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Commercializing Science: Turning Life Science Discoveries Into Lifesaving Products – Part 1: Overcoming Barriers to Commercialization of Original Research

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Abstract

What is the message? Developing a life science product is extremely complex and difficult: there are many steps along the way when a would-be biotech entrepreneur can be derailed. This is especially true of academic scientists seeking to bring their discoveries from bench to bedside. Translational science, fundraising, and commercialization require a wide array of skills and a lot of luck. Focusing on Stanford University, this paper details some common pitfalls experienced by scientists seeking to commercialize their original research, as well as some attributes common to many success stories. It suggests means of mitigating common sources of failure to enable more scientific discoveries to be developed into lifesaving products.

What is the evidence? Interviews with several individuals with experience across parts of the life sciences research, development, and commercialization value chain. Emphasis on university-based principal investigators with experience translating basic science from their laboratories into for-profit life sciences firms. Analysis and interpretation of publicly available data from multiple sources.

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To read the companion paper, Commercializing Science: Turning Life Science Discoveries Into Lifesaving Products – Part 1: Overcoming Barriers to Commercialization of Original Research, click here.

Introduction

Patients benefit from investment in basic science research through the translation of science into novel medical products and services. Yet, despite the demand for innovation from patients and providers, it is incredibly challenging to translate discoveries made in academic laboratories into products that benefit patients. Since the beginning of large-scale government funding of university research in the 1940s, the process has worked as follows: (1) government funds academic scientists to do research; (2) scientists make discoveries and publish their findings; (3) eventually (often after years or decades), industry identifies one idea or synthesizes multiple findings into a technology, which can then be developed into a product.[i]

The Bayh-Dole Act of 1980 was enacted to encourage universities to commercialize government-funded research. The act clarified ownership of intellectual property resulting from government-funded studies, formally transferring ownership and a responsibility for translation and licensure to universities. It enabled a new pathway whereby scientific discoveries are shepherded directly from the laboratory into startups, then into industry, which then have an opportunity to develop products.[ii]

However, the post-1980 pathway from academic science to commercialization remains challenging. There are a handful of locations in the world where translation is most efficient in the life sciences, the most notable being the Bay Area and the Boston / Cambridge region.[iii] This paper represents the collective experience and wisdom of several participants in the scientific discovery and commercialization process (largely based in the Bay Area) and seeks to

understand the process of commercializing discoveries and challenges involved in bringing scientific ideas to patients. The perspective is largely one of examining the business risk of drug development; it does not address the scientific risk (i.e., around the validity of the underlying scientific hypotheses). It concludes by discussing implications of this work and potential ideas for overcoming barriers to commercializing research.

Context: How the Process Works From Bench To Newco

The pathway by which life science discoveries in the lab translate into commercialized products for patients proceeds roughly as follows:

- Scientists (principal investigators, postdoctoral students, and graduate students) conduct laboratory-based research. They discover new biological targets, tool molecules, or develop potential platform technologies, and demonstrate initial proof of concept.
- Principal investigators work with university technology licensing offices to file relevant patent applications on discoveries.
- Scientists publish their initial findings in academic journals.
- Scientists continue to conduct translational experiments (e.g., target validation, additional *in vitro* studies, animal studies for efficacy and safety) to further prepare for translation into clinical development.
- Scientists apply for non-dilutive funding from the Small Business Innovation Research (SBIR) and/or raise private angel funding. They form a startup company and start recruiting a management team while doing additional translational science. University personnel may move into the startup or may serve as advisors.
- The startup, equipped with a preliminary management team, raises venture capital investment.
- The startup works with the university technology licensing office to in-license patents related to the discovery. In the meantime, the VC(s) helps recruit additional management personnel. The management team makes important strategic decisions (e.g., which indications to pursue). The startup is now in the pre-clinical development stage.
- The startup continues to develop technology while raising money. Management works towards successfully hitting developmental milestones agreed upon with investors. Preclinical studies are completed and an Investigational New Drug (IND) application is filed

with the Food and Drug Administration (FDA).
- The startup moves into the clinical development stage with human clinical trials (Phases 1, 2 and 3). Clinical development requires significant investment, which requires further venture rounds or partnership/sale to larger pharmaceutical firms. For the fortunate few with successful clinical trials, the startup receives approval of their new drug application (NDA) by the FDA. The startup becomes a commercial stage company.

Of note, while this somewhat formulaic playbook works for therapeutics, it does not apply neatly to diagnostics or scientific tools. That said, it remains useful for illustrative purposes.

