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Commercializing Science: Turning Life Science Discoveries Into Lifesaving Products – Part 2: What Makes Life Sciences Innovation Ecosystems Tick

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Abstract

What is the message? The benefits of economic clusters have been well observed: proximity of firms and other institutions associated with a given industry enables increased productivity and innovation. In the life sciences, the San Francisco Bay Area and Greater Boston area are the world's preeminent biotechnology hubs. What present-day institutions enable such robust engines of innovation? What historical occurrences or decisions led to the formation of these economic clusters in the first place? This paper highlights the critical components of the system – research universities, academic hospitals, biotechnology firms (large and small), and venture capital – and the roles that they play in turning science into lifesaving products. It further draws lessons for other regions of the world attempting to build their own biotech innovation hubs.

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.

Timeline: Submitted: December 14, 2021;accepted after review: March 31, 2022.

Cite as: Kevin Ho. 2022. Commercializing Science: Turning Life Science Discoveries Into Lifesaving Products – Part 2: What Makes Life Sciences Innovation Ecosystems Tick. *Health Management, Policy and Innovation* (www.HMPI.org), Volume 7, Issue 2.

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

In 1976, Herb Boyer and Bob Swanson founded Genentech, Inc., and along with it, the biotechnology industry. Genentech was founded based on technology developed by Boyer, a professor at UCSF, and Stanley Cohen, a professor at Stanford University. Boyer and Cohen's recombinant DNA technology was patented with the help of Stanford's Office of Technology Licensing, then licensed non-exclusively to Genentech and other companies. Genentech, based in South San Francisco and seeded with an investment from Kleiner Perkins, successfully developed the first synthetic human growth hormone and human insulin, thereby proving the scientific and commercial viability of biotechnology.[1] Its success inspired a generation of biotech startups in the San Francisco Bay Area and beyond.

While the birth of biotechnology was serendipitous, it is not entirely an accident that it occurred in the San Francisco Bay Area. Genentech's founding built on a legacy of innovation, from Hewlett Packard to Fairchild Semiconductor, from Intel to Atari. It developed in the fertile ecosystem of world-class university research and talent, risk-seeking financial capital, and a culture of entrepreneurship and labor mobility.

Today, the Bay Area and Greater Boston area are the world's preeminent biotechnology hubs. These two metro areas and economic clusters are uniquely effective at taking scientific discoveries, often made locally, and developing them into commercial products that help patients. More than half of all life sciences venture capital funding in the US consistently goes towards these two geographies.[2] While other regions of the United States and globally have attempted to create their own Silicon Valleys and Kendall Squares, no other geography has yet to achieve comparable bench-to-bedside throughput.[3] [4]

This paper reviews the elements – the institutions and intangibles – that have made these regions so successful at taking basic science and developing commercialized products. Academic research has described the important role of geography in the innovation process: the power of economic clusters has been well documented.[5] [6] [7] [8] This paper provides additional context, details specific Bay Area (especially Stanford University-based) and Greater Boston institutions and their histories, and offers considerations for other regions seeking to develop life sciences innovation ecosystems.

Major Institutions

Universities, hospitals, industry, and financing form the foundation of innovation ecosystems. When these complementary resources and capabilities cluster together, they provide both the raw materials and the developmental capacity to turn scientific discoveries into products. This is especially valuable in biotech, where a wide array of specialized functions must come together to turn an idea for a drug into something that helps patients.

World-class research universities amenable to entrepreneurship

Research universities are the foundational anchors of any innovation ecosystem. They employ scientists and engineers who generate and refine new ideas; they provide institutional support (e.g., funding, job security, facilities) for research; they train new talent. Furthermore, research universities have staying power: they are unlikely to move or go out of business. As such, research universities are the anchor tenants around which other parts of the innovation ecosystem are built.

