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China's Biotechnology Development: The Role of US and Other Foreign Engagement

**A report prepared for the U.S.-China Economic
and Security Review Commission**

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Executive Summary

American policymakers have a keen interest in understanding the interaction between the US biotechnology sector and industry developments in China. This high-technology complex is key to economic competitiveness and national security in the years ahead. The US is today the leading biotech nation in the world, a position earned through a century of innovation and healthy market conditions that fostered success. China, meanwhile, is an increasingly important player in biotechnology, given a huge population and effort to advance, and it has great potential to lessen the gap with the US in certain areas. Collaboration with America through investment, education, trade, R&D, and talent flows was critical to China's biotech catch up since the 1980s. The current flow of capital, people, and ideas between the Chinese and US biotech industries reflects the reality of increasing economic globalization that creates benefits to both sides but has recently come under debate given concerns that China's economic, political, and security evolution is not as aligned with American interests as previously assumed.

As a major element of China's biotechnology growth, Chinese biotech companies are utilizing US firms to acquire technologies and data that bolster their current capabilities through a variety of channels, including bi-directional investment, corporate and academic partnerships, and recruitment of US-trained researchers (both foreign- and Chinese-born). A leading segment of China's biotechnology industry going forward will use big data in healthcare with technologies such as genomics and precision medicine. Through investments and research partnerships with US institutions, Chinese biotechnology companies are acquiring technologies crucial to advancement in the field as well as amassing large collections of clinical and genetic data on US residents.

This report reviews the development of China's biotechnology industry and the role foreign trade, investment and other linkages—particularly with the United States—have played in its evolution. We find that integration and collaboration run deep, and that disrupting these linkages would bring high costs for innovation, US welfare and public wealth. Continued investment by the US in its own biotechnology industry will go a long way toward limiting the effectiveness of China's efforts to close the biotechnology gap between the two countries. At the same time, the US needs to address concerns arising from China's current policy directions, including better screening of investment and other engagements for potential national security risks and the protection of sensitive data. Our key findings are summarized below.

The development of China's biotech industry

- China's biotech industry has grown rapidly over the past decade but still remains less than a tenth the size of the US biotech industry in terms of market size. China's biologics market is estimated at 30 to 40 billion yuan (\$4.7 to \$6.2 billion) and their agricultural biotech market is around \$8.1 billion, while estimates place those US markets at \$118 billion and \$110 billion, respectively. Overall, the US maintains a superior biotechnology innovation capacity through world-class research training and strong governmental support of R&D, but China is seeking to close that gap through its top-down government strategy and coordination, talent recruitment programs, high R&D spending across the industry, and capacity for high-tech R&D.
- China's biotechnology sector is dominated by biologics and other medical technologies. As with other parts of the world, this segment is growing quickly due to rising demand from patients and the high value of the products relative to traditional pharmaceuticals. China's products, however, are largely biosimilars rather than innovative new biologic products. Contract research and manufacturing also make up much of the segment. Though these activities represent a low end of the biotechnology value chain, they are nonetheless high-tech and high-skill, and build a solid foundation of technology for future innovation.
- Chinese biopharmaceutical companies are developing some innovative biologics using cutting-edge technologies such as Chimeric Antigen Receptor T-cell therapy (CAR-T) and CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats)-based editing of cells, both of which can be used to treat cancer. Advancement by Chinese companies in these areas may be

due in part to looser regulations and more relaxed attitudes to the controversial topic of gene editing.

