that matter. Therefore you give equity or shares in your company tied to a vesting schedule, allowing your cofounders and early employees to participate in the ownership of your company. Initially these company shares will be worth very little, but the idea is to incentivize high-quality work that will drive up the value of the shares with a large potential up-side to the shareholders. Equity is also a vehicle to recruit an experienced entrepreneur, senior advisor, or consultant with unique expertise to help your company.

Get quality legal advice

A good lawyer will become a key advisor in the early stages of your company, so it is crucial to seek out quality legal advice in the field of your startup (a lawyer with experience in real estate can help little when it comes to a company inventing cardiovascular implants). Yes, it is pricey, but you really get what you pay for, so it is worth spending slightly more to set up the foundation of your company correctly. Many large law firms have special incentives for startups, often with fees deferred until a funding event happens. In terms of company formation, make sure you choose the company structure that fits your business model best. For example, if you will need to incentivize early advisors with equity and if you will need to seek private capital to bring your product to market, a C-corporation makes more sense. If you will be operating as a service and do not depend on raising investor dollars, you might consider a Limited Liability Corporation (LLC). A "quick and dirty" online site to register your company may seem appealing now, but try to avoid it—fixing all the problems later will cost more money, and it will create unnecessary paperwork and transactions.

Your intellectual property (IP) is also one of your most valuable assets, so make sure you secure it early and well. If you are filing your own patent, craft the claims so that your technology is protected as broadly as possible; if you are licensing IP (for example, from a university), do this early and seek your lawyer's counsel to make sure the license terms are acceptable.

Money, money, money—search under every rock

There are many sources of early-stage funding: Small Business Innovation Research (SBIR)/Science and Technology Translation Research (STTR) and other federal grants, angels, venture capital (VC), foundations, crowd funding, friends, and family. Explore them all, but be prepared to roll up your sleeves and write some grants. SBIRs and STTRs are grants by any federal government agency that has an annual budget larger than $100 million. Familiar sources such as the National Institutes of Health, National Science Foundation, Department of Defense, and Department of Energy participate and provide these types of grants. The process is involved and competitive, but many successful companies, including Refactored Materials, started on the backs of these grants. Most VCs and angels have moved farther down the pipeline to where the technology has been de-risked, so government grants are certainly worth your time and effort. As an example, one-third of Startup in a Box graduates started operations on the back of SBIRs.

Finally, leave no rock unturned. It is always helpful to start building relationships with your potential future investors to understand what is needed for a "yes" later on and ask for advice before asking for money (the old adage, "if you want money, ask for advice," is certainly true in the early-stage investment world).

Respect your investors

Research your investors before meeting with them. Find out what their investment interests are and in which space they usually participate. This will help you spin your story appropriately in terms of specific application (if you have several possible ones), amount to ask for (some large investors cannot give you seed money), and your use of the funds.

Sooner or later, you will run into the rumor that you should not talk science with investors. Know that this is just a myth; sophisticated life science investors will want to understand the technology into which they are putting their cash. In the words of engineer and statistician William Edwards Deming, "In God we trust, all others must bring data."

Your investors will know more about the market than you will. This means that you do not need to dwell on the point that cancer is an important problem. Listen to your investors' advice even before they become your investors. Their insight can help you identify opportunities and refine your strategic thinking.

Be unfocused at the beginning, but learn to identify opportunities

This advice applies to technologies with more than one application, such as platform technologies; in such situations, it might be difficult to pick which application or market to pursue first. It is useful to think of having a strategy that includes an earlier or easier path to revenue. Large markets may be alluring as a first battlefield, but they are often plagued with regulatory and market risks. Find out whether there is a better route to establish your proof of concept, even if it is in a smaller market. Having a direct path to market will allow you to move quicker on fewer funds; this will make it easier to tackle the larger and more challenging market later on. Refactored Materials realized that ballistic armor and medical devices would be challenging markets to crack, and they received much interest from the textile industry. The door is open to come back to the other applications in the future, but the silk textile market is primed for disruption.