One way to think of great research universities is as pools of talent. Great universities attract star scientists, who then attract other star scientists. Bob Langer, one of twelve Institute Professors at MIT, cites the example of Arthur Kornberg, a Nobel Prize-winning biochemist, as being important to the rise of biological sciences at Stanford. When he became Head of the Biochemistry Department in 1959, he attracted other talented scientists (e.g., Joshua Lederberg) to the university. Talented scientists like Langer, Kornberg, and Lederberg develop great ideas that serve as the raw material for scientific innovation. Importantly, they also provide mentorship and serve as role models for other scientists.

While great science is required for commercialized innovation, it is not sufficient. Academic culture is critically important. Universities that anchor innovation ecosystems have also proven to be supportive of entrepreneurship and amenable to relationships with commercial entities. Here, UCSF and Stanford provide contrasting examples. Typical of most university faculty until the last few decades, J. Michael Bishop, Chancellor of UCSF, viewed commercial activity with skepticism and believed that potential conflicts of interest could contaminate academic integrity.[9] He preferred for UCSF scientists to focus on basic science rather than applied research.

In contrast, Stanford University was created to "qualify its students for personal success, and direct usefulness in life."[10] At Stanford, education and research were meant to be practical, and the institution was, from its inception, amenable to collaboration with industry. Frederick Terman, Dean of Stanford's School of Engineering and eventual Provost, further promoted this relationship with industry: he established Stanford Industrial Park and encouraged technology companies to move in, created a program through which industry engineers could study part time at Stanford, and encouraged Bill Hewlett and David Packard to start a business rather than stay in academia.[11] Niels Reimers, founder and former Director of Stanford's Office of Technology Licensing (OTL), formalized the means by which Stanford supported its scientists in patenting technology by allowing them to benefit financially from patent licenses. His revenue-sharing model encouraged university-based researchers to disclose their ideas and inventions, thereby increasing their rate of commercial success and netting proceeds for both individual inventors and the university.[12] The model paid off immediately in the form of the Boyer-Cohen patent; this success bred confidence in this model of university-supported commercialization of science.

Medical schools and hospitals

In the life sciences, scientists often develop technology to prevent, treat, or cure disease. Doing so often requires clinical development to gain approval by the Food and Drug Administration (FDA) and other regulatory agencies. It requires an understanding of how therapeutics, diagnostics, medical devices, and tools may be used in the clinic.

Clinicians understand clinical medicine intimately, in a way that pure bench scientists often do not. Enabling interaction between clinicians and scientists can thus be useful for developing biotechnology for medical applications. Working with physicians helps scientists identify tangible problems, brainstorm technological solutions, and circumvent bottlenecks. Hospitals also have access to patients and samples (e.g., tumor biopsies) and are sometimes equipped to run clinical trials. These resources can also be highly valuable for laboratory research.

Stanford's world-class medical school and hospitals represent an important advantage for its life science researchers. Housing both academic medicine and research facilities under one administrative roof enables seamless collaboration and increases the rate at which people with different skill sets serendipitously meet each other at retreats and seminars.

MD/PhD students further strengthen the connective tissue between bench and bedside at Stanford. People who understand both molecular and human biology can, for example, avoid selecting an animal model that is not representative of human biology prior to the initiation of clinical trials. Understanding how drugs work in the clinic can help avoid early mistakes around administration, formulation, and safety profile.

The value of medical schools and hospitals to life sciences innovation will only become more important over time. While small molecule blockbuster drugs required mass manufacturing and huge clinical trials (neither is conducive for a university-based clinical setting), newer, curative modalities (i.e., cell and gene therapies) require artisanal manufacturing and small clinical trials (given their high therapeutic indices), which make them ideal for an academic setting. Institutes at Stanford, like the Center for Definitive and Curative Medicine (CDCM) and Chemistry, Engineering, & Medicine for Human Health (ChEM-H), were developed with an understanding of these circumstances.[13] [14]ChEM-H recently hired a full-time clinical operations coordinator to support testing in human subjects and is actively seeking to recruit MD/PhDs.

