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We Need An Entrepreneurial Culture in Chemistry: Do You Have What It Takes to be a Chemistry Entrepreneur?

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> *Many scientists intrinsically understand that their discoveries might translate into important, highly profitable entrepreneurial enterprises," says Madeleine Jacobs, executive director and CEO of the American Chemical Society, which published a report last year on chemical entrepreneurs (C&EN, Nov. 7, 2011, page 47). "But making a discovery or patenting an invention is only the beginning of creating a company. Bringing that idea or invention to commercialization and creating a successful company requires a different set of skills and knowledge than carrying out basic research.* [1]

1.1 Introduction: Disruptive Innovation in Chemistry is in High Demand

When I think about the future of chemistry entrepreneurship, the term limitless comes to mind. Chemistry is associated with more than 96% of all the world's manufactured goods today. Over the last 25 years, there has been an explosion of innovative and disruptive chemistry companies entering the market and using chemistry to create products ranging from food, beverage, supplements, biofuel, drugs, diagnostics, and skin care, naming a few. So, if you have a chemistry or biochemistry background, a good idea, and want to start your own company – now is the time to do it. The market is ready to keep rewarding those who bring innovative, disruptive solutions based on science.

However, for many scientists, this innovation process works backward. The product is created before they even know it has value. One of the main reasons the market has a growing interest in chemistry companies is that they are often established with a central mission to solve a problem. They may not have a solution yet, but they have a strategic plan to find one.

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As a scientist entrepreneur, your time should be spent exclusively on how your business can use science to address a specific problem. Chemists are naturally looking to do something that has never been done before, so the ideation and innovation process comes naturally. Many chemistry entrepreneurs come not with creating an idea but also turning that idea into a successful, thriving business.

1.2 Examples of Innovation in Chemistry Catching the Eye of the Mainstream Market

About 10–15 years ago, the term "innovation" started to become a cliché. Every company was touting innovation when what they were doing, in reality, was nothing more than ordinary. Adding buckwheat, the latest and greatest "super grain" to your vegetable soup product is not innovation. Real innovation should mean creating or inventing something that never existed.

If we look at the buzzword landscape today, it is all about "disruptive" innovation. While I think the word disruptive is also overused, some cool companies are doing some cool things worthy of being called disruptive.

1.2.1 Food and Nutrition

Imagine a world where a steak was not from a cow, and eggs were not from a chicken instead were manufactured in bioreactors. Recently, there has been a tremendous amount of activity in the category of engineered food. These five companies collectively raised over $500 million in the past few years, and chemists founded all.

1.2.1.1 Just (formerly Hampton Creek)

A plant-based food company founded in 2011 launched Just Mayo, an eggless mayo product, in 2013. Just is included here because they have a very sophisticated high throughput screening model for identifying ingredients from plants that can be used to formulate products.

1.2.1.2 Impossible Foods

Founded in 2011 by Stanford biochemistry professor Patrick Brown, Impossible Foods develops plant-based alternatives for meat and dairy. The company uses chemistry to look at animal products down to the molecular level and then identifies plant-based proteins and nutrients to create new products. Their first product, the Impossible Burger, was launched in 2016.

1.2.1.3 Perfect Day

Founded in 2014 to create sustainable, animal-free dairy products, Perfect Day is developing novel fermentation methods for manufacturing dairy proteins.

1.2.1.4 Endless West (formerly Ava Winery)

Founded in 2016, Ava Winery is now rebranded under Endless West. This company started off trying to reverse engineer the usual grape fermentation wine-making process to develop a more synthetic means of replicating wine. It looks like they may have had some initial challenges with synthetic wine. However, their rebranding has positioned them to focus on synthetic spirits such as whiskey or rum.

1.2.2 Sustainable/Renewable Chemistry

There has been much activity in synthetic biology over the past few years, with numerous startups jumping into space in just the last two decades. Advances in the speed and cost of deoxyribonucleic acid (DNA) synthesis and gene editing have made it much easier to engineer microorganisms to be used as factories producing food ingredients, drugs, biofuels, specialty chemicals, and more in an environmentally safe and sustainable way.

1.2.2.1 Ginkgo Bioworks

A synthetic biology biotech company was founded in 2009 by a scientist from the Massachusetts Institute of Technology (MIT). The company has a rapid, high throughput development process for genetically engineering microorganisms to act as factories to manufacture chemicals that can produce food, drugs, cosmetics, or pretty much anything for that matter.

1.2.2.2 Modern Meadow

Founded in 2011, this company uses a yeast fermentation process to make collagen used to produce leather or "biofabricated" leather without the cow.

1.2.2.3 Genomatica

This San Diego-based bioengineering company develops biobased, sustainable processes to manufacture industrial chemicals that can be used for food packaging, auto parts, clothing, tires, carpets, and more. They successfully commercialized a process to make bio-BDO for plastics and butylene glycol for cosmetics.

1.2.2.4 Zymergen

Like Ginkgo Bioworks and Genomatica, Zymergen is a synthetic biology company that genetically engineers microbes to manufacture chemicals. In a world that seems skeptical of words such as "synthetic" and "genetic engineering," it is hard to ignore innovation that could dramatically impact sustainable and more environmentally suitable production.

1.2.3 Biotech/Pharma

Innovative and emerging technologies are changing the landscape across the entire pharmaceutical industry. Today, the innovators of drug development are the smaller and quite often startup biotech and pharma companies. Large pharma companies'

development process has shifted from R&D to acquiring the innovative small companies that demonstrate success and paying handsomely for them. This trend has a healthy pool of investment dollars to further fuel the innovation in smaller startups.

1.2.3.1 Moderna Therapeutics

This company was founded by Harvard researchers in 2010 who developed a method for modifying mRNA to dedifferentiate human cells into stem cells. Their drug development platform has received a tremendous amount of publicity, and as a result, the company has raised well over a billion dollars in equity financing. Since the original draft of this manuscript, Moderna has become quite famous by utilizing this model to create a Covid-19 vaccine. They now have an $87 billion market capitalization, amazing what can happen to a disruptive company in a short time.

1.2.3.2 Unity Biotechnology

This biotech company is aiming its drug development platform toward finding a cure for aging. It seems like that might be a lofty goal, but in reality, they are focused on developing drugs for the many diseases of aging. Their platform centers around senescent cells (those that are stuck, neither dividing nor dying). Unity Biotechnology was created based on licensed technology from the Mayo Clinic and the Buck Institute. Their focus on the science of aging has made the company a media darling that has received tremendous interest in the venture capital (VC) funding community.

1.2.3.3 CRISPR Therapeutics, Intellia Therapeutics, and Editas Medicine

These are the three main companies battling for a position in the CRISPR gene editing drug development. They all had in common that they are all focused on developing platforms around CRISPR-Cas9 technology. Intellia and Crispr are co-founded companies by Doudna and Charpentier and backed by the UC Berkeley CRISPR patents. Editas was created around the Broad Institute, MIT, and Harvard patent. Historically, there has been a tremendous interest in gene therapy as a way to cure diseases or conditions, and CRISPR seems like it might be a very promising path to fixing past failures in the category, which is why we see so many companies battling for control.

1.2.4 Diagnostics

Personalized medicine or nutrition is one of the hot areas in pharmaceuticals, foods, and supplements. Imagine a world where you could actively monitor your health through devices (such as a Fitbit or Apple watch). Another diagnostic testing (such as blood, sweat, or urine), to receive drugs, supplements, or food specific to your health needs. Without innovation in diagnostics, it will be virtually impossible to enable the idea of personalized medicine. Tests are being developed to rapidly screen and provide early detection for diseases or conditions that previously were detectable only through symptoms and a biopsy. There was also an explosion of

at-home tests, in which sample kits are sent to and taken by the consumer, then sent to a lab for testing. These at-home test kits have also led to several startups combining at-home testing with personalized medicine/nutrition solutions. The company uses the testing data to prescribe vitamins, medicine, or nutrition programs to improve health and wellness. There was some early success in both areas, which led to an explosion of VC financing activity over the past few years.