- China's drug approval policies create advantages for Chinese developers of biopharmaceuticals and other drugs. Drugs manufactured in China and drugs not previously approved outside of China receive fast-track review. The duration of market protection via data exclusivity for newly approved biologics is maximized when clinical trials are performed in China and the drug is not yet approved elsewhere.
- Investment in the agricultural biotechnology segment is low in China, despite a stated goal of deepening capacity in this area. China is not a major producer of genetically modified (GM) crops, with the exception of cotton for export. Regulatory burdens and lack of consumer support have led to a lack of GM commercial activity, although China is investing in GM research. The recent purchase of GM seed producer Syngenta by ChemChina may signal a turning point in this regard, although catching up to the US in the foreseeable future is not likely due to the size of the lead the US has.
- The development of China's biotech sector is fueled by many commercial factors including high expectations for future market size, cheap labor, and abundant talent, but industrial and technology policies play an important role as well. China is pursuing a comprehensive, long term strategy to become a leader in biotechnology, creating globally competitive domestic firms and incentivizing the relocation of biotechnology manufacturing, design, and operations to China. Biotechnology is named as a Strategic Emerging Industry, and plans such as Made in China 2025 and the 13th Five Year Plan prioritize its development. To implement these and other policies, the Chinese government is supporting the biotechnology industry through R&D programs like the 863 Program and through investment in infrastructure, development of research parks, and recruitment of overseas talent.
- China is following a strategy of using international resources to further the advancement of China's own industries, including biotechnology, as emphasized in Made in China 2025. China is specifically targeting foreign capital as a mechanism to increase investment in Chinese technology companies to both bolster their domestic capabilities as well as increase their global integration and access new markets.
- As China's biotechnology industry develops, we are likely to see continued advancement in medical biotechnology, especially in biologics, genomics, and molecular diagnostics. Chinese biologics companies may move further toward producing innovative drugs. Given investments in agricultural biotechnology R&D, this segment may begin to see commercialization should restrictive policies and attitudes change. Due to a sizable lead, though, the US is not likely to lose its standing in the global biotech sector provided it maintains its investment in the industry.

The Role of Foreign Firms and Technology in the Development of China's Biotech Sector

- The development of China's biotechnology sector is closely tied to interaction with foreign entities. Initially this interaction was limited to inward foreign direct investment (FDI), but in the past decade it has been characterized by two-way flows in all investment channels, including greenfield investments, venture capital (VC), and other portfolio investments.
- Of all inward channels, FDI has likely contributed the most to the development of China's biotech industry, but VC is increasingly present. The establishment of operations on the ground in China through FDI provides foreign operators opportunities for transfer of intellectual property rights (IPR), integration into global supply chains, and overall sharing of expertise and practices. The most common type of FDI in China, acquisitions and greenfield investments, peaked in the mid-to-late 2000s. Of the 236 foreign mergers and acquisitions (M&A) in the Chinese pharmaceutical and biotechnology industries occurring since 2000, 84 percent took place between 2003 and 2011; 78 percent of greenfield investment occurred after 2008. Inbound VC saw modest activity starting in 2007, averaging 5.6 funding rounds and \$140 million per year until a sharp increase to over 15 rounds and \$590 million per year from 2015-2017.

- Only in the past decade have outbound Chinese acquisitions, greenfield FDI and VC become important channels of interaction. Chinese outbound M&A in the pharmaceutical and biotechnology sectors took off quickly starting in 2014, reaching over \$1.5 billion in 2015 alone and further increasing to over \$3.5 billion in 2017, driven by Chinese companies positioning themselves for global growth. Chinese VC in the global biotech industry has been steadily increasing since 2013, reaching a record of 53 funding rounds with a total value of \$3.8 billion in 2017 alone. Chinese cross-border activity in biotech is concentrated on North America and Europe, with more modest but still important activity in Asia (Singapore) and Oceania (Australia).
- Non-investment channels to foreign technology and know-how are also important to China. Use of foreign licensing and patents was limited in the past but has increased in the last five years (although obscure legal structures and the lack of disclosure requirements globally make a thorough assessment of these relationships complicated). Overseas training of Chinese students and researchers and their repatriation to China—through explicit government directives such as the Thousand Talents Program—is a channel that has become increasingly important in the past decade. Chinese entities have also been charged as perpetrators of espionage and other illicit activities to obtain technology and know-how, though limited public access to alleged details makes independent conclusions partial at best.
- There is no regime for global coordination or regulation of foreign investment, and thus no effort to focus on biotechnology specifically. Most nations with which China has extensive biotechnology ties follow liberal economic norms that constrain government intervention, for example screening only M&A for issues like national security, competition concerns, and control of dual-use technology.