Companies

Biotechnology companies, large and small, serve several functions in an innovation ecosystem:

- They introduce academics to industry. Scientists who have been trained through academia typically lack prior exposure to the industry dynamics and the various functions required for industrial biotech R&D. Nearby biotech companies often hire university-based scientists in a consulting capacity and provide valuable exposure in the process. Edgar Engleman, for example, experienced his first exposure to biotech through consulting for Bay Area firms seeking their scientific expertise.
- They provide additional training for scientific and management talent. Graduate students and postdocs that do not plan to continue in academia can join biotechnology companies and continue their scientific training. Larger companies, especially, serve as excellent training grounds for future managers of biotech firms. Genentech, which has had outstanding corporate and scientific leadership, "incubated" many biotech management teams, and is the foremost example of this in the Bay Area.[15]
- They serve as a reservoir for talent. In addition to providing training, biotech companies give students a reason to remain in a geographic location even after they are no longer associated with their university. A corporate ecosystem also makes it easier for someone to move his or her family to a given area to work at a risky startup – even if that startup fails, he/she will likely be able to find employment nearby without having to uproot family again. Biopharma companies absorb talent and retain it in an area, especially during times of turnover.

It is important to have companies of different sizes for a true innovation ecosystem to function well. New York, New Jersey, and Philadelphia are home to large pharmaceutical firms (e.g., Pfizer, Merck, Bristol Myers Squibb) but a relative dearth of small, innovative firms. The Bay Area and Boston, in contrast, have both large firms (e.g., Genentech and Gilead in the Bay Area, Pfizer, Novartis, and Biogen in Boston) and a host of smaller biotechs. The large companies soak up talent and provide basic scientific and management training, while the small biotechs develop new ideas and encourage movement of talent between organizations.

Venture capital

Venture capital firms provide the investment capital that is the commercial lifeblood of R&D-oriented startups. Biotech companies, like other R&D-oriented firms, require substantial upfront funding for many years before profits can be made. Biotech VCs evaluate these firms on technology and management talent and determine how to allocate capital to the most promising ideas. This is not easy – it requires substantial technical expertise and a willingness to commit large sums of money to risky projects. Notably, biotechnology investment is the domain of specialized firms, generally with a focus on specific stages of technology.[16]Beyond capital, VCs, armed with experience serving on boards across multiple firms, provide mentorship and support in recognizing and responding to the challenges.

Finally, established venture capital firms have large networks of management talent. They help new startups quickly build the talented management teams required to move fast and utilize funding efficiently. Once a company gets started, VCs dig into their rolodexes to facilitate business development and partnering deals and raise later stages of financing. Overall, they serve as the connective tissue across biotech innovation ecosystems.

The Bay Area's VCs provide a critical advantage for the region's ability to commercialize scientific discoveries. Without Kleiner Perkins, Genentech may never have had the capital to run its first experiments.[17] While Sand Hill Road's technology VCs receive most of the national media limelight, the region's life sciences VCs generate stellar returns, as well. The high density of these technically savvy, founder-friendly investors means that scientists and management teams in the area can find money and mentorship when their ideas are promising.

Supporting institutions

While major institutions are required for any innovation ecosystem to function, supporting institutions improve the efficiency with which ideas are developed into commercialized products. Stanford boasts a plethora of supporting institutions that facilitate development of promising ideas into products for patients. These range from education and mentorship programs designed to familiarize students, postdocs, and faculty with industry dynamics and basic business skills to incubation programs that guide innovators through critical steps on the path to commercialization and offer mentorship from industry experts.

A non-comprehensive list of these supporting institutions is provided in a companion paper.

Additional Factors

Beyond local institutions, additional factors play a role in a region's ability to turn commercialize science. Many of these – history and culture, for example – are intangible. Others, like proximity, may be at least a partial function of geography. They are often difficult to influence, but critically important.