1.2.4.1 23andme

Founded in 2006, 23andme has become a household name due to all of the advertising and sponsorship programs they ran to engage consumers in DNA testing. The company is named for the 23 pairs of chromosomes in a human cell. They are quickly moving from ancestry-based DNA service to genetic testing services for health and wellness.

1.2.4.2 Grail Diagnostics

This startup cancer diagnostics company was a spin-out from Illumina and entered the space with too much fanfare raising over $1 billion in financing – not bad for a startup. Grail aims to develop a blood test to detect cancer early before symptoms begin.

1.2.4.3 Viome

Viome is a personalized nutrition company that combines an at-home diagnostic testing kit with a nutritional program based on that data results.

1.2.5 Cautionary Tales

Success in chemistry entrepreneurship brought a healthy supply of funding to the entire field. It was only natural that this success might lead to some failures as well and attract bad actors. Being an early chemistry innovator is difficult. The more money you raise, the farther you have to fall when things go wrong. In the end, even the early innovators that fail usually blaze the trail for new ones who often go on to succeed or blaze trails of their own.

1.2.5.1 Theranos

This company blew up terribly. I cannot imagine that anyone does not know about this story. Theranos was going to disrupt and reinvent the entire blood-testing business. They developed an all-in-one device called Edison to do all of the testing needed from a single drop of blood from a finger prick. It sounds great when you say it like that, and on that basic premise, Elizabeth Holmes, the founder, raised around $1 billion, with a valuation as high as $9 billion. Unfortunately, their device was a fantasy. To provide blood test results, Theranos relied on the same blood testing equipment and technique other blood testing labs employed. They were trying to fake it until they made it, or at least that was the plan until an investigative writer from the Wall Street Journal exposed the company as a gigantic fraud. The US Attorney is currently indicting Holmes in San Francisco for fraud, and the company has been formally dissolved.

1.2.5.2 Solazyme (TerraVia)

This company was founded in 2003 to utilize microalgae to create renewable fuels. Using their algal molecular biology platform, they found that the process created other compounds valuable for health and nutrition. The company successfully received millions of dollars in government grant money to develop commercial-scale algal oils. Solazyme went public on the NASDAQ in 2011 and raised almost $200 million in the initial public offering (IPO). As the oil price continued to decline, however, it becomes difficult to support the use of algal oil as a cost-effective, renewable energy source. Solazyme officially changed its name to TerraVia in 2016 to focus on food, nutrition, and personal care. However, the debt accrued during their time as an algal oil business left them in a precarious position. TerraVia filed for bankruptcy protection in 2017.

Tips for Readers

As capital market interest in the space continues to grow, these companies will get more and more competitive, which can be both a good and bad thing. The competition among financiers grows in the category, as does a phenomenon called FOMO or fear of missing out. That means that they sometimes start making poor investment decisions by not spending as much time doing due diligence as they should. This behavior can sometimes fuel a "fake it until you make it" mentality within the startup community. Fake it until you make it may work in the internet, software, and app development. However, it is unacceptable in markets, products, or services that can impact human health.

As you can see, it is a great time to be a chemistry entrepreneur. There are many early signs of success, and that success will bring additional interest and funding. Now that we have established a need for chemistry in business, let us look at how to start and run a successful chemistry business.

1.3 Unique Challenges for Chemistry Entrepreneurs

Everyone loves a plot twist. We root for the heroes of stories like those behind Facebook or Apple, where soon-to-be global companies began in college dorm rooms or parent's garages. However, these tales are not the reality for a chemistry entrepreneur. Our kind of innovation requires specific facilities and expensive equipment. The only exception to that rule would be a PhD student or professor coming up with an idea during already funded research. Although discoveries such as those come with complications of their own.

This may not come as a surprise, but the biggest challenges facing the chemistry entrepreneur have nothing to do with chemistry. They come from personality and business savvy.

1.3.1 The Most Important Trait of Every Chemical Entrepreneur

One of the first and most important traits you will need is also one of the most important challenges you will face. It can be particularly tempting for chemists to value their inventions over the works of others. The field, after all, can be rather competitive and non-collaborative. To be a successful chemical entrepreneur, you will need the ability to identify ideas worth commercializing, whether you invented them or not.

In my experience, chemists are trained to find something truly unique. It is part of the culture in chemistry to find a new theory, do the research to prove it, and publish in a top-tiered peer-reviewed journal (perhaps even get the patent). What chemists are not trained to do is figure out whether their invention could create a viable product. This can be especially difficult for chemists as many of their innovations may not easily translate into a product.

One of the best examples of this is 3 M's Post-It note. Spencer Silver accidentally created a weak glue that seemed to serve no purpose until Art Fry applied it to paper and made sticky notes. Without this ingenuity and collaboration, Spencer's adhesive may have never been commercialized at all.

I have seen hundreds of university inventions or patents over the last 20 years resulting from years of hard work and research. Only a small fraction of those inventions were worth further evaluation, and only an even smaller fraction proved to have commercial value. Recognizing the difference between the two sets apart those who merely want to be a successful chemistry entrepreneur from those who become one.

Educating and Preparing Chemists to be Entrepreneurs

Another unique challenge presented to the chemistry entrepreneur is education. According to a recent Wall Street Journal article, chemistry as a major is on the decline [2]. One-third of all college freshmen in the United States pursue a STEM major, but only 1.2% of those students become chemists. Recent numbers show this percentage is still on the decline. Even those students who do join as chemistry majors soon transfer out to pursue another program.

This is a problem for the field. It creates problems for those in the chemistry businesses looking to hire chemists. Undergraduate programs are too rigid and leave little room for students to pursue side passions. We need to reinvigorate these programs at the university level, to entice students into becoming chemists and retain those who already want to be one. It is important to note that companies looking to hire students with a technical background in chemistry also desire students with practical business and commercial experience or awareness. Just because you have a chemistry degree does not mean you understand what the day-to-day jobs or responsibilities would be if you worked in pharmaceutical quality control or research lab.

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In the 2015 Survey of Employers (CBI), it was noted that 34% of businesses said that the quality of STEM graduates was not good enough, and 46% said they lacked business and commercial awareness in the workplace [3].

As an employer in chemistry, I can confirm that most straight out of school applicants we interview do not understand how to apply the chemistry they learned in a business environment. Three main areas need to need to incorporate into the undergraduate curriculums to fix this problem. First, both classroom and laboratory courses should integrate real-world business examples of chemistry at work. For example, while learning about high-performance liquid chromatography (HPLC) in the analytical chemistry laboratory, students should be challenged with something more than a simple mixture of amino acids. Students should be doing work on real-world drug samples, where they have to prepare the sample and run it as if they were working in the quality control department for a pharmaceutical company. Second, chemistry curriculums should include or integrate education about how chemistry is used in business. There are so many different types of companies that utilize chemistry such as pharmaceutical (Pfizer), biotechnology (Amgen), food (Nestle), beverage (Pepsi), cosmetic (Estee Lauder), consumer products (Procter&Gamble), chemical (Dupont), diagnostics (Labcorp), agrochemicals (Monsanto), dietary supplement (ChromaDex), the list goes on. Many different types of chemistry are being utilized by different departments such as quality control, manufacturing, research and development, product development, and many others, even within these companies. Students must learn how the chemistry they are learning is applied in business and how that might translate to career opportunities. Finally, it is important to bring in people from the outside world to speak and interact with students, preferably former students working in chemistry labs for these types of businesses. If these topics were part of the curriculum, it is safe to say that the survey numbers would probably improve dramatically.

Emory University in Atlanta and Davidson College in North Carolina are two examples of programs that recognize this trend and attempt to challenge the norm. For example, Davidson's new curriculum requires students to take one course each in five foundational areas. It then allows the up-and-coming chemists to choose from a range of higher-level classes on subjects such as medicinal chemistry and immunology. Both universities move beyond the traditional format and on to a new chemistry style based on interdisciplinary foundational courses and various electives.