Chinese Investment in the US Biotechnology Industry

- Chinese investment in the US biotechnology sector was small but has grown rapidly in the past five years, surpassing \$500 million per year since 2014. While the sector accounts for only two percent (\$3.8 billion) of cumulative Chinese investment in the US in 2000-2017, the recent pick-up has been resilient to a sharp overall drop in Chinese investment in North America in 2017-2018. In 2018, the health and biotechnology industry became the top recipient of Chinese capital in the US, surpassing real estate and entertainment.
- Chinese investment in US biotech in 2000-2017 predominantly (96 percent) came in the form of acquisitions and startup financing: 67 percent of Chinese capital can be attributed to acquisitions of US companies, while VC and other portfolio investment contributed 29 percent. Greenfield FDI in R&D centers and manufacturing remained small (4 percent).
- Almost all Chinese investment occurred in medical-related segments. 70 percent of total Chinese investment has been in biologics and contract research and manufacturing (which support the biologics industry), reflecting China's stated policy interest in biopharmaceuticals and demand on the healthcare market and mirroring the high level of biologics development activity occurring domestically in China. Another 22 percent was in genomics, molecular diagnostics, and precision medicine. Correlation between Chinese investment and the level of existing domestic activity in the target biotech segments indicates that Chinese investment is focused on reinforcing existing capacities back home rather than expanding into newer fields.
- Chinese investment in the US biotechnology sector is overwhelmingly private—only 3 percent of the total Chinese investment in biotech since 2000 came from formally state-owned actors. The role of state-owned investors is much smaller in biotech than in overall Chinese investment in the United States (24 percent). However, the Chinese government can influence investment decisions of Chinese firms through various channels including investment approvals, industrial policy, and informal coercion.
- Recent US regulatory reforms enhance tools to address biotechnology investment security concerns. The Committee on Foreign Investment in the United States (CFIUS) was previously limited to reviewing inbound M&A from China and other nations; VC transactions that stayed

below a certain equity threshold were not scrutinized. In August 2018, new investment screening and export control legislation expanded these reviews to encompass foreign VC transactions meeting certain criteria, and to impose restrictions on the licensing and transfer of critical emerging technologies (which could include certain biotechnology areas).

- The potential for Chinese outbound investment growth remains large, but policy uncertainty in both China and the United States clouds the near-term outlook. China continues to impose various restrictions on outbound investment, and the US is introducing additional restrictions. These developments cast a shadow over expanded Chinese capital flows to the US in biotech and other sectors.

China's Involvement in US-Based Research Organizations

- Chinese companies and researchers play an important role in in US biotechnology innovation through US-based R&D centers and incubators plus corporate and academic partnerships. The large cohort of Chinese researchers in US academic institutions and companies has long been core to the US innovation ecosystem.
- China's biotech companies have sought to engage with US biotechnology innovation by creating US-located R&D centers and incubators. They are attracted to the concentration of elite biotech companies and academic research institutes in major centers like Boston and the San Francisco Bay area. Some locales offer financial incentives for biotechnology that the companies are also looking to take advantage of.
- China recruits students and researchers trained in the US to relocate to China. Over 350,000 Chinese students are studying in the US. Through programs offering incentives such as high salaries, laboratories, and startup financing, China has recruited thousands of researchers, both Chinese-born and foreign, to relocate to China since the programs began in 1994; the Thousand Talents Program alone has recruited over 2,600.
- Research partnerships between US and Chinese academic institutions or biotech firms spur scientific advancement and are generally beneficial to the US economy. Partnerships are often designed to leverage expertise in specific fields, such as cancer therapeutics or precision medicine.
- Partnerships between US and Chinese institutions also marginally increase the potential for theft of intellectual property (IP) and trade secrets. Close research collaboration can offer opportunities for individuals and companies to illegitimately or illicitly obtain and transfer US IP to China. But this reality is not limited to China or Chinese nationals, and is generally inherent to high-innovation industries.
- The US has limited regulations on foreign involvement in US research. Open collaboration is a cornerstone of scientific research and innovation, and foreign-born researchers are an integral part of US biotechnology. The United States must maintain a balance between open collaboration and access to foreign talent with the potential losses due to leakage or theft of IP and technologies.

China's Access to US Healthcare-Related Data

- The Chinese government has formulated policies to support the use of big data and modern techniques to drive new discoveries and cures by analyzing large healthcare, genomic, and other personal health data sets. China's State Council treats the role of big data in health and medicine as a national priority, and China is building national and regional health and big data centers in Fuzhou, Xiamen, Nanjiang, and Changzhoi. China has also launched a 60 billion yuan (\$9.3 billion) precision medicine initiative that will benefit from this capability.
- China's biotech companies have access to healthcare and genomic data on US persons through various channels, including investments and partnerships. At least 23 companies with a nexus to

China are certified according to the Clinical Laboratory Improvement Amendments (CLIA) and accredited by the College of American Pathologists (CAP), giving them direct access to US medical and health data via their participation in our healthcare system.