Identify your white-hot risk, and use your time wisely

There are many risks in the way of taking a scientific technology to market: technical/scientific risk, regulatory risk, market risk. Higher risk in any of these areas correlates directly with the difficulty of getting money (since the uncertainty of return on investment for investors is higher). Convincing investors to accept these risks strongly affects early stage companies, as they have the largest number of unknowns. Your goal as an entrepreneur is to focus on answering the questions that will help you address and decrease those risks. Understand what the major risks are that stand between you and getting to market, and focus your time on them.

Test and build your business model—no, you do not need a business person—yes, you can use a scientific approach, too

As a startup, one of your most important tasks will be to discover your business model, that is, how your company fits into the market. What is your value proposition? Who are your customers and partners? Do you understand how your product fits into the entire process or patient care procedure? If you are developing a diagnostic for a disease that has no current therapy, why will people be inclined to use (and pay for) your product? You might have answers to all

these questions, but at the moment they are really just hypotheses. The best way to validate these and develop your business model is to talk to relevant partners directly in a process developed by Steve Blank and called "customer discovery" (Blank and Dorf, 2012). The founders are the best people to do this validation, since they have a deep understanding of the technology and can make changes to the model (or pivot) if necessary. So, in Blank's words, "Get out of the building!"

Be lean

Money is the lifeline of a startup, and you will never have enough. You must use it wisely when you have it, and take it whenever you can. Make a budget and prioritize to ensure that your resources are going toward your key activities, and follow this plan with superb execution: in other words, be a *lean startup*. For example, you do not need to hire a full-time business person from the beginning; instead find someone who is willing to work with your company as an advisor or interim CEO in exchange for equity and reduced (or no) pay. If they believe in your company, they will be incentivized to help the company grow.

When being lean, you often need to find a middle ground that allows you to focus on your core skills. Trying to save some money by attempting to cram "Accounting 101" might not be a wise use of your time. Conversely, you do not need to hire a full-time accountant; outsource the company's accounting work, and pay by the hour or service.

Tell a story without giving away your secrets

An idea alone is not enough to make a company; you need execution and feedback from others. You will need to learn how to talk about your idea without revealing the "secret sauce" with investors and potential partners: in fancy terms, this is called having a nonconfidential discussion. While you are in the process of filing a patent to protect your IP, it is useful to learn how to describe the problem you are solving and your approach without revealing confidential details. Being able to describe your idea in nonconfidential terms will also allow you to avoid having to ask for a nondisclosure agreement (NDA) when you have an introductory discussion with a potential partner. Oh, and whatever you do, don't ask VCs for an NDA for an initial pitch: they will not sign them, and it makes you seem naive.

Inform yourself

Staying informed is the key to success: talk to entrepreneurs in the field, and find resources at your institution (career office, technology transfer office, entrepreneurship groups) that can help you learn about entrepreneurship and connect with alumni who have started their company or joined a startup. Reach out to faculty who have founded companies, and try to get connected with the entrepreneurs that drove their company.

Do not give up, and get ready for the best roller coaster ride!

Despite the plethora of (at times daunting) things to think about, I have not yet met a single entrepreneur who regrets starting a company. There will be ups and downs, much as in academic science, but as with any goal worth pursuing, it will all be worth it. In the case of Refactored Materials, it will be revolutionizing a centuries-old industry by enabling spider silk production for multiple applications at a large scale and in an environmentally conscious way.

ACKNOWLEDGMENTS

I acknowledge Douglas Crawford, Regis Kelly, Richard Yu, and Filip Ilievski for constructive discussions and thoughtful feedback on this Perspective.

REFERENCE

Blank S, Dorf B (2012). The Startup Owner's Manual: The Step by Step Guide for Building a Great Company, Pescadero, CA: K&S Ranch Press.