There is also an interesting publication worth reading by Wolfgang Runge and Stefan Brase at the University of Karlsruhe called *"Education in Chemical Entrepreneurship: Towards Technology Entrepreneurship for an in Chemistry-Related Enterprises."* It summarizes their experience in executing a "Theory-to-Practice" model for teaching technology entrepreneurship and intrapreneurship [4].

Economics used to be referred to as the "dismal science," but chemistry is now taking its place. If we capitalize on this movement toward chemistry entrepreneurship across multiple markets worldwide, we need to rethink how we groom those who lead it.

1.3.2 Chemistry Accelerators, Incubators, and Academic Spin-offs

Raising money for an early-stage idea in chemistry can be very difficult or very expensive. It means you do not get the funds necessary to get to the next stage, or if you do find someone willing to finance the company, you will find yourself giving away the majority of the company right out of the gate. Finding a cost-effective way to get to a proof of concept or prototype will dramatically improve your ability to get that seed round or Series A.

Incubators and accelerators have become an increasingly important early-stage funding option for chemistry startups over the past few years.

Y Combinator is an American seed accelerator, started in March 2005. They have a very interesting incubator model, whereas they invest a small amount of money, $150 000, in many companies twice a year. The startups all move to Silicon Valley for three months to refine their business models and prepare them for pitching investors. The most important thing they do at YC is not providing the funding, but their experience in helping these very young startups with their ideas. Y Combinator has spawned several highly successful companies and is consistently ranked at the top of US accelerators. YC has companies such as Dropbox, Airbnb, and its chemistry participant Ginkgo Bioworks in their portfolio.

Incubators are not new, but many university and corporate incubators have popped up over the past few years. Historically, incubators have not been very successful, but the concept is beginning to turn a corner, and they are starting to achieve results.

In October 2016, MIT announced creating a startup incubator called The Engine, which will provide funding, workspace, and access to equipment and experts to help them during the early stages of establishing a product or a business. The Engine has a straightforward application process that references the Heilmeier Catechism, created by George H. Heilmeier, former DARPA director, who established a set of questions to help the Agency evaluate these types of proposals [5].

The Heilmeier Catechism

1. *What are you trying to do? Articulate your objectives using absolutely no jargon.*
2. *How is it done today, and what are the limits of current practice?*
3. *What is new in your approach, and why do you think it will be successful?*
4. *Who cares? If you are successful, what difference will it make?*
5. *What are the risks?*
6. *How much will it cost?*
7. *How long will it take?*
8. *What are the mid-term and final "exams to check for success"?*

This is a simple yet brilliant approach to evaluating these types of early-stage opportunities.

In 2017, DuPont and the University of Delaware established the Delaware Innovation Space (DIS) incubator, a chemistry incubator, right on their own Experimental Research campus in Delaware. The DIS provides opportunities for students, an outlet for intellectual property developed at the university, and a way of creating value from DuPont's decommissioned assets. Even more interesting was that the establishment of the incubator was not too long after they made cutbacks in their central research unit.

One of the reasons incubators are important has to do with visibility. Scientists can see a place on campus where they can talk to somebody and try to find a way to take their interests and research and transfer them into a startup. Without incubators, these scientists may not know where to start or how to take their ideas to market. Incubators also relieve the founders of many pressures of getting a business up and running, to focus on developing and innovating.

The visibility angle is half the battle. How do we find more chemists that have an entrepreneurial spirit and are willing to take the necessary risks to make entrepreneurship happen?

1.3.3 Do Something, do Anything, even if it is Wrong

The best way to learn is by doing. The problem is that many people never get to the doing phase. Why? The primary reason is the fear of making a decision.

As a kid, when I was struggling to decide about something, my father would always say, "Do something, do anything, even if it is wrong." I always remember thinking, what the hell does that mean? It was not until years later that I finally figured it out, right or wrong, just decide and get moving. The biggest mistake you can make as an entrepreneur is hesitating to decide, primarily out of fear of failure. No one can be right every time, and you will not know if you were right or wrong until you have either tried and succeeded or tried and failed.

Failure is part of the process. Great chemists and entrepreneurs learn to harness failure by learning from their mistakes. It is amazing what clarity failure can bring, not always knowing what to do, but what not to do.

When it comes to chemistry and research, chemists seem to understand the link between failure and success. Some of the biggest commercial success stories in the field of chemistry started as accidental findings from failure.

1.3.3.1 Penicillin

Penicillin was first discovered in 1928 and is perhaps the most widely used antibiotic in the world today. Sir Alexander Fleming found penicillin during the cleanup of a failed microbiological experiment attributed to a careless lab technician handling the experiments while he was on vacation. Accidental mold contamination of the microbiological experiment led to an unexpected finding. From his failure, the world got penicillin.

Tips for Readers

Failure can provide great insight. Take time to evaluate failure. If Alexander Fleming did not take the time to look at his failure, we might not have penicillin today.

1.3.3.2 Post-It

In 1968, Spencer Silver was trying to develop a strong adhesive for 3M. Instead, he developed the opposite, a weak but reusable glue that could easily be lifted from the surfaces it was on. There was no real-world application for Silver's reusable glue until 1974 when a colleague in new product development, Art Fry, who was aware of the adhesive, conceived of using the glue as a way of holding bookmarks in his hymnal while singing in his church choir. From this, Post-It notes were born.

Tips for Readers

As chemists and scientists, sometimes we are too close to the invention to identify practical commercial use for the technology. Surround yourself with people with backgrounds and experience in different markets or fields and communicate with them. This will increase your chances of finding an application for your invention.

1.3.3.3 Saccharin

In 1879, Constantin Fahlberg, who was researching new uses for coal tar, had spilled some chemicals on his hands and forgot to wash his hands before eating. He found a super sweet substance on his hands, and saccharin was born. Ultimately it took many years for the market to find any commercial value in saccharin. It did not become popular until the 1960s and 1970s, when the Sweet'N Low brand started to take hold.

Tips for Readers

It is hard to imagine replicating this discovery in the lab safety environment we work in today. However, it is still a great example of an accidental chemistry invention.

1.3.3.4 Teflon

While researching new chlorofluorocarbon refrigerants, Dupont chemist Roy Plunkett produced tetrafluoroethylene (TFE) gas stored in cylinders before use. When they tried to use the cylinders of TFE, no gas came out, and when they opened them,

they found a white powder. Despite the failure, Plunkett chose to analyze the white powder and found it chemically inert, heat resistant, and low surface friction, which ultimately became a new polymer called polytetrafluoroethylene known as Teflon. This accidental discovery ultimately took years to develop into a cost-effective commercial product. It took a team of chemists and engineers in polymer research to evaluate the chemical properties of Teflon and identify commercial applications.

1.3.3.5 Viagra

More recently, Pfizer chemists came up with a compound called sildenafil citrate. They were testing high blood pressure, a heart drug candidate that failed during clinical trials but exhibited some very interesting side effects. Even with the news of this interesting side effect, the development team was dangerously close to shuttering the program. One persistent R&D team member was begging for a small amount of additional funds to further evaluate the side effect, which ultimately led to the development of what we know as the little blue pill called Viagra.

Tips for Readers

Do not be so quick to throw failures away. Whether you work for a significantly larger company or a small startup, sometimes it can be hard to resist a quick exit from a failed project. Failure is often a critical part of the R&D process and costs significant time and money. However, failure also delivers data, results, and experience, which can have tremendous value in the right hands. In the Viagra example, an unexpected finding delivered value well beyond the initial focus of the study.

If you are not afraid to take risks in chemistry research, why would you be afraid to take risks in business? When it is all said and done, good chemists and entrepreneurs will not regret their failures anywhere near as much as they regret the chances they did not take.