- Compared to other nations, the US has fewer protections on sharing of medical and healthcare data, including internationally, facilitating foreign access to data on US persons. The EU's General Data Protection Regulation (GDPR) protects identifiable information more strongly than any US regulations, including the Health Insurance Portability and Accountability Act (HIPAA). China's laws go even further, preventing export of data on Chinese persons and requiring a permit for each research use of genomic information.
- China's efforts to acquire US health data combined with limited data protections by the US raise questions about national security. Theoretically, access to private information on security-sensitive US persons creates a risk of blackmail and may reveal health conditions exploitable in a targeted attack, although no public reports suggest this has yet happened or is a current aim of the Chinese Government or industry.
- China has numerous laws requiring or authorizing access to private-sector data by the central government, ostensibly for national security reasons. While it is difficult to discern the level of access afforded to the Chinese government through these laws, their vagueness when it comes to oversight could allow collection of data to go relatively unchecked.
- The US is not moving as aggressively as China to advance the use of big data in healthcare, and that could, over time, open an innovation gap. The US can prevent this outcome by investing in its own infrastructure, knowledge base and scientific enterprise.

Recommendations

This report is primarily focused on providing data and analysis, but we offer a few conclusions and recommendations based on the findings:

- (1) China's approach to the development of its biotechnology sector mirrors the state- and industrial policy-driven approaches causing concerns in other high-tech sectors, thus **it is important for the US to analyze the potential long-term risks from those non-market interventions and formulate appropriate policies to respond to these challenges**. The liberal US market approach can only be sustained if the US has adequate policies in place to mitigate against economic and security risks posed by China's statist approach to innovation without stifling US innovation. While a comprehensive investigation of policy options needs to be performed, for example, through an interagency effort led by the White House, the subsequent recommendations provide some specific avenues to focus on.
- (2) **Increase international efforts to bring China's approach to innovation policy and market access more in line with standards in other major biotech markets**. Given the small number of regions with major stakes in biotechnology, and the US's current global leadership in the industry, international coordination to address potential security and economic concerns requires just a few nations to participate, increasing the prospects for success. Potential remedies range from incentives (e.g., free-trade agreements or industry-wide standards setting) to deterrents (e.g., tariffs). Identifying appropriate economic or diplomatic interventions requires a thorough assessment that factors in the rapidly evolving nature of biotech as well as the broader suite of policies currently being deployed or considered by the US across all industries.
- (3) **Ensure that CFIUS and export control reform implementation results in a measured approach toward biotech that is based on careful deliberation and data gathering, not broad inclusion of all biotech R&D activity**. The Foreign Investment Risk Review Modernization Act (FIRRMA) and Export Control Reform Act (ECRA) legislation resulted in a process to identify emerging and foundational technologies important to US national security, which will be subject to special scrutiny going forward. Identification of these technologies must

be done deliberately and systematically. Poor implementation could be counterproductive to innovation and long-term US competitiveness in biotech. During this process, delineating fundamental research from foundational and emerging technologies that could be exploited by malicious adversaries will be difficult yet critical; we propose three potential criteria for defining fundamental and emerging technologies that permit continued basic research:

- a) The technology has been reduced to marketable commercial practice in at least one application, clearly distinguishing it from current definitions of fundamental research (see National Security Decision Directive-189);
- b) The technology has some plausible, if not demonstrable, link to a specific risk to national security, reducing the potential for inadvertent inclusion of technologies with limited or no feasible national security contributions; and
- c) The technology can be controlled such that embargoed countries are unlikely to acquire it or a technology with the same end-use easily through sharing of fundamental research, minimizing the potential for ineffective regulation.