Common Challenges

Scientists face several challenges throughout the process of commercializing their research, something that they typically have not trained for and do not know how to do. The most commonly raised challenges are detailed below.

Short timeline and bandwidth constraints

Researchers typically have only two years and six months after filing for a provisional patent application to find a licensee (often his/her own venture-backed startup) for that patent application.[1] Over this short time, several additional activities need to occur:

- The basic research must be published in an academic journal.
- Additional translational research must be conducted to confirm initial findings and de-risk sufficiently to encourage venture capitalists to finance the idea. This step can be extensive and onerous – there is typically a large gap between the state of research immediately post-publication and the studies that must be done to raise investment, as scientists race to publish their research as quickly as possible in a competitive environment.
- A team to manage the startup must be recruited.
- Capital must be raised to fund the startup.

In addition to these activities, researchers must continue to do their day jobs at the University. Further, once the company is established, the University might place restrictions on the inventors/faculty given the potential conflict of interest between their University and company roles. Given these short timelines and intense demands, scientists face difficulty juggling

competing responsibilities – there are simply not enough hours in a day nor days in a year to do it all. If a given scientist has not yet achieved tenure, it can be risky to spend so much time on translational research that will not support his/her case for tenure.[2]

To compound these challenges, commercializing science requires bridging the gap between academia and industry, two sets of institutions with misaligned incentives and a large cultural gap. While academia rewards basic scientific research, which is more likely to be published in prestigious journals, industry seeks to maximize profit and prioritizes translational research. Academics sometimes view industry-based drug development as intellectually unsophisticated, while industry scientists view academic work as unreliable and not replicable.[iv]

Lack of know-how and experience

Developing a drug requires a long series of complex, difficult, and nonintuitive steps. It requires varied skill sets and knowledge. From pitching the right investors for a specific disease area to good manufacturing practice (GMP), from recruiting and managing a team to working with the FDA, the sheer number of intermediate steps required to commercialize a drug increases the opacity of the entire process. Missing any of these could be a fatal roadblock.

Academics who have never undergone the process of raising money and developing a drug often do not realize just how much time, money, and effort is required. After all, the biotechnology industry operates under an apprenticeship model, where most people who have learned to translate their research and start companies do so by watching others with more experience. Even knowing everything in the playbook is an inadequate substitute for executing; as with surgery, a textbook cannot teach everything. For scientists who have no experience in commercial activity and lack ready access to people who have successfully navigated this process, translation can become an unachievable objective.

Lack of experience can also increase business risk. It can lead to unrealistically high expectations regarding scientific founder ownership stake and influence on a startup's day to day operations. Without full understanding of all the steps and skill sets required to bring a drug to market, scientific founders may underestimate the value brought by investors, management, and employees. This can cause friction within new startups that cripples their chances of success.

Recruiting talent

Given the complexity and risks involved in the process, good management is critical for success in life sciences commercialization. Drug development requires a wide variety of specific skill sets and experiences, and these requirements change over time as a company progresses from pre-clinical to clinical to commercial stages. For a startup, cash flows are the primary metric, with management and investors carefully monitoring burn rates required to achieve milestones at each development stage. Mistakes or delays can leave a startup short of cash at critical periods. Experienced leadership allows a biotech startup to (hopefully) avoid mistakes.

Investors understand that many great technologies fail due to poor management, and often care more about the management team than even the technology of a potential portfolio company. Many are not interested in funding a company unless a strong team is already in place.

Unfortunately, good, experienced management is in high demand and difficult to recruit to early stage companies. CEO talent is especially make or break, and especially rare: very few people can lead a ten-person company, grow it to a 50-person company, and eventually take it public. Furthermore, team dynamics are critical – many programs have failed due to intra-team dysfunction. Finally, retention of key staff can be nearly as difficult as recruitment – departure of a key scientist for greener pastures can tank an early-development program. These personnel challenges – recruiting and retaining a talented management team that works will together – will only intensify as more biotech companies receive venture funding.

Raising money

Biotechnology startups must constantly raise money to remain solvent while developing products that take years to reach the market. Raising capital, especially early on, requires the ability to do great science *and* be able to sell that science to investors. This combination is rare in academic scientists, who also often do not understand the market for their discoveries and pathways for translation.