History

Innovation ecosystems cannot be built overnight. It takes time for major institutions to mature, then develop trust and productive cross-institution working relationships. At an interpersonal level, it takes time to develop strong, informal networks of experienced executives and scientists who understand the biotech industry. Hardware can be built quickly, but software takes time to develop.

Here, the Bay Area and Boston benefit from a decades-long head start on the rest of the country. California and Massachusetts were home to elite universities and recipients of significant federal government spending on science and engineering starting in the 1940s, both in the form of grants to top research universities and contracts awarded to defense contractors. This federal funding attracted technical talent and seeded a culture of engineering. Venture capital followed government funding to take advantage of this non-dilutive seed financing and nascent talent pool. Over decades, a dense infrastructure connecting academia, industry, and venture capital developed. Important institutional support – bankers and lawyers with business models tailored for startups – sprang up to support local ideas and businesses.[18]

Culture

As institutions take root and grow, they shape the norms, business practices, discussion, and people in an area. In other words, they shape culture, and this culture, in turn, shapes institutions.[19]

The Bay Area has historically been where revolutionary things happen. In Silicon Valley, innovators have, for decades, left comfortable jobs behind, questioned authority, and created entirely new industries.[20] These practices eventually created a culture where commercializing new ideas is neither strange nor especially scary. This strong entrepreneurial culture then self-selects for entrepreneurial people and converts prior non-entrepreneurs who “catch the bug.” In contrast, until recently, East Coast universities and companies were seen as more hierarchical and conservative than their West Coast counterparts. Broadly, academics were less willing to step out of their ivory towers to associate with industry. Aspiring entrepreneurs were less willing (and able, due to enforceable noncompete agreements) to leave large employers and set out on their own.

At Stanford, a cultural bent toward industry and entrepreneurship has important practical implications. Startup culture is the norm, and a part of typical interpersonal interactions. When seemingly everyone is willing to start a company, the social barrier to doing so diminishes. For professors, pursuing entrepreneurial ideas takes time, but does not detract from tenure decisions. The acceptance and promotion of entrepreneurship at Stanford fosters selection bias: on balance, comparatively industry-oriented, entrepreneurial students and faculty elect to study and work at Stanford over other universities.

This cultural dynamic creates a virtuous cycle in the life sciences. Commercially minded professors can maintain tenure while exploring entrepreneurial ideas. Entrepreneurial students actively seek to work with these commercially minded professors. With guidance from their commercially minded professors, entrepreneurial students spin companies out upon graduation, thereby enabling those professors to remain in academia while remaining involved with the startups that arise from their labs. These commercially minded professors continue running academic labs and mentoring the next generation of entrepreneurial students. Over time, such a dynamic creates a self-perpetuating, critical mass of people with great ideas and enthusiasm for collaboration with VC and industry.

Proximity of ecosystem players

In a world where remote work is commonplace, important elements of life sciences innovation – ideas, talent, and capital – can interact across distances. However, geographic proximity remains critical; while working remotely can be productive, laboratory research requires working in person.

Geographic proximity fosters personal connections, which are critical in a biotechnology industry that operates under an apprenticeship model. Being physically close together enables learning and collaboration: novices can ask uncomfortable questions; experienced scientists and managers can provide better mentorship over coffee than through a screen; venture capitalists can better diligence new companies and support portfolio companies that are just a short drive away.

Physical proximity also increases the chance of serendipitous interaction. Stanford and other university campuses are designed to house a high density of talented people who may meet serendipitously and produce innovative work. Word-of-mouth success stories can be inspiring for building a culture that facilitates commercialization of science.

In short, geographic proximity between academia, medicine, industry, and financing can create a superstructure akin to a protein complex that enables extremely efficient enzyme function. As in other areas of knowledge economy, agglomeration effects in the life sciences are significant. For this reason, companies founded elsewhere often move to the Bay Area or Boston to gain proximity to talent, capital, and culture.