Successful people never stop learning, evolving, or changing themselves for the better, even when they have found success.

Tips for Readers

As an entrepreneur, you cannot be afraid of failure. Unless you are very lucky, you will need to fail repeatedly to land on something that will work eventually. The road to success is paved with failure. Like my father told me when I was a kid, do something, do anything, even if it is wrong.

1.3.4 You have your Discovery; now you need a Patent

Another challenge or pitfall for chemists is the patent process. As technical experts, we think we understand how to structure patent claims. However, the patent process can be a costly and complicated exercise, as it will require patent lawyers' expertise. You could take the patent filing challenge on yourself, many have tried, but most fail. Whether you came up with the idea while doing your research or found something you can license, you will need money to bring the invention to the next stage: filing or licensing a patent.

1.3.4.1 Provisional Patent

The provisional patent process can be a good way to get started on protecting your invention. For example, your invention is still very conceptual, and you do not have enough data to enable the idea fully. This process gives you one year to do your research and provide the data necessary to file a patent application. However, if the provisional patent is not drafted properly, it could cause problems during the application and prosecution phases.

1.3.4.2 Patent Application

Suppose you want to have a patent with protectable value. Much work goes into the application. There are many factors in filing a solid patent application, such as structure of claims, patent search, prior art, and international considerations, to name a few.

1.3.4.3 Patent Prosecution

Once your patent application has been filed, that is only the beginning. The patent application will be assigned to a patent examiner, and the fun begins. Many people underestimate the amount of work that goes into the prosecution phase. It can take years and much money to get a patent application, and in many cases, the patent issued can be vastly different from what was initially proposed.

1.3.4.4 Structure of the Patent Claims

There are many ways of structuring patent claims. A truly great invention could be worth very little if the claims are not structured properly. This is perhaps one of the most important reasons you want a solid patent lawyer working on the application. Some chemists believe that since they are technical experts, they know how to structure claims, which is a big mistake. There are many complicated nuances in getting the language correct, and doing it poorly could cost you big time.

1.3.4.5 Patent Search and Prior Art

One of the main reasons many patents do not issue or are later overturned is prior art. You need to do a thorough search for any prior art that could be problematic during prosecution or future defense of the patent. This is another good reason to have patent counsel, as they have access to the tools and staff necessary to do this kind of in-depth investigative work.

1.3.4.6 Publishing Before Patenting

One common mistake with researcher inventors is the publication of the research underlying their invention. We can all admit that finding something innovative, groundbreaking, and the novel is very exciting stuff. However, if you intend to file a patent, you need to hold the publication until after you have a solid invention disclosure in place. I cannot emphasize this point enough, as valuable licensed patents had vanished right before my eyes, knocked out by an early publication of the research. This is yet another good reason to have patent counsel advising right from the beginning.

1.3.4.7 PCT International Patent

Most inventions have an international scope. The Patent Cooperation Treaty (PCT) allows you to expand your patent scope from the US to pretty much every country if you wanted to do that. When you file the PTC application, you can choose all countries or pick the highest value countries. Once a PTC application is filed, you will have a timeline by which you will need to file a formal application in that country. The PTC process can cost hundreds of thousands of dollars, and that is just the filing fees. It does not include the translation, formatting, and filing of an application in each country.

1.3.4.8 Protectable Patent Value

The goal is to obtain a patent that can defend and protect your invention. The problem is that not all patents are equal. There are strong, weak, and mediocre ones. Patents that have survived challenges or were successfully defended in litigation have considerably more value than patents that have never been challenged.

1.3.4.9 Selecting the Wrong Lawyer for the Job

There are good and bad lawyers. There are also many different types of patent lawyers, such as prosecutors and litigators, and each has varying degrees of familiarity with our field. Some may have experience working with chemistry, while some may have no technical background whatsoever. Finding a good attorney to cover all of the items listed above can be challenging and does require some due diligence. Since this will be such a big expense, it is worth spending the time interviewing and selecting the right lawyer for the job.

There are many pitfalls and traps when navigating the patent process, which is why it is better left to a qualified, trained professional. There is a great guidance document created and updated by the American Chemical Society (ACS), "*What Every Chemist Should Know About Patents*," that goes into a lot more detail about the patent process [6]. It can help familiarize yourself with the patent process and lingo before you start working with a patent lawyer. However, I would not suggest navigating this incredibly valuable and complex process on your own.

Ultimately, how valuable a patent depends on how defendable in the face of a challenge. Obtaining a solid patent that is defendable in the commercial world can be very complicated, expensive but, in the end, will be very valuable if done properly. Find a good patent lawyer and let them do the heavy lifting.

Tips for Readers

Suppose you are considering filing your patent, without a patent attorney, especially for those working in the field of chemistry. In that case, there is a very low likelihood that the patent will deliver any substantial protectable value. Do your best to find a way to obtain the funds to have a patent attorney do the work. However, if the money is not available, do not let that hold you back. Start by filing a provisional patent, which will buy you one more year to find the funds to hire a qualified attorney. At the same time, you continue to work and develop the idea to enable the invention better.

Case Study 1.1

The CRISPR patent wars

If you are an aspiring chemistry entrepreneur and you have not been following the patent battle over CRISPR, you need to start reading up on that story. CRISPR-Cas9, which turned out to be a ridiculously simple way of editing genes, is perhaps one of the biggest stories in chemistry over the past decade.

It all started in 2012 when Jennifer Doudna, from UC Berkeley and whom many consider the creator of CRISPR, published the first paper on the enzyme in *Science*. Further advances followed when Feng Zheng, at the Broad Institute, co-authored a paper in *Science* in February 2013. Ever since, UC Berkeley, Broad, Harvard, and MIT have been locked in a patent battle over CRISPR-Cas9. In September 2018, the US Court of Appeals for the Federal Circuit issued a decisive ruling, awarding CRISPR-Cas9 gene editing to the Broad Institute.

Tips for Readers

This CRISPR patent battle is the perfect example of why you should spend the time and money on intellectual property and take the patent process very seriously. Just put yourself in Jennifer Doudna's shoes and imagine you were the inventor of a revolutionary new technology that someone else outsmarted you on the patent front.

1.4 Invention is Only the Beginning of Creating a Company

Now that you have your product, or at least a prototype of it, and have done the best you can to protect its patent, the next logical step is to form a company – maybe.

Just because you have a protected invention does not necessarily mean it has to be a company. For all of you that might watch Shark Tank regularly, you will often hear the sharks' comments to the presenter that they have a product, not a company, and more so than not, that statement will lead to an "I'm out." The first step is to assess whether your product is enough to form a company.

If your invention is indeed only a product, do not be discouraged, many inventions are licensed, distributed, or sold. Licensing or selling a patent to a company with the resources necessary to get a product to market, or better yet, using the invention for improving an already existing product, can be a very financially lucrative option.

If you decide to start a company based on your invention or idea, there are still many critical decisions. At what point do you need to raise money to capitalize the company for success appropriately? As the founder, are you going to be the right person to run the company as the CEO? How are you going to get your invention to commercialization? When the product is ready, how are you going to market or sell it? All of these are crucial decisions that will impact the future success or failure of your company.

1.4.1 Know your Role: Founding CEO vs. Founder vs. Inventor

I have seen many inventors make the classic mistake of thinking that since they created the product or idea, they also need to start and lead the company. It is quite common for founders to lead the company during the early formative years. This is when the founder should be doing some serious self-reflection focused around one question: Am I the person who can take this company to the next level?

In a recent article in *Science*, the concept of "founders and joiners" was discussed about chemistry [7]. There are two styles of entrepreneurs: the ones who will found a company and the ones who take a risk by joining a company at an early stage. As a rule, "founders" are significantly more risk-tolerant and have a stronger interest in management, whereas "joiners" are more interested in functional work activities, such as research and development.