It is even harder to raise money for truly novel ideas. Venture capitalists often prefer to invest in technologies with which they are familiar, rather than ones that present additional scientific risk. Even some of Stanford’s faculty who are most successful in translation have had difficulty

finding investment for their most groundbreaking ideas. Jennifer Cochran, for example, has found investors more receptive to antibody-based therapeutics than therapeutics based on engineered cysteine knot peptides ("knottins"). Carolyn Bertozzi, despite her academic accomplishments and commercial track record, has faced relative difficulty raising money for glycoscience-based startups (i.e., Palleon Pharmaceuticals and InterVenn Biosciences) compared with her easier success for startups developing more widely understood technologies (e.g., Lycia, which is developing a protein degradation technology).

Technology licensing resource constraints

Given the substantial resources required to file patent applications, pay internal staff and external consultants, and hire legal support, technology licensing offices must be selective about the commercial potential of the science they support through the patenting and licensing process. Increased selectivity can have a positive effect – the high bar encourages researchers to think big (i.e., develop technologies applicable to large markets). On the other hand, bandwidth constraints force tech licensing offices to make tradeoffs based on limited information. For scientists navigating this process without full knowledge of the process and constraints, technology licensing offices can appear to be another roadblock to translation.

Developing valuable products that are not rewarded by the market

Translating scientific discoveries through venture-backed startups only works when these startups have the potential to be worth billions of dollars and generate positive returns for venture capital firms. This method does not work for products with more limited markets or for products without novel intellectual property. Despite years of work to raise venture and philanthropic funding for pediatric cancers, Crystal Mackall has had difficulty upending the physics of the market and building a "business case" for pediatric therapeutics that do not also work in adult cancers. The same issue – lack of market incentive – applies to next-generation antibiotics to fight the coming antibiotic resistance crisis.[v] Public policy measures, like the Orphan Drug Act or modifications of payment models are needed to incentivize development in these valuable but financially unattractive markets.[vi] [3]

Where Success Comes from on an Individual Level

Scientists typically attribute their own success in translating ideas from laboratory to startup to a mixture of skill, experience, and luck. A closer glance suggests that these advantages break down into several specific success factors.

Mentorship

Biotech is commonly described as an apprenticeship-based industry. To learn the ropes, it is important to see how things are done well, and useful to have someone you can ask questions of. Mentorship is thus invaluable – it enables scientists without any commercial experience to skip unnecessary steps and sidestep risks, thereby increasing speed and chance of success.

Many scientists who have seen success in commercializing their ideas worked with mentors who had prior experience with the biotech industry. A 15-minute conversation with Paul Yock yielded Tom Soh connections that saved him three months of cold outreach. On a longer time horizon, Ravi Majeti benefited from Irv Weisman's mentorship in developing his discovery of CD47 into a clinical stage monoclonal antibody housed within Forty Seven, a biotech startup ultimately acquired by Gilead Sciences. Garry Nolan gained early exposure to industry as a PhD student when Leonard Herzenberg invited him to observe contract negotiations with pharmaceutical firms.

Ability to sell

Academic scientists have universally honed their grant writing abilities over years of practice. However, raising capital from private investors and writing grants require different skills, and can be difficult for scientists. Specifically, raising money requires the following:

- Strong communication ability. Raising startup financing requires scientists to develop pitch decks that tell simple, compelling stories; they must then deliver sales pitches repeatedly with confidence and clarity. Scientists sometimes dive deeply into the details of their science without pausing to discuss higher level implications, thereby causing potential investors' eyes to glaze over.
- An ability to empathize with investors. Crafting a compelling story requires tailoring messages for specific audiences. Different types of investors – government, disease-specific foundations, venture capitalists – have different assumptions and goals. A good

salesperson understands what the buyer wants and messages appropriately.
- The ability to paint a big vision with conviction, while remaining realistic about potential challenges and risks. Venture capitalists seeking home run returns will not invest simply based on a reasonable two-year development plan – they need to be convinced of the potential for a billion-dollar exit. Many scientists, trained for years not to make claims they cannot back up, find it difficult to truly *believe* and sell the story of a big exit.

Network

Having access to a dense network facilitates fundraising and recruitment of a management team, the most critical bottlenecks in the early stage of commercialization. Given the number of pitches that VCs see every day, personal connections can be a prerequisite for an opportunity to pitch the right investors. Relationships also increase the chance of raising multiple funding rounds, even in the face of development setbacks, and facilitate recruitment of talented management teams.

Track record and experience

Any kind of experience, especially past success, helps tremendously in subsequent attempts to commercialize scientific discoveries. Experience builds wisdom and understanding – of what errors to avoid, what VCs are seeking to fund, and how to be self-critical about subpar ideas. Experience in commercializing products also facilitates rapid network building; multiple successes over time can build a reputation for scientific excellence and startup acumen. For this reason, venture capitalists proactively reach out to some investigators (e.g., Irv Weissman, Stephen Quake) who have progressed multiple ideas successfully from bench to bedside.