Government support

Beyond the financial support for basic research provided in the form of grants from the National Institutes of Health (NIH) and National Science Foundation (NSF), the government provides additional non-dilutive funding for biotech startups. The federal government's Small Business Innovation Research (SBIR) grants enable biotech startups to grow early on, before seeking dilutive VC funding. These grants are often the first funding that a biotech startup receives. State governments provide additional financing. The California Institute for Regenerative Medicine (CIRM), for example, has received $8.5 billion in taxpayer funding since its founding 2004 to support stem cell research.[21] The founders of many Bay Area biotech companies, including Forty Seven and Graphite Bio, received CIRM funding to develop their technologies within an academic setting before incorporating and taking on private investment.[22] [23] In Texas, the Cancer Prevention and Research Institute of Texas (CPRIT) plays a similar role.[24]

More importantly, government can shape the physical and human environment in a way that encourages innovation. The example of Cambridge's Kendall Square illustrates the impact that government initiatives can have on stimulating an academic and industrial renaissance.

In the early 2000s, the Boston area was already home to a few established biotech firms (e.g., Biogen, Genzyme, Vertex Pharmaceuticals). At the time, however, Boston lagged behind the Bay

Area in terms of biotech revenue, jobs, and research and development funding.[25] A 2003 report on Massachusetts' competitive positioning in life sciences developed by Michael Porter found that Boston fell behind the Bay Area in life sciences employment, wage growth, and patent output.[26] Porter identified the Boston area's world-class universities and hospitals, as well as its existing biotech industry and high density, as critical advantages. Despite the availability of raw material for a dynamic biotech ecosystem, Boston remained in second place and in danger of falling further behind.

Around this time, the Massachusetts state government initiated a deliberate effort to stimulate the local biotech economy by retaining existing firms and expanding the footprint of the industry. A 2003 economic development bill included tax credits for life sciences companies that promised to create jobs in the state. Over the next few years, Bristol Myers Squibb, encouraged by $67 million in tax breaks and other incentives, built a $750 million R&D facility in Cambridge.[27] Around this time, Novartis invested $250 million to move its worldwide R&D headquarters to Cambridge (after reportedly turning down offers of state-sponsored assistance).[28] [29] Merck and Pfizer, among other companies, also established R&D operations in the area. Meanwhile, venture capital firms and incubators sprang up; tech companies moved in.[30] As a result of this work, Ranch Kimball, Massachusetts' Secretary of Economic Development from 2004 to 2007, was named "Outstanding State Executive" nationally by the Biotechnology Innovation Organization (BIO).[31] Thomas Finneran, president of the Massachusetts Biotechnology Council, called Mitt Romney "the best life scientist governor of the U.S."[32]

The Massachusetts Life Sciences Initiative, enacted in 2008 under Governor Deval Patrick, built on the success of the early 2000s success by committing $1 billion in life sciences investment and tax incentives over ten years.[33] Meanwhile, the Kendall Square area, heart of Cambridge's biotech ecosystem, developed from a "Nowhere Square" of post-industrial parking lots to a re-zoned, revitalized, mix-used hub of activity with apartments, hip restaurants and bars, and retail alongside offices and labs.[34] Today, Kendall Square can genuinely lay claim to being the "the most innovative square mile on the planet."

Implications for Existing and Developing Innovation Ecosystems

It takes a village to take an idea from the lab and develop it into a commercialized product. In this case, some villages function more effectively than others. Below, I lay out suggestions for continued progress, both for regions that are working to build biotech ecosystems and innovation hubs that are already the envy of the rest of the world.

Higher density increases innovation

Stanford is the only top-five engineering school that is also home to a top medical school and world-class hospital.[35] In contrast, scientists at UC Berkeley who want to work with clinicians at UCSF must drive up to an hour across the Bay Bridge and enter a different institution to collaborate. This contrast highlights a significant advantage that Stanford enjoys: having the major academic components of a biomedical innovation ecosystem physically on the same campus and organizationally under the same administration, enables more frequently serendipitous meetings and seamless collaboration.