In a recent study, 4000 PhDs were interviewed about their opinion on this topic. Forty-six percent expressed interest in joining a startup as an employee, while 11% expected to start their own company one day. The article also cited that mandated entrepreneurship training is likely to be inefficient in fostering the "founders and joiners" relationship.

Let us look at the GEN (Genetic Engineering & Biotechnology News) annual "Top 10 Under 40" list. You will find a pretty consistent mix of researchers, business executives, and entrepreneurs, with only four out of ten in the business and entrepreneur category. Until the 2017 list was published, entrepreneurs were not even included in the mix. I think that speaks volumes about the chemistry community's mentality in the past, where the recognition was focused on the researcher. The recent pivot to include entrepreneurs is also an excellent sign, as the rewards continue to move towards starting new companies. Let us face it, even with the recent change, six out of ten that receive recognition are researchers, and only two of four in the business category are entrepreneurs. However, we have got to start somewhere.

Tips for Readers

You may be a great researcher and inventor. You might even have some entrepreneurial spirit, but that does not necessarily mean that you will be the CEO guiding the company you created to the promised land. It takes much self-awareness to identify your role with the company as it develops. It takes a strong person to step aside from running the day-to-day operations, and I have seen many examples of success from an early decision to let someone more qualified step in and run things. I have also seen the flip side with the founder and inventor determined to be the CEO to run the company to the ground. Seek counsel from employees and outside relationships and listen to what they have to say.

1.4.2 Raising Money: Acquiring the Right Money at the Right Time

The one question I am asked most often when speaking with startup entrepreneurs is, "How much of my company do I need to give up for the amount of money I need?" That is a challenging question to answer. Ultimately it will be a function of valuation. How much money do you need to raise, and what valuation can you get based on your progress? Any early-stage company will find out pretty quickly. When it comes to valuation, you can walk into the meeting with a model to justify the value of the company, but ultimately it will be a negotiation. As a startup, you need to start becoming familiar with financing jargon like seed round, Series A, and Series B.

Seed Round. *The first rounds of funding for a new company, where this money is used for early product development and initial market research. Typically anywhere from $50 000 to $1.5 million. Anything above that range could be viewed as a Series A round.*

Series A. *This is the first round of financing after the seed capital has been secured, and the product and market development were successful. Typically anywhere from$2 million to $10 million. This is typically the funding round that will make the company into a real operating business with actual employees and possibly get you to revenue, depending on the nature of the business.*

Series B, C, D, …. *Suppose you were lucky enough or good enough to make it through your seed round and Series A. In that case, you would have a healthy operation that will not require additional capital, but for those that do you will continue to follow the letters in the alphabet after A, until you stop raising money. As long as the company's valuation continues to increase with each round, you should be in good shape. However, if the business or product hits a snag and you face a notorious down round to keep things going, buckle up because the smooth ride you may have enjoyed is about to become a roller coaster ride.*

The first thing you need to consider your financing options, and when you are pitching, you need to approach groups that are most likely a good match for the type of funding round you are seeking.

1.4.2.1 Self-funding

The more money you put in on your own, especially during the early stages of development, the better off you will be. It does not matter where the money originated. If it is cash, taking a second mortgage on your house, or credit cards, investors like to see that the entrepreneur has skin in the game. One of the first questions I ask any entrepreneur asking me for money is how much have you personally invested in this company? If you believe in your product or business and have the capital to self-fund your company through the seed round, you would be crazy not to take that risk.

1.4.2.2 Friends and Family

This is usually a good option during the early stages of the company and shows a different skin-in-the-game type. If you believe in the company, invention, or discovery enough to take money from friends and family and put them at risk, you must feel pretty good about the opportunity. It is very common to see friends and family participating in the seed round, especially if the product or company does not require more than $500 000 to get to proof of concept.

1.4.2.3 Angel Investors

If you have access to high net worth individuals who like to make seed investments in startup companies, there is a good fit between yourself and the company. This can be a very favorable way of financing the company in the early days. If you do not have a list of millionaire or billionaire investors on your speed dial, there are other ways to find and pitch angel investors. Here in California, an angel investor group called Tech Coast Angels, has about 300 members and consists of experienced CEOs, current and former entrepreneurs, venture capitalists and some generally high net worth individuals. Groups like this accept applications or proposals and are very active in funding startups. Angel investors usually only focus on the early rounds, some only focus on seed round investments, and others will focus on Series A rounds. If you are pursuing angel investors, it is worth the time to identify investors that will be the best fit.

1.4.2.4 Accelerators and Incubators

As discussed in Section 1.3.3, it can be a lot more challenging to get a chemistry startup going than other businesses, largely because you will need access to some pretty expensive equipment and laboratory resources to prove a concept. Accelerators and incubators that can provide access to these resources and funding are often a cost-effective to get through the initial startup phase and make it easier to obtain additional financing.

1.4.2.5 Debt

A startup or early-stage company can obtain debt as a non-dilutive way of financing. However, I would not recommend any early-stage company that pre-revenue or losing money to consider debt a viable option. Almost every company that took on a debt too early resulted in the company filing bankruptcy, including a few companies that achieved over $1 billion. Debt can be a very useful tool for companies that have an established business with predictable cash flow. However, the minute you take the debt for startups burning cash, the clock starts ticking pretty much immediately. I have seen startups take debt instead of an equity deal, thinking they are getting a

better deal to avoid dilution. They ultimately had to raise money via an equity offering significantly below the valuation they would have had, so they can pay off the debt and still not have enough cash to grow or run the business.

1.4.2.6 Strategic Investment

Many large companies have found out the hard way that size can kill innovation. As a result, most large companies have created venture funds to make strategic investments in innovative startup companies to provide capital and resources while maintaining a placeholder position as the company develops. This can be a great way to finance a startup, but you need to be careful about how the deal terms are set up. You would not want to find out several years later, after you are successful, that your only option is to sell to that investor. Many consumer products, food, and pharmaceutical companies have created venture funds to make strategic investments in innovative startups. Many of the innovative companies identified in Section 1.2 have received strategic investments from these corporate VC arms.

Food Company VCs: Large food companies like Nestle, Coca Cola, Kraft Heinz, Campbells, General Mills, Kellogg, and Tyson Foods have all started VC operations. Primarily driven by pressure, successful startup brands and e-commerce growth make it easier for startups to reach the consumer directly.

Consumer Brand Company VCs: Large consumer product companies like Procter&Gamble, Unilever, Colgate-Palmolive, and Church and Dwight have all suffered from nimble e-commerce startups Dollar Shave Club and Honest Company, and have reacted by establishing VC investment arms to do early-stage investing in these types of businesses.

1.4.2.7 Private Equity

These private capital investment funds typically acquire or invest in late-stage private companies and are not normally known for making early-stage investments. The largest and most well-known PE firms are Blackrock, The Carlyle Group, and Kohlberg Kravis Roberts (KKR). These PE firms typically look to purchase undervalued companies or assets that they can break-up, streamline, or fix. As a startup, I would not expect to see PE firms knocking on your door anytime soon.

1.4.2.8 Venture Capital

VCs are a form of private equity known for financing high-risk, high-reward startups, and early-stage companies. As you can imagine, any investment firm willing to make a bet on a high-risk venture will want a large share in the company to justify the risk. The earlier you take VC money, the more you will pay inequity, so my advice is to bring the company as far as possible before going to a VC. You will be in a better position to negotiate if you have made substantial progress. Sometimes you hear people refer to VCs as vulture capitalists, and there is some truth in that, but VCs have also been very helpful in financing some of the most well-known, innovative companies worldwide. There are VC firms of just about every shape and size you can think of, just like any form of financing. It is worth your time to find a VC that would be the best fit for what you are trying to accomplish. VCs will tend to focus their investments and expertise on specific industries, so dealing with a tech or internet VC might not be a good fit for a chemistry oriented business.