Entrepreneurial mindset

Given the significant differences in incentives and culture between academia and the industry, successful translation of basic research requires a willingness to work in the chaos, frustration, and uncertainty of a biotech startup. Scientists seeking to play a role in commercializing their research must be comfortable with ambiguity, willing to start a company and operate in a structure very different from that of an academic lab.

Naivete can also be very helpful in lowering the activation energy required for starting a

company. Sometimes, scientists stumble into entrepreneurship without knowing the negative implications. Tom Soh started CytomX after applying for an SBIR grant to fund his research and realizing that he *had* to house his newly funded work in a commercial entity to make use of the funding.

Luck

As with any entrepreneurial activity, a substantial amount of success in translating research into commercialized products comes down to luck. This is especially salient in the life sciences, a field characterized by unknown unknowns. Development of Rituxan, the first and perhaps most famous monoclonal antibody treatment, would have died an early death had Ron Levy not met David Ebersle through a chance encounter at Stanford. Their conversation over lunch convinced Ebersle to push for Genentech to fund continued development of Rituxan just as IDEC, its parent company, was running out of money.[vii] Rituxan went on to become the world's top selling oncology drug for nearly a decade, with sales eventually peaking at nearly $9 billion annually.[viii] Many other drugs on the market experienced similar near-death situations, only to be serendipitously rescued on the path to commercialization.

Addressing the Challenges

Given the daunting path from bench to bedside, universities, other organizations, and individuals have developed novel programs to address the challenges outlined in this paper. Several solutions have been designed at Stanford University and in the Bay Area at large to accelerate translation of discovery to the market.

Wraparound drug development support

Stanford's SPARK program in translational research provides invaluable guidance for faculty, postdocs, and graduate students through the step-by-step process of translational research and commercialization of lab discoveries. It convenes industry mentors who, along with faculty and staff, provide high-touch support for translation. The program also provides $50,000 per team per year to fund the translational work that may be necessary to test preclinical hypotheses.[4]

The university developed the Innovative Medicines Accelerator (IMA) to support faculty in one

key aspect of drug development: medicinal chemistry. While the IMA is brand new (founded in 2019), it has been able to recruit medicinal chemists to facilitate development of small molecule drugs.

Stanford's Chemistry, Engineering & Medicine for Human Health (ChEM-H), an institute designed to bring multiple drug development disciplines under one roof, has moved to support its researchers by hiring a full-time clinical coordinator to handle clinical operations (e.g., trial design, biostatistics, patient recruitment, collaboration with contract research organizations, institutional review board interactions).

The Center for Definitive and Curative Medicine (CDCM) was developed with an understanding of commercialization needs: it supports clinical development of cell and gene therapies through proof-of-concept trials.[ix]

Reduced Barriers to Gaining Know-How and Experience

Today, researchers gain valuable introductions, mentorship, and experience through ad hoc conversations following presentations, at convenings, and through informal relationships. Despite these venues for knowledge-sharing, many scientists still feel lost when it comes to what is required to commercialize a life science product. At Stanford, several programs have been developed to introduce scientists to basic business concepts and provide a baseline level of mentorship and guidance.

Ignite, a 4–8-week program offered through the Graduate School of Business (GSB), teaches business fundamentals to graduate students and postdocs interested in commercializing their ideas.[x] It is built around turning a scientific idea into a "venture project."

The Accel Leadership Program, a 6-month program, prepares technically minded students (both undergraduate and graduate) to start and lead startups through workshops, projects, and exposure to industry leaders.[xi]

The Faculty Entrepreneurship Leadership Program, started by Jennifer Cochran based on her own experience commercializing technology, offers a two-quarter bootcamp for STEM faculty to gain knowledge and skills to commercialize their laboratory research.[xii] It exposes Stanford

faculty to industry leaders and introduces scientists to fundraising, negotiation, intellectual property, management, and industry collaboration.

Finally, frequent events (e.g., conferences, like Stanford Drug Discovery Symposium; networking events; classes with a slate of guest speakers from industry), expose researchers to stories of success, help answer basic questions, and enable introductions to people with complementary skill sets for commercializing discoveries in the lab.[xiii]

Network of future biotech management talent

Difficulty recruiting experienced management talent is one of the most common causes of failure for biotech startups. The apprenticeship model prevalent in the biotech industry has resulted in a shortage of management talent, as the recent explosion in company formation and funding has outpaced the rate at which talent has "graduated" from older startups. Additionally, many scientists with great ideas do not have networks dense enough to rapidly recruit teams to manage their startups.