- (4) Enhance ethics and IPR programs to provide better protections from theft of US intellectual property.** US institutions in both academia and the private sector can better protect themselves from economic threats with a strengthened understanding of IPR, research ethics, and the risk of IP theft, as well as education on how to recognize and report insider threats. US government agencies such as the National Institutes of Health, Bureau of Industrial Security, and the State Department should produce guidance for universities and companies engaging in science and technology research and international collaboration that support scientific advancement while protecting IPR. Expanding access to this knowledge will enable academic and private institutions to better weigh the risks and benefits of foreign talent and to prevent loss of data or technology through theft by foreign nationals of any country.
- (5) Provide incentives to retain foreign-born students in technological fields.** Professional opportunity is the primary driving factor for Chinese students remaining in the US after training. The US biotech sector is vibrant enough to provide that opportunity despite challenges foreigners may face in trying to stay in the US, but as China's biotechnology sector continues to develop, the balance may start to tip. Expanded investment by the US government in basic and applied biotechnology research will help ensure that the best opportunities for professional development are on US soil, either in academe or industry. Simultaneously, modifications to US immigration policy, such as expanding H-1B visas, creating portable work authorizations, and easing the path to permanent residency of foreigners trained at the best US research institutions, would help ensure that talented workers who wish to stay can easily do so.
- (6) Develop federal guidance for international data agreements.** Access to aggregated data on US citizens by Chinese or other foreign firms does not inherently disadvantage the US unless data access is not shared equitably among all partners. The US government should develop specific guidance on how to structure such partnerships so that US interests are maintained. This approach is preferable over more stringent prohibitions on foreign access to data, which could raise costs for R&D in the US; with access to the same data, US entities are collectively more capable of innovating than their Chinese counterparts.
- (7) Enhance cybersecurity measures to protect personal data on US citizens.** Legal protections on data access, no matter how stringent, will not prevent unauthorized access by China or other foreign governments. Recent healthcare cybersecurity breaches in the US suggest that enhanced measures to protect personal data from hacking are necessary. Yet, while the healthcare industry is receiving increasing numbers of cyberattacks, we see no particularities that suggest protecting genomic and healthcare-related data requires unique cybersecurity measures.
- (8) Update and Expand the National Bioeconomy Blueprint.** A refresh of this high-level, executive document would underscore the importance of the biotechnology industry to the greater US

economy and illustrate how the federal government can support its future growth. A new Bioeconomy Blueprint should accomplish the following: measure the productivity of the US biotechnology industry and draw forecasts and goals for the expected growth of the sector; provide an updated view of biotechnology as the global industry it is, including an assessment of US dependence on foreign industries and recognition of rising players on the world stage; and perform an analysis of the health and stability of the US biotechnology sector, including identifying which segments are strong, which are vulnerable to foreign competition, and which may be key to future growth of the sector.

Introduction

Many of the major technological advances of the twenty-first century will come from the fields of biology and biotechnology as discoveries in life science research are developed into new therapies, materials, fuels, and other products.¹ Indeed, the global biotechnology industry is already a large and growing market segment. In 2016, the total market size was estimated at \$370 billion, and could reach more than \$700 billion by 2025.² The US is home to the world's largest and most advanced biotechnology sector, with 440 publicly traded companies employing 136,000 people and generating \$112 billion in revenue, plus thousands of startups that are on the leading edge of innovation.³ Industry growth averaged 13 percent annually in 2009-2016 and promises to contribute significantly to future US Gross Domestic Product (GDP) growth.⁴

The development of a highly competitive biotech sector was nurtured by a market-oriented, liberal approach to technology policy that has been typical for the US over the post-War period.⁵ That approach meant a limited role for government, primarily confined to regulation (intellectual property rights [IPR] protection, competition policy to avoid market-distorting practices and ensure a level playing field, etc.) and an emphasis on market forces (e.g., a financial system that encourages disruptive innovation) as well as a liberal international agenda (openness to foreign investment with minimal restrictions, immigration policies, support of US companies' global expansion to reach scale, etc.). The exception was heavy government funding for basic research and development (R&D) through national laboratories and universities, and investment in research within the defense industrial sector. For the most part this support was neutral with regard to winners and losers or specific technologies, with peer review determining funding recipients.

In recent years, two factors have triggered a debate about whether this approach is still the right one. The first is technological progress, which has blurred the lines around what is and is not concerning from a security perspective, and between civilian and military applications. Innovations that were perceived as entirely benign with regard to security concerns just a few years ago are now seen as potentially concerning, as they have evolved to take on new characteristics, including in the biotechnology sector. For instance, researchers at Stanford University and elsewhere have created microbial strains that produce opioid drugs, potentially eliminating the need to cultivate poppies and, via further engineering, potentially enable new drugs to be developed.⁶ Yet this same technology could be misused by criminal organizations or "home brewers" with the potential to increase drug abuse and upend drug interdiction efforts.⁷ As biotechnology, like information technology, becomes ever more ubiquitous for national security, the question arises whether we need to rethink and expand existing exceptions to foreign investment in such technologies.