1.4.2.9 Investment Banks

These financial institutions help companies look to raise money in equity offerings through the public markets, i.e. IPOs. Using the public markets is not common for startups. It is usually done during the later phases of the money-raising process, in most cases as a way of providing liquidity for the early-stage investors and founders.

Large investment banks. *Goldman Sachs, JP Morgan Chase, Morgan Stanley, and Citigroup are the best examples of large full-service investment banks.*

Medium-sized banks. *Jeffries, Lazard, Oppenheimer, and William Blair*

Small investment banks. *Cowen, Roth, HC Wainwright, and Craig Hallum*

There are several ways to become a public company, and the IPO is the route most people think of when considering going public, but there are other routes of bringing a company public. IPOs are very glamorous and exciting events, especially for the founders and management team of the company, but pulling off a successful IPO is not as easy as it sounds. The very high profile and successful IPO we all get to see on CNBC make it look easy. However, the reality is that most IPOs never even make it to the market. Suppose the investment bank cannot find enough interest in the offering, which usually decreases the offering price. In that case, the company and its key shareholders will eventually get to the point that it is no longer worth going public.

Another common route to becoming public is through a reverse merger, also known as a reverse IPO, which is the acquisition of a public company by a private company so that the private company becomes public due to the merger. Many bankers and investors do not favor this route. However, it can be a very efficient and cost-effective way of becoming a public company if done properly. ChromaDex became public due to a reverse merger in 2008, which proved to be a very successful route to become public and continue to raise the capital we required to grow the business. Like any of the financing options listed here, you need to do your homework for the process to go well.

ChromaDex uplisted to NASDAQ in April 2016. That is me ringing the opening bell.

In the end, you will find the most successful startups got there by using a combination of these financing options. Generally, the longer you can operate without taking investors, without dramatically impacting the growth of the company, the better off you will be. Ensure you are raising money for the right reasons and asking yourself if the additional investment capital helps you accelerate your business plans.

The money you raise is not there to make you feel comfortable. You are an entrepreneur. It is your job to be uncomfortable. Any sense of comfort from having cash in the bank will quickly be replaced with the discomfort that comes with reporting to investors.

Tips for Readers

One thing I have found to be true over the many years I have been doing this is that you can do your best to predict how long and how much money you will need to get your business going, but in the end, it always takes twice as long and requires more than double the amount of capital you would expect. You may think it is painful giving away a huge chunk of your company during your initial seed financing, but that is nothing compared to the pain of doing a down round after you run out of money after failing to meet your initial objectives as a startup.

Tips for Readers

It is not uncommon for financing deals to go bad before and sometimes after they are completed. In my experience, most go bad because there was not a good fit between the company and the financier. It can be fascinating to have an individual or a group willing to invest millions of dollars in your company or idea, but that is no reason to abandon common sense. Ensure that you do an appropriate amount of due diligence on people or businesses that you choose to finance your company. Background checks are generally pretty easy to do. However, the best way to manage their money is by researching the portfolio of companies they are currently invested in and the companies they have exited. If that information is not publicly available, you will need to ask for it, including a list of founders or CEOs at each company you can call and interview.

1.4.3 Can you get the idea for Commercialization?

"Build it, and they will come" is not a business model. One of the industry's main problems is that many great inventions never make it to commercialization. A chemist-scientist could have the greatest product innovation on the planet, but it

is dead if it cannot be successfully commercialized. Moreover, the best product is not always the winner.

Failed commercialization is a common problem with scientist founders who believe their technology is so good it will sell itself. Some will succeed with this, but the odds are heavily stacked against it.

Another key reason for commercial failure is product-market fit. Two great examples of this are Post-it Notes and Teflon. Spencer Silver's accidental weak glue would probably never have had commercial success without Art Fry finding a product-market fit. Roy Plunkett's Teflon might not have found commercial success without an experienced team of engineers and product developers identifying a product-market fit.

To set yourself up for success, you have to build a business plan, find a way to fund it, and then hire a team to execute that plan. When you build your team, you want to find people committed to the company and stay for a long time. You do not want to train people and have them leave.

Another key issue is establishing a sales and marketing team. A common pitfall is that scientists do not often understand sales and marketing. However, there is a caveat to that: If you are a biotech company, you do not need to focus heavily on sales and marketing. Instead, it is more important to put your energy toward a developmental plan to get the drug to market.

If success comes, be prepared to grow. There have been stories where success killed the company, so it is possible to fail by succeeding.

1.4.4 When you are Ready to Commercialize, which path do you take?

Innovation in chemistry rarely creates and a plug-and-play consumer-ready product. In most cases, innovation in chemistry is going to enable a better or improved consumer product. An excellent example of this is the airbag. The idea of an airbag existed long before the chemistry innovation occurred that would enable the concept to work. The airbag probably would not be in cars today if not for the chemical at the heart of the airbag reaction called sodium azide.

Suppose we assume that your technology is consistent with other innovations in chemistry, meaning that it is not a consumer product on its own. In that case, there are several ways of bringing your invention to market.

1.4.4.1 Licensing Deal

Instead of creating and selling a product, and perhaps avoiding the complication of building a company, you could pursue a licensing strategy. You would identify the company or companies that would be the best fit for your invention and do some form of an exclusive or non-exclusive licensing deal so they could integrate the invention into their business or product. Economically, these deals typically include upfront, milestone, and royalty payments, which would also require the licensee to bear the cost of development. This route, if executed properly, can be an efficient, low-risk, and lucrative model.

Tips for Readers

A quick word of caution when dealing with large companies: it is not uncommon for companies to license technology only to "put it on the shelf." They will license the invention with no intention of ever using it and therefore keeping anyone else from using it as well. If you pursue this path, I would highly recommend having an experienced contract attorney familiar with these types of negotiations, as there are ways of protecting yourself against this type of behavior.

1.4.4.2 Business-to-Business (B2B)

In this scenario, you would establish a company that would produce a product sold to other businesses to use in their products. It is common in chemistry that those inventions or ideas are not consumer products but rather fixes or improvements to a manufacturing process such as scale, efficiency, safety, or cost. I have always loved the BASF tagline, "We don't make a lot of the products you buy. We make a lot of the products you buy better." Many of the chemical companies like BASF that provide innovation in chemistry exist not to produce consumer products but work with consumer goods companies to improve the sold products, which can be a very lucrative business.

1.4.4.3 Business-to-Consumer (B2C)

There is little doubt that the most lucrative path to commercializing your chemistry innovation is bringing a consumer product to market. However, this is also the riskiest path. It is challenging to translate innovation in chemistry into a successful consumer product. That said, money flows to innovative chemistry companies that have identified a problem with a path to identify a solution, which is ultimately a much more efficient way of creating high-value consumer product innovation. Companies like Just, Beyond Meat, and Impossible Foods are great examples of companies that followed that path, and I expect the trend will continue.

One thing is pretty clear, the less you know about how your chemistry invention can be used in the real world, the less it will be worth. The more you know about its value, the more economic value you will be able to capture along the way.

Tips for Readers

Access to capital/financing will play a big part in determining the best route to commercialize. The more money you have, the more options you have. One piece of advice I would offer is do not choose a path of commercialization without the money necessary to succeed. Whatever the amount of time and money you think you will need to commercialize, double it, and you still may fall short.

1.5 Do you have the Traits of an Entrepreneur?

I first realized that I would be an entrepreneur when I was in my third year of college. I can remember the exact moment it happened. At the time, my girlfriend was a fashion merchandising major, and she was tasked with putting together a detailed business plan for her concept of a fashion store. It included designs and idea boards for the store and products. Somehow, she managed to convince me to help her with what turned out to be a huge project. Please bear in mind that I was a 19-year-old chemistry major with no prior business training whatsoever. She struggled with the project, so I looked at the outline provided, and the main three items were product line design and selection, store design and budget, and a financial plan forecast. Since she was a fashion major, I figured let us start with the more difficult task of designing the store, so I handed her a couple of blank sheets of paper and asked her to draw a concept for the store's front and a floor plan. The response is one that I will never forget because when I looked into her eyes, I saw a combination of confusion and panic all at the same time. How could a blank sheet of paper elicit such a response?