Venture capital firms provide a stopgap solution to the shortage of management talent by temporarily filling empty leadership positions with their own staff and serving as part time executive recruiters. However, they do little to train the next generation of management talent. Furthermore, a startup is usually limited to the networks of its own investors.

In the Bay Area, informal networks help to train and nurture talent. For example, one chat on GroupMe has grown from a small group of young business development and strategy managers seeking peers to socialize with during the JP Morgan Healthcare Conference into to a hundreds-strong support group. Today, members use the group chat to get information, seek advice, and post job opportunities.

Conclusion

Translating scientific discovery to clinical products that benefit patients remains a significant challenge. Based on interviews, many of these challenges have been identified. One Bay Area institution has developed several overlapping efforts to address these challenges, but the effort required to impact patient care remains significant. A companion paper examines these

challenges from an ecosystem perspective.

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References

[1] At the end of this two-and-a-half-year period, university technology licensing offices must file for the patent in question (~$85,000 to cover North America, Europe, Japan, and China). Universities are typically unwilling to pay for expensive patent applications without reasonable certainty that a commercial entity will license the resulting intellectual property. Researchers often receive help from university technology licensing offices and other supporting groups in finding licensees.

[2] Translational research also often requires funding separate from basic science research, which must be applied for separately. This is also a time-consuming process.

[3] Carolyn Bertozzi's Thios Pharma developed a treatment for a rare disease indication prior to the Orphan Drug Act. It boasted great science, great preclinical data with an IND-ready asset, and a good management team, but shut down after it was unable to secure Series B funding. Years later, after the passage of the Orphan Drug act, another company pursuing the same indication successfully raised funding and commercialized its product.

[4] $50,000 is often not enough to fund all the translational work required to de-risk a drug. SPARK teams sometimes seek additional funding.

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[i] Leyden DP and Menter M. The legacy and promise of Vannevar Bush: rethinking the model of innovation and the role of public policy. *Economics of Innovation and New Technology*. 2018; 27(3): 225-242. https://doi.org/10.1080/10438599.2017.1329189

[ii] Mowery DC, et al. The growth of patenting and licensing by U.S. universities: an assessment of the effects of the Bayh–Dole act of 1980. *Research Policy*. 2001 (30):99-119. doi.org/10.1016/S0048-7333(99)00100-6

[iii] Owen-Smith J, Powell WW. Accounting for Emergence and Novelty in Boston and Bay Area Biotechnology. *Research Gate.* 2006. DOI: 10.1093/acprof:oso/9780199207183.003.0004

[iv] Begley C G and Ellis L M. *Nature* (2012): 483. Raise standards for preclinical cancer research. https://doi.org/10.1038/483531a

[v] Plackett B. Why big pharma has abandoned antibiotics. *Nature Outlook.* 2020 Oct; 586:S50-S52. https://doi.org/10.1038/d41586-020-02884-3

[vi] Gandhi N, Schulman KA. New Medicare Technology Add-On Payment Could Be Used As A Market Support Mechanism To Accelerate Antibiotic Innovation. *Health Aff* (Millwood). 2021 Dec;40(12):1926-1934.

[vii] Colin C. The Lunch. *Genentech: A Member of the Roche Group.* 7 Jul 2016. https://www.gene.com/stories/the-lunch

[viii] Pierpont, T M, et al. Past, Present, and Future of Rituximab—The World's First Oncology Monoclonal Antibody Therapy. *Frontiers in Oncology*. 4 Jun 2018. https://doi.org/10.3389/fonc.2018.00163

[ix] Stanford Medicine. Center for Definitive and Curative Medicine. https://med.stanford.edu/cdcm

[x] Stanford Graduate School of Business. Stanford Ignite. https://www.gsb.stanford.edu/exec-ed/programs/stanford-ignite

[xi] Stanford Technology Ventures Program. Faculty Entrepreneurship Leadership Program. https://stvp.stanford.edu/alp

[xii] Stanford Technology Ventures Program. Faculty Entrepreneurship Leadership Program. https://stvp.stanford.edu/felp

[xiii] Stanford Medicine. Stanford Drug Discovery Symposium 2022. https://med.stanford.edu/cvi/events/2022-drug-discovery-conference.html