Second, the rise of new players with fundamentally different political and economic systems as leaders in technological innovation presents new challenges, first and foremost China. China's different political and economic realities likely require adjustments to traditional US thinking. China is a Leninist-style one-party state based on rule-by-law not rule-of-law. China's economic ambitions and intentions present challenges for more liberal economies. In the past, the US generally overcame such threats by sticking to its liberal economic norms until challenger experiments with non-market mechanisms failed of their own weakness. China's size and staying power already present a more challenging case. Since 1978 China's leaders have generally endorsed and worked toward a market-re-orientation. There is much present debate about

¹ Shreef Mehta, "Biotechnology: The Technology of the Twenty-First Century," in *Wiley Encyclopedia of Management*, ed. VK Narayanan Cary Cooper, Gina O'Connor (Hoboken, NJ: Wiley, 2015).; Anne Glover, "The 21st Century: The Age of Biology" (Presentation at the OECD Forum on Global Biotechnology, Paris, November 12, 2012).

² Grand View Research. *Biotechnology Market Analysis By Application (Health, Food & Agriculture, Natural Resources & Environment, Industrial Processing Bioinformatics), By Technology, And Segment Forecasts, 2018 - 2025* San Francisco, CA: Grand View Research, 2017.

³ Ernst & Young Global Life Sciences. *Beyond borders: Biotechnology report 2017 – Staying the course*: Ernst & Young LLP, 2017.

⁴ Authors' compilation, from Ernst & Young Global Life Sciences, *Beyond borders: Biotechnology report (2010-2017)*.

⁵ Robert H. Wade, "The Paradox of US Industrial Policy: The Developmental State in Disguise," Chapter 14, *Transforming Economies: Making Industrial Policy Work for Growth, Jobs and Development*, (Geneva: International Labor Office, 2014)

⁶ S. Galanie et al., "Complete biosynthesis of opioids in yeast," *Science* 349, no. 6252 (2015): 1095-100.

⁷ K. A. Oye, J. C. Lawson, and T. Bubela, "Drugs: Regulate 'home-brew' opiates," *Nature* 521, no. 7552 (2015): 281-3.

the fidelity of that reform, with some emphasizing the progress and others the shortcomings; but most observers—including in China—agree that Communist Party control, nationalism, state planning, and suppression of liberal economic discussion have been prominent in recent years. This trend has shaken up US and other advanced economy debate about the right mix of engagement and self-protection should China continue to take a markedly non-market economic course in the years ahead.

Beyond economics, China is a geopolitical competitor of the United States and is increasingly challenging US foreign policy interests in Asia and other regions. These realities present a particular set of concerns about potential leakage of dual-use technology or the infiltration of critical infrastructure. China also poses unique economic concerns, priding itself on a distinctive economic model that entails the political guidance of the Communist Party in all domains, including in the commercial sector. Working hand-in-glove with government institutions, the Party has deep influence on both state-owned and private firms in the marketplace, including in biotech.

The re-assessment of the decades-old US policy of engagement toward China is most pronounced in innovation and technology-intensive sectors where the national security implications of technological advancement is most concerning. The debates in the information and communications technology sector (ICT) are illustrative. In the ICT arena, China-related concerns have impelled authorities in the US to embrace new approaches to shield certain assets, such as de facto prohibition of Chinese acquisitions of major semiconductor companies, expansion of the foreign investment screening and export control regimes, more forceful counterespionage efforts, and stricter oversight of company management decisions.⁸

Similar debates are taking place in biotech. However, analysis of China's rise in the global biotech industry and its connections with the world has been fragmented and the empirical foundations have been weak. This report aims at filling this gap by providing a thorough analysis of China's biotechnology sector, its interactions with US and other foreign players, and related policy questions. We utilize proprietary data, original research, and interviews with experts to draw a detailed picture of China's biotech industry and its connections with the world, with a particular focus on the United States.