Similarly, Cambridge benefits from higher density than the Bay Area. Kendall Square represents a tight geographic radius, where biotech firms, VCs, and university labs often occupy the same buildings. An MIT student can graduate, start a new job, then move to a different company without changing his or her daily commute. Boston-area institutions have built on this physical density by removing administrative barriers and increasing “organizational” density. For example, the Broad Institute, established in 2004, enables seamless collaboration between Harvard and MIT scientists.[36] Collaboration between academia and industry in the Bay Area, on the other hand, requires commuting long distances. No formalized institution akin to the Broad exists to encourage collaboration between Stanford, UCSF, or UC Berkeley.

Given the importance of density, it may be instructive to compare the relative sizes of various life sciences innovation clusters.[37]

Innovation ecosystem	**"Corners" of triangle**	**Area (square miles)**
Boston / Cambridge	Harvard, Mass General, Brigham and Women's (MIT / Kendall Square fall in the middle)	3.3
Research Triangle	Duke, North Carolina Chapel Hill, Raleigh	102
Bay Area	Stanford, UCSF, UC Berkeley	186
Loxbridge Triangle	Oxford, Cambridge, London	1,251
Texas Triangle	Austin, Houston, Dallas/Fort Worth	13,392

The Boston / Cambridge area is two orders of magnitude more compact than Research Triangle or the Bay Area, which are both an order of magnitude smaller than Loxbridge Triangle. The "Texas Triangle," comprised of three Texas cities that are combining resources in the hope of creating a new biotech hub, is so large that it barely qualifies as a single "cluster" compared to the other geographies.[38] The sheer size of this Texas Triangle suggests that significant efforts to increase organizational density must be made for the region to function as a cohesive innovation ecosystem; investment may be more effective if concentrated on one corner of the triangle rather than dispersed across the entire 13,000-square-mile region.

Institution-building takes time

Major institutions are not typically built overnight. The Bay Area's success in commercializing scientific discoveries are built on the culture and infrastructure of Silicon Valley, the venture capital of Sand Hill Road, and the flow of ideas from Stanford, UCSF, and UC Berkeley. The Boston area's biotech renaissance started in the early 2000s and gathered steam quickly over the next decade, but relied on critical institutions – world-class universities and hospitals and a handful of well-respected biotech firms – that were already in place. Given the extended time and effort required to create an ecosystem capable of turning laboratory discoveries into commercial products, regions seeking to develop biotech clusters should understand their weaknesses and build on their existing strengths.

Public policy is critical for developing innovation clusters

The rise of Kendall Square since the early 2000s, with a heavy assist from the Massachusetts state government, demonstrates the substantial role that public policy can play in enabling the development of life sciences innovation ecosystems. Life sciences research has been heavily subsidized by government funding since the creation of the NIH; more recently, it has become clear that government can also play a large role in shepherding ideas through the process of development and commercialization.

The Chinese government has taken this lesson to heart and poured billions of dollars of investment into developing a homegrown biotechnology industry. The last decade has witnessed an explosion in the amount of venture capital available to Chinese biotech firms and a growth of biotech startups, many of which are developing novel therapeutics for export to Western markets. The Chinese biotech industry is concentrated in three clusters: Beijing-Tianjin-Hebei, Shanghai, and the Pearl River Delta (i.e., Guangzhou, Shenzhen, and Hong Kong); local governments in each of these regions have supported industrial development with government funding and supportive policies. While the Chinese biotech industry is still in its relative infancy, it has made tremendous progress in a few short years, thanks in large part to enormous government investment.[39]

Thanks to its decades-long head start, the United States still leads the world in life sciences innovation. However, in recent years, the federal government has invested less in life sciences research – between 2002 and 2015, NIH funding declined in inflation-adjusted 2022 dollars and, as of 2021, has still yet to reach 2002 levels.[40] Here, the federal government would do well to look to the example set by state and local governments that have supported the translation of new ideas to commercial products.