I could visualize the entire store design and floor plan in my head, down to the smallest details, front door, signage, window graphics, flooring, shelves, racks, lighting, displays, sitting area, just to name a few. The difference was that I just needed to transfer what was in my head to the paper. Was I some retail clothing store savant? Far from it. I had spent plenty of time shopping in clothing stores, but that was about it. It just seemed intuitive and logical to me, almost easy, which was not the case with her. Once we had the outline in place, her creative side kicked in, and she designed a store that was way beyond anything I would have been able to visualize. This experience showed me that I had some of the key traits of an entrepreneur that others lacked. I had the vision, curiosity, decisiveness, risk tolerance, and reasoning. What came naturally to me did not come naturally to everyone, and I could use that to my advantage.

Even before graduating with a chemistry degree, I knew that I was not destined for a life at the bench. I knew I wanted my career to be involved in the field of chemistry, so the next logical step was to look at options on the business side of chemistry. I will not bore you with the details of a 21-year-old kid trying to find his way. However, I did end up getting very lucky to find a sales job at a small but entrepreneurial analytical chemistry company in Los Angeles, and I loved analytical chemistry.

It did not take me long to figure out that I was pretty good at selling chemistry. This provided me with other opportunities within the company to be even more entrepreneurial. While helping my girlfriend on her college project, those traits I found were coming in very handy in the real world. While talking with customers, I would identify product needs that were not part of our product offerings. If the opportunity appeared to be lucrative, I would research the product, identify additional customers with the same need, find a viable supplier with a suitable wholesale price that would provide good margins for the company, test the product details and pricing with the customer, and prepare mock-up marketing materials. If everything lined up, I would pitch management to consider adding the product line to our catalog.

The point is, I did not have any clue I wanted to be a chemistry entrepreneur until I did it. That is the whole spirit of this business. I knew I had something valuable, I made a plan, and I went for it.

Case Study 1.2

The Path to ChromaDex

When I graduated from Valparaiso University in 1991, I did what every chemistry major was supposed to do – get a job working in a lab.

My time at the quality control lab did not last long. After a year, I decided that I needed to move on to something different. I knew that I still wanted to stay in chemistry and use my education for something productive. I loved science and the chemistry side of things, but I did not want to work in a laboratory.

What were other options there for someone with an undergraduate degree in chemistry? After all, there are plenty of businesses that involve chemistry. There must be jobs outside of the lab that require chemistry. The decision was clear. I moved towards the business side of chemistry and landed a job in 1992 with the technical sales division of a growing analytical chemistry business. By 1993, my technical sales success led to an opportunity to set up and run international subsidiaries for this growing analytical chemistry business. These technical sales and management jobs allowed me to be very entrepreneurial. However, this was still not enough, and something was still missing.

In 1998 I decided to leave and pursue what would become ChromaDex. I was 29-years-old, which was the ideal time for starting a business. I had minimal obligations, family, or financial, and was perfectly positioned to take this type of risk.

Tips for Readers

and think you want to start your own business, the best way to learn how the business side of chemistry works is to get a job working in the industry. You will learn the basics of how these businesses operate and how they interact with their customers.

Case Study 1.3

ChromaDex Unique Business Model

ChromaDex is a NASDAQ public company built on a natural products chemistry platform that utilizes business relationships with universities to track and license research-backed ingredient technologies. The company began in a

(Continued)

Case Study 1.3 (Continued)

spare bedroom of my house in 1999 and is now a publicly-traded leader in its field.

For many years, we have been the go-to company for anything related to the research, development, or testing of foods, beverages, supplements, sports nutrition, skincare, and related products. ChromaDex has a solid brand and reputation firmly rooted in science and innovation of natural products. As such, our expertise allows us to get a very early look at university research. We also have business relationships with many of the world's largest consumer products companies. This advantage puts us in a unique position to cherry-pick highly valuable intellectual property based on solid research, and more importantly, relevant to the consumer product markets. We have used this strategy to develop a portfolio of novel ingredients, including our flagship nicotinamide riboside (NR). This is all based on university licensed research and patents.

Finding and licensing these opportunities is less than half the battle. University patent technologies are never plug-and-play. Licensing the patent is only the first step in what ultimately becomes a long and expensive development process to take it from a dream to reality. We are in a unique position to license the patents because we have the expertise, assets, and capabilities to take it from an idea to a developed commercial product. On top of that, we know how to sell and market it successfully. Sounds simple enough, right? Not quite. Most of these innovators do not fail because they had the wrong idea. They fail because they underestimated the difficulty in turning that idea into a commercial product.

Case Study 1.4

The Nicotinamide Riboside (NR) TRU NIAGEN Story

NR is a vitamin B3 metabolite that was first described in 1944. However, its true function was unknown until Dr. Charles Brenner identified NR as an NAD+

precursor in his 2004 Cell publication. I started following Dr. Brenner's research on NR as an NAD+ precursor in 2006, while he was at Dartmouth. I quickly recognized that NAD+ was a very important part of the healthy aging story and that NR was the most effective way of raising NAD+. As a result, ChromaDex began actively pursuing the research behind both NR and NAD+ in 2009. It took a few years to do our due diligence and get everything in position for licensing the patents, but after that, things started to move very quickly.

- ChromaDex licensed the Cornell patents (Dr. Anthony Sauve) in 2011.
- The Cornell patent was the base we used to start developing the commercial manufacturing quantities of NR. Before ChromaDex started making NR, it was not easy to find even a few grams of NR for research. We achieved metric ton scale for NR by the middle of 2013.
- ChromaDex launched NR as an ingredient under our NIAGEN brand in May of 2013.
- ChromaDex licensed the Dartmouth (Brenner) dietary supplement and food-related patent in 2013.
- ChromaDex licensed the Washington University (Dr. Jeff Milbrandt) patents in 2013.
- ChromaDex licensed the Dartmouth (Brenner) NR pharmaceutical patents in 2014.
- During the period between 2013 and 2015, ChromaDex performed numerous safety and toxicology studies, beyond the already published studies, to prepare for regulatory filing with the US FDA.
- In 2014, ChromaDex started its first human clinical trial on NR.
- In 2015, the first human clinical study of NIAGEN®, NAD+ metabolomic analyses were completed in blood for various time points over 24 hours. For the first time, the study also established an effective dose range for NR in humans.
- In 2015, ChromaDex submitted and received notification of New Dietary Ingredient (NDI) status from the FDA for our patented NR.
- In 2016, ChromaDex submitted and received notification of Generally Regarded as Safe (GRAS) status from the FDA for our patented NR.
- In 2016, ChromaDex's second study, a 140-participant trial evaluating the effect of repeated doses of NIAGEN on NAD+ metabolite concentrations in blood, urine, and muscle in healthy adults, analyzed the impacts of three dose levels of NIAGEN compared to a placebo. The recruitment and dosing portions of the trial have been completed. We are finalizing the analysis of data from this trial, and we are working on the timing of the release of top-line data, which we expect to report over the coming months.
- ChromaDex completed our pre-IND meeting with the US FDA in November of 2016 to develop of NIAGEN as a drug in treating of Cockayne Syndrome.

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This rare pediatric orphan disease that results in a significantly shortened lifespan for the affected children.