Defining Biotechnology

To understand the scope and scale of the biotechnology sector requires a definition of the word *biotechnology* itself, yet curiously there is no common or fixed definition for the term. In its broadest definition, and the one we use in this report, biotechnology means *modern advances in science and technology derived from discoveries and advances in the life sciences*. This broad-scope definition includes the biotechnologies of the rapidly growing medical biotechnology sector, like personalized medicine and molecular diagnostics, as well as biotechnologies in other economic sectors, such as industrial bioproduction in manufacturing and genetically-engineered crops within agriculture.

Within medicine, we consider the spectrum of new biotechnologies improving public health and treatment outcomes. We have classified these technologies into four categories: (1) biologics, i.e., biologically-derived products used to treat or prevent disease, (2) genomics, the study of the entirety of an individual's DNA sequence, (3) personalized medicine, or technologies that can be used to tailor treatment for an individual, and (4) molecular diagnostics, the use of DNA sequence to diagnose a disease. Within this scope are *biopharmaceuticals* (a subset of biologics), but, notably, not the *traditional pharmaceutical industry*. These two industries are closely related, and both entail the development of therapies for disease, yet they remain distinct. By and large, the biopharmaceutical industry develops therapeutics through the manipulation of living cells, whether it is, for example, using cells to produce large, complex molecules such as antibodies (which, due to their complexity, cannot be synthesized chemically and therefore must be produced by living organisms) or engineering cells to directly target cancer, among

⁸ Ian Talley, "Chinese Access to U.S. Semiconductor Industry May Be Curbed," *The Wall Street Journal*(2017), <https://www.wsj.com/articles/chinese-access-to-u-s-semiconductor-industry-may-be-curbed-1483397701>; Thilo Hanemann and Daniel H. Rosen. *Chinese Investments in the United States: Recent Trends and the Policy Agenda* New York, NY: Rhodium Group, 2016.

other applications. Traditional pharmaceuticals, in contrast, are therapeutics derived from small molecule drugs (for example, penicillin, ibuprofen, etc.) that are chemically synthesized. Traditional pharmaceutical drugs are frequently identified by high-throughput screening of libraries of chemicals to identify desirable therapeutic effects, or by chemically modifying existing drugs; the technological advances, therefore, are not derived from advances in biology. Of these two industries, we focus solely on the biopharmaceutical industry as it is a rapidly evolving sector that features modern and emerging biological technologies.

Outside medicine, the range of biotechnology applications in development is broad. For example, we include the accelerating developments in agriculture, such as genetically modified (GM) crops created by companies such as Monsanto and DuPont as well as new advanced efforts, such as the attempts to engineer beneficial soil microbes by companies such as Pivot Bio. Industrial biotechnology is transforming the chemicals sector via the development of engineered microbes that produce chemicals of interest at lower cost and lower environmental impact. These chemicals include fuels, evidenced by the partnership between ExxonMobil and Synthetic Genomics to create algae-based biofuels.⁹ Industrial biotechnology is also accelerating advances in manufacturing, through, for example, engineered silks developed by Bolt Threads, as well as the attempts to design a fully-automated robotic life science workstation by companies such as Transcriptic. Compared to medicine and healthcare, many of these other sectors are just beginning to be influenced by biotechnology, so the number and size of investments within them are smaller, though we included all examples we could identify. In the data we gathered and analyzed, we excluded technology advances where the breakthrough is not in the life sciences. For example, advances in automation within dairy farming, though part of agriculture, would be excluded because the advances are neither biological nor contribute to life science advances (and instead are within robotics and automation).

Report Organization

The report is structured as follows. Chapter 1 describes the evolution and current status quo of China's biotech sector, discusses the underlying policies, and offers a look into its direction in the future. Chapter 2 provides an overview of the role that foreign involvement around the world—through investments, partnerships, and other channels—has played in the development of China's biotechnology industry. Chapters 3 through 5 then offer a deep dive into three aspects of US biotech engagement with China. Chapter 3 analyzes the investments made by Chinese companies into the US biotech industry, including direct investment, venture capital and greenfield investments. This chapter also includes a discussion of US regulatory tools available to monitor such investments and safeguard against economic or national security threats they may pose. Chapter 4 discusses partnerships and other less formal interactions between the Chinese and US biotechnology sectors, including the role of Chinese researchers training in the US. In Chapter 5 we look at how Chinese firms are using US healthcare and healthcare-related data and the impacts that may have on the US. The report concludes with a synthesis of the major findings and recommendations for US policymakers in light of the broader question of re-calibrating economic engagement with China.