There remains room for improvement

From the 1950s through the 1970s, the epicenter of American technology rested around Route 128 in Massachusetts, not Silicon Valley in California. Digital Equipment Corporation, Raytheon, and Lotus Development Corporation were all founded and headquartered along “America’s Technology Highway,” and contributed to Massachusetts’ economic dynamism through the 1980s. The rise of Silicon Valley, however, shifted the worldwide epicenter of technology westward.[41] Today, Route 128 is something of a footnote in the collective 21st century understanding of information technology.

The Bay Area is the birthplace of biotech – it showed the world that scientists collaborating across institutions (Stanford and UCSF) could come up with a groundbreaking idea, then turn it into a world changing technology and company with the help of venture capital financing. However, the Boston/Cambridge area has since surpassed the Bay Area as the world capital of biotech. In the meantime, neither the California state government nor local governments have made concerted efforts to support the growth and development of the life sciences industry (with the exception of stem cell research). Without additional attention, it is not inconceivable that the Bay Area biotech ecosystem could further lose its preeminence in the coming decades. The COVID-19 crisis and the rise of remote work environments will certainly put the existing model to the test.

For Stanford and the Bay Area as a whole, the major pieces of the puzzle are clearly established, but this is a dynamic environment. Stanford, for its part, continues to blend academia and industry under Marc Tessier-Lavigne, President of the University and former Chief Scientific Officer at Genentech, and Lloyd Minor, Dean of the School of Medicine and promoter of Stanford's role in enabling precision biomedicine through translational research.[42] [43] Ongoing efforts to deepen networks and increase the likelihood of serendipity will continue to make the whole even greater than the sum of its parts.

Acknowledgements

I would like to thank the Stanford University faculty and researchers who provided important information and perspectives for this paper:

- **Carolyn Bertozzi, PhD**, Director of Stanford ChEM-H, Professor in the School of Humanities and Sciences, Stanford
- **Matthew Bogyo, PhD**, Professor of Pathology, of Microbiology, and of Immunology, Stanford
- **Scott Boyd, MD, PhD**, Associate Professor of Pathology, Stanford
- **Jennifer Cochran, PhD**, Chair of the Department of Bioengineering, Professor of Bioengineering, Stanford

- **Scott Dixon, PhD**, Associate Professor of Biology, Stanford
- **Edgar Engleman, MD**, Professor of Pathology and of Medicine, Stanford
- **Linda Grais, MD, JD**, former CEO, Ocera Therapeutics, former Partner at InterWest Partners
- **Kevin Grimes, MD, MBA**, Professor of Chemical and Systems Biology, Stanford
- **Stephen Johnson, JD**, Lecturer, Stanford Graduate School of Business, former Partner, Kirkland & Ellis
- **Perry Karsen, MIM**, Chairman, Graphite Bio
- **Robert Langer, ScD**, Institute Professor, MIT
- **Josh Lehrer, MD**, CEO, Graphite Bio
- **Ron Levy, MD**, Professor in the School of Medicine, Stanford
- **Crystal Mackall, MD**, Professor of Pediatrics and Medicine, Stanford
- **Ravindra Majeti, MD, PhD**, Professor of Medicine, Chief of the Division of Hematology, Stanford
- **Garry Nolan, PhD**, Professor of Pathology, Stanford
- **Matthew Porteus, MD, PhD**, Professor of Pediatrics, Stem Cell Transplantation, Stanford
- **Stephen Quake, PhD**, Professor of Bioengineering and Professor of Applied Physics, Stanford; President, Chan Zuckerberg Biohub
- **Michael Snyder, PhD**, Professor of Genetics, Stanford
- **Tom Soh, PhD**, Professor of Radiology, Electrical Engineering, Stanford
- **Ansuman Satpathy, MD, PhD**, Assistant Professor of Pathology, Stanford
- **Mona Wan, MBA**, Associate Director of Licensing, Office of Technology Licensing, Stanford
- **Joseph Wu, MD,** Director of Stanford Cardiovascular Institute, Professor of Radiology, Stanford

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