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Edited by Javier García-Martínez and Kunhao Li

Chemistry Entrepreneurship

With a Foreword by Robert Langer

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Foreword

Javier García Martínez and Kunhao Li have put together what I believe is a fascinating book – to my knowledge the first of its kind – on chemistry entrepreneurship. I feel privileged to contribute to it, as well as to write this foreword.

The basic goal of the book is to provide guidance to chemists, biochemists, chemical engineers, and scientists in related disciplines on how to start a company that can create products from their research, as well as the elements of being an entrepreneur coupled with being a scientist. There are eight chapters, which I will discuss briefly below.

The first chapter is aimed at explaining what it takes to be a chemistry entrepreneur. It discusses examples of innovation in chemistry in food and nutrition, sustainable/renewable chemistry, biotech/pharma, and diagnostics, followed by a discussion of key challenges like patents. It then discusses invention being only the beginning of creating a company and examines raising money and getting one's key ideas to commercialization.

The second chapter is from our laboratory and discusses starting companies in the biomedical field. There are six examples: Advanced Inhalation Research, Kala Pharmaceuticals, Moderna, Sigilon Therapeutics, Suono Bio, and Vivtex. We also discuss why to start a company (e.g. to have the largest impact on patients), when to start a company, and related issues.

Next, transferring technology from the lab to the market is evaluated. Such issues as entrepreneurship and technology transfer, pursuing commercial product/service, and extracting technologies from research institutions are examined. This is followed by a discussion of technology discovery and development and customer discovery and development. A case study of the Naval Research Laboratory's development of Self-Decontaminating Materials is also evaluated.

The fourth chapter involves financing and business development, such as balancing ambition with reality. It then discusses challenges in financing hard tech startups such as fundraising the right way, including what kind of investors you should raise funds from and how to generate interest from investors.

The next chapter discusses battery entrepreneurship, including finding a market for your technology. There is a focus on energy storage markets such as portable electronics, drones, and medical devices; grid energy storage and renewable energy; industrial batteries and back-up power; home energy storage; electric vehicles; and

other nascent energy storage markets. It then covers battery startup case studies and lessons learned from these case studies, such as market challenges, technical challenges, financial challenges, and team challenges. Finally, it evaluates strategies for startups and academic inventors, such as funding strategies, strategic partnerships, intellectual property (IP) management strategies, technology licensing, press relations (PR), and marketing strategies.

The sixth chapter covers growing a business in the chemical industry. It examines strategic market segmentation, such as situations where one has a solution looking for a problem as well as a problem looking for a solution. In addition, roadmaps for scaling a chemical business, finding the right niche, pivot strategies that can work, selecting the best path to market, licensing vs. manufacturing, and strategic market assessment are examined. It also evaluates building economies of scale, including gaining customer traction, customer testimonials, pricing models, market entry and initial sales, and direct sales vs. distributors. Finally, the chapter discusses growing to a commercial scale and includes such factors as best practices, financing, growth constraints, primary and secondary markets, in-sourcing vs. outsourcing, growing too fast, hidden landmines, and overcoming competitive threats.

The next chapter discusses new models to foster big pharma and chemistry entrepreneurship. It examines issues specific to universities and research institutions, biotech companies, venture capital, patient associations and charities, public administration, and contract research organizations (CROs). It also provides considerations for would-be entrepreneurs such as reflections on collaborations with Big Pharma and areas of collaboration between chemical companies and Big Pharma, as well as novel business models.

The final chapter discusses the economic need for chemically based start-up companies. It discusses promising programs such as National Science Foundations (NSF's) I-Corps and also evaluates non-dilutive funding opportunities, angel funding, and accelerators.

Overall, I found this to be a very unique book with many real life lessons and case studies for potential entrepreneurs. I expect we will see more and more companies started in the future by chemical entrepreneurs, and this book illustrates critical examples and lessons from which all of us can learn.

Professor Robert S. Langer, MIT

Preface

When someone decides to embark on the adventure of publishing a new book, a process that usually requires years of work and a lot of sleeplessness, you should think hard about why you want to do it. Likewise, when a person decides to purchase a book, it is convenient that the reader knows why the authors decided to dedicate themselves to writing it and what can be expected from it. In these first pages, I would like to answer those two questions in a clear and brief way, why we decided to edit "Chemistry Entrepreneurship" and what you will learn after reading it.