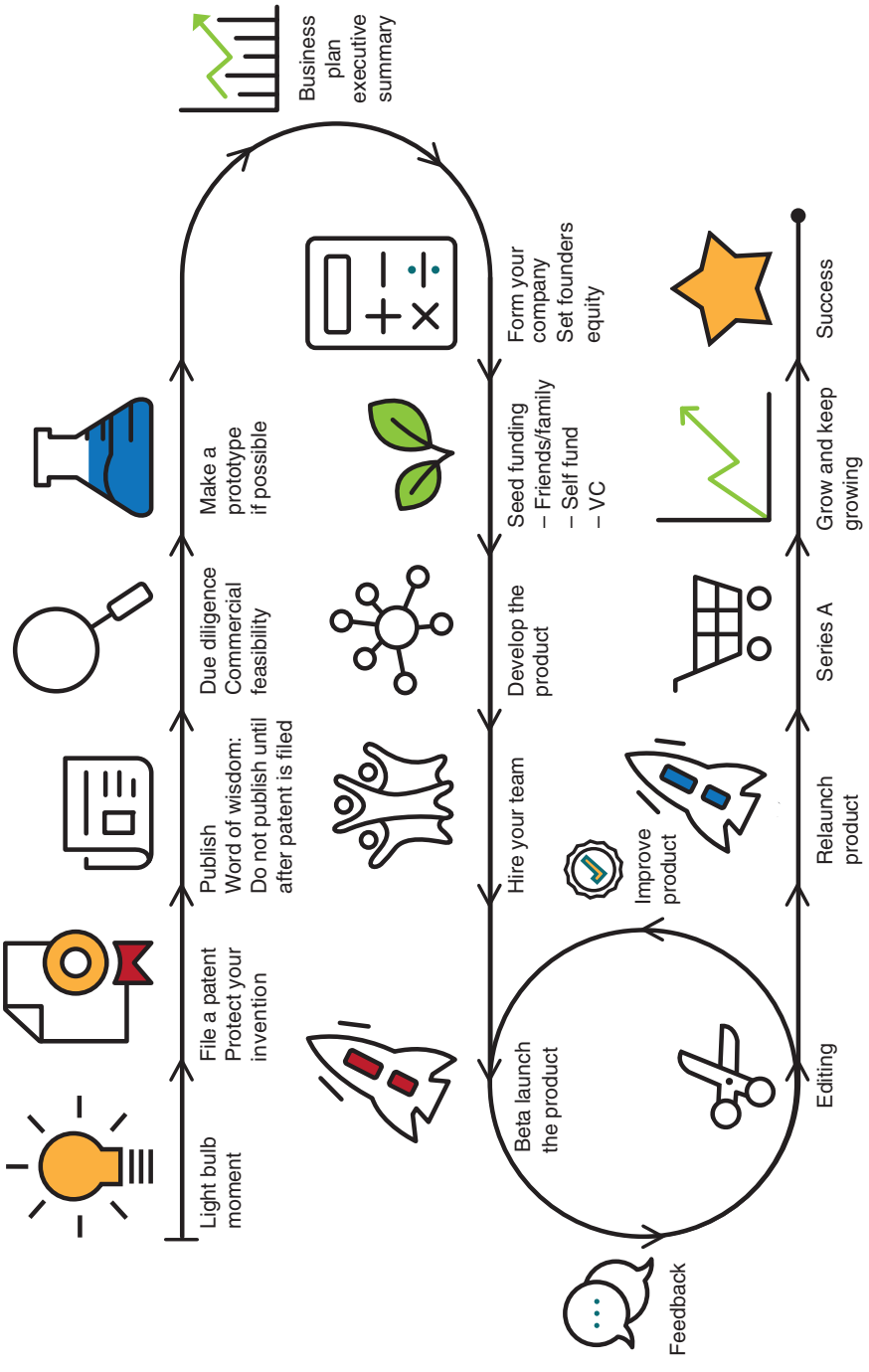
- Since launching NIAGEN in 2013, ChromaDex has signed over 160 collaborative research agreements with numerous prestigious universities and research institutions worldwide.
- In 2017, ChromaDex pivoted from selling NIAGEN as an ingredient to selling our consumer product brand TRU NIAGEN.

1.6 Summary: Do You Have What It Takes?

It does not matter if you have the most innovative and disruptive technology in the industry. If you cannot bring it to market, it will die. If you bring it to market without the proper patents or preparation for success, it will die. Success as a chemistry entrepreneur is a delicate balance that requires patience and a plan, even when it seems like there is not the time for either.

The industry is currently moving so quickly that even companies like ChromaDex struggle to keep up with new technology opportunities. We have had to pivot our business model to continue building upon our reputation as a viable partner in commercialized technology. That kind of success will inevitably open doors for many others. All we need is more people willing to walk through them.

We need more chemistry entrepreneurs. We need more researchers with the talent for identifying promising discoveries, who are also willing to learn how to commercialize them. There are a lot of truly disruptive technologies already out there. Overall, I would say the best way to figure out if you have got what it takes to be a chemistry entrepreneur – is to become one.


Light bulb moment
File a patent Protect your invention
Publish Word of wisdom: Do not publish until after patent is filed
Due diligence Commercial feasibility
Make a prototype if possible
Business plan executive summary
Form your company Set founders equity
Seed funding – Friends/family – Self fund – VC
Develop the product
Hire your team
Improve product
Beta launch the product
Feedback
Editing
Relaunch product
Series A
Grow and keep growing
Success

Recommended Readings and References

1 Jacobs, M. (2011). *Chemical & Engineering News* (7 November), p. 47. https://cen.acs.org/articles/90/i34/Researchers-Want-Entrepreneurs-Need-Know.html.
2 Korn, M. (2015). Chemistry departments try to attract more students by retooling the major. *The Wall Street Journal (US Edition)* https://www.wsj.com/articles/chemistry-departments-try-to-attract-more-students-by-retooling-the-major-1428880862.
3 Ghatora, B. and Strutt, R. (2017). Incorporating entrepreneurship skills into chemistry and related curriculums. *New Directions in Teaching of Physical Sciences* 12 (1) https://journals.le.ac.uk/ojs1/index.php/new-directions/article/view/2335/2275.
4 Runge, W. and Brase, S. (2009). Education in Chemical Entrepreneurship: Towards Technology Entrepreneurship for and in Chemistry-Related Enterprises. Self published. https://www.researchgate.net/publication/228801210_Education_in_Chemical_Entrepreneurship_Towards_Technology_Entrepreneurship_for_and_in_Chemistry-Related_Enterprises.
5 G. Heilmeier (1992). "Some Reflections on Innovation and Invention," Founders Award Lecture, National Academy of Engineering, Washington, D.C., as published in *The Bridge*, National Academy of Engineering.
6 McLeland, L. (2002). *What Every Chemist Should Know About Patents*, 3e. https://www.acs.org/content/dam/acsorg/about/governance/committees/what-every-chemist-should-know-about-patents.pdf.
7 Roach, M. and Sauermann, H. (2015). Founders and joiners. *Science* 348 (6240): 1200. https://science.sciencemag.org/content/348/6240/1200.3.

Author Biography

Frank L. Jaksch, Jr., co-founded ChromaDex®, Inc. in 1999, brought the company public in 2008, listed the company on NASDAQ in April 2016, and serves as Executive Chairman. Under his leadership, ChromaDex has focused on developing a comprehensive natural products chemistry business, expanded into international markets, and built an impressive roster of Fortune 500 customers.

As it is built on science, ChromaDex (NASDAQ: CDXC) has been transformed into an integrated, global nutraceutical company devoted to improving the way people age. Its flagship ingredient, NIAGEN® nicotinamide riboside, sold directly to consumers as TRU NIAGEN®, is backed with clinical and scientific research, as well as extensive IP protection. TRU NIAGEN® is helping the world AGE BETTER®.

Mr. Jaksch holds a Bachelor of Science degree in Chemistry and Biology from Valparaiso University in Valparaiso, Indiana, and serves on the Natural Products Association (NPA) board. Mr. Jaksch was the co-editor of Current Opinion in Biotechnology: Analytical Biotechnology in February 2014, highlighting new technologies for quantitative analysis of natural products. He also co-authored "The Handbook of Analytical Methods for Dietary Supplements" with Drs. Mark Roman and Mingfu Wang, which was published by the American Pharmacists Association in June 2005.