About the motivation of this book, I think the best way to summarize why we decided to edit it is because there was nothing similar and I would have loved to have it when I decided to found Rive Technology in 2006 to commercialize the technology I discovered at the Massachusetts Institute of Technology. Chemistry Entrepreneurship is the first book to explain how to become a chemical entrepreneur, from creating a business plan to selling the company. At MIT, I was fortunate to have many people who helped me create Rive Technology. As a Fulbright post-doc there, I had no idea about how to create, grow, and sell a company. I was almost fully tied up with conducting my research and advancing my academic career. Fortunately, I had a lot of help from industrial veterans. Thanks to my co-founders, Dr. Larry Evans, a former MIT professor and then recently retired founder and CEO of Aspen Technology, leader of chemical process simulations, and Mr. Andrew Dougherty, an business executive at Aspen, who joined the company we founded together, Rive Technology, full time a year later, we managed to protect the intellectual property, raise a total of $87 million, build a winning team with some of the most respected people in the industry, secure great strategic partners, and finally sell our company to W. R. Grace, a leading multinational chemical company. It has not been an easy process and I have had to learn a lot along the way with experts in almost every aspect of protecting, licensing, and commercializing chemical innovations. My co-editor, Dr. Kunhao (Eric) Li, who worked with me at Rive Technology and now is a Director of R&D at W. R. Grace, and I decided to put together this guide book so that anyone who wants to start a business in the chemical sector can do so with the resources, advice, and information at their fingertips.

Another reason why we decided to edit and publish this book is that we strongly believe that Chemistry Entrepreneurship is a topic of great importance. Many innovations never leave the lab because those who made those discoveries do not know

how or have not considered commercializing those technologies. We hope that this book will inspire them to become entrepreneurs. The society will benefit from more discoveries reaching the market, as those innovations could not only create jobs and wealth but also help solve some of our most pressing problems from fighting climate change to curing new illnesses.

One of the key messages we want to convey with this book is that it is not necessary to make a great scientific discovery in order to create a company. Many successful businesses are based on new types of business, on improving practical aspects or reducing costs. As frequently said, an entrepreneur is a person who where others see a problem, he or she sees a business opportunity. The chemical sector, despite its size, maturity, and resources, presents numerous opportunities for improvement, whether toward a more circular economy or its decarbonization. On the other hand, commercialization of a discovery, product, service, improvement, or new business model in the chemical sector does not always (and rarely does) involve the creation of a new company. There are many other ways to reach the market without having to found a company, such as licensing a patent, a joint development agreement, or selling rights. It is very important that we think about which of these and other business models suits the best. This book tries to provide you the resources to help you make these important decisions.

Despite the fact that many chemists, especially in academic institutions, make discoveries that are potentially the seeds of new businesses, the average chemists receive very little training on how to patent, write a business plan, or create a company from their formal education. We are glad to see that in recent years there are increasing interests in formal and informal trainings on entrepreneurship at various educational levels. We hope that this book will be useful to both those learning and teaching those courses.

We would like to thank the authors of the different chapters of this book, who themselves have been actively engaging with chemistry entrepreneurship, for sharing their knowledge and first-hand experience in this book. We are especially grateful to Professor Robert Langer of MIT, a leading scientist and serial inventor and entrepreneur, for writing the Foreword for the book, in addition to contributing an excellent chapter with his colleagues. We also want to thank Wiley who believed in this project from the beginning and helped produce this book in your hands.

"Chemistry Entrepreneurship" is meant to be a practical guide instead of an academic book for chemists and chemical engineers who want to start a business to bring chemical innovations to markets. In each chapter, there are highlighted "Tips" or "Key Takeaways," figures, images and diagrams that help emphasize and visualize the basic concepts. Each chapter also has at least one case study to exemplify how the concepts are applied by real-life entrepreneurs at different stages of a chemical start-up, the resources available to new chemical entrepreneurs, the common mistakes and consequences, etc. We believe that these case studies offer unique learning experience to the readers. In addition, each chapter ends with a thematic drawing as visual summary of the main idea the authors have decided to highlight in his contribution. We hope you find this book a visually attractive, easy to read, and useful to your own entrepreneurial endeavors.

Lastly, I wish you all the success in creating and growing your own chemical start-ups in near future!

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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.

Chemistry Entrepreneurship, First Edition. Edited by Javier García-Martínez and Kunhao Li.

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.

(Continued)