⁹ "Cell Factories," Synthetic Genomics, <https://www.syntheticgenomics.com/cell-factories/>; "ExxonMobil and Synthetic Genomics Algae Biofuels Program Targets 10,000 Barrels Per Day by 2025," ExxonMobil, updated March 6, 2018, <http://news.exxonmobil.com/press-release/exxonmobil-and-synthetic-genomics-algae-biofuels-program-targets-10000-barrels-day-202>

1. China's Biotechnology Sector

Key Findings

- China's biotech industry has been growing rapidly in the past decade but still remains less than a tenth the size of the US biotech industry in terms of market size.** China's biologics market is estimated at 30 to 40 billion yuan (\$4.7 to \$6.2 billion) and their agricultural biotech market is around \$8.1 billion, while estimates place those US markets at \$118 billion and \$110 billion, respectively. Overall, the US maintains its lead through world-class research training and strong governmental support of R&D, but China is seeking to close the gap through its top-down government strategy and coordination, talent recruitment programs, high R&D spending across the industry, and capacity for high-tech R&D.
- China's biotechnology sector is dominated by biologics and other medical technologies.** The segment is growing quickly due to increasing demand and the high value of the products relative to traditional pharmaceuticals. While Chinese biotech companies develop few innovations (instead producing biosimilars or performing contract research and manufacturing), they still provide a high-tech and high-skill foundation for future innovation, with potential demonstrated in some cutting-edge technologies like CAR-T and CRISPR.
- China's drug approval policies create advantages for Chinese developers of biopharmaceuticals and other drugs.** Drugs manufactured in China and drugs not previously approved outside of China receive fast-track review. The duration of market protection via data exclusivity for newly approved biologics is maximized when clinical trials are performed in China and the drug is not approved elsewhere.
- Investment in the agricultural biotechnology segment is low in China, despite a stated goal of developing the technology.** China does not grow much GM crop, with the exception of cotton for export. Regulatory burdens and lack of consumer support have led to a lack of GM commercial activity, although China is investing in GM research. The recent purchase of GM seed producer Syngenta by ChemChina may signal a turnaround in this market, although catching up to the US in the foreseeable future is not likely due to the size of the lead the US has.
- The development of China's biotech sector is fueled by many commercial factors—such as a massive future market, cheap labor, and abundance of talent—but industrial and technology policies play an important role as well.** China is pursuing a comprehensive, long term strategy to become a leader in biotechnology, especially medical biotechnologies. Biotechnology is named as a Strategic Emerging Industry, and plans such as Made in China 2025 and the 13th Five Year Plan prioritize its development. As a result of these and other policies, the Chinese government is supporting the biotechnology industry through investment in infrastructure, development of research parks, and recruitment of overseas talent.
- China is following a strategy of using international resources to further the advancement of China's own industries,** including biotechnology, as emphasized in Made in China 2025. China is specifically targeting foreign capital as a mechanism to increase investment in Chinese technology companies, including biotechnology, to broaden their international footprint.
- As China's biotechnology industry develops, we are likely to see continued advancement in medical biotechnology, especially in biologics, genomics, and molecular diagnostics.** Chinese biologics companies may move further toward producing innovative drugs. Given investments in agricultural biotechnology R&D, this segment may begin to see commercialization should restrictive policies and attitudes change. Due to a sizable lead, though, the US is not likely to lose its standing in the global biotech sector provided it maintains its investment in the industry.

This chapter sets the scene of China's standing in the global biotechnology industry with a thorough description of the country's current capabilities and industry landscape. Following this characterization is a review of China's high-level policy plans that have contributed to its biotechnology development and a discussion of the outlook for its future advancement.

1.1. Current State of China's Biotechnology Industry by Segment

1.1.1. The Biotechnology Market at a Glance

Biotechnology as a global industry is a strong market force and is growing rapidly. In 2016, the total global market size was estimated at \$370 billion and predicted to reach more than \$700 billion by 2025.¹⁰ In the four major biotechnology centers combined (US, Canada, Europe, and Australia), the medical biotechnology industry has seen consistent growth of 7 to 25 percent since 2012 with revenues of \$139 billion in 2016, generated by 708 (publicly traded) companies employing more than 200,000 people.¹¹ The US is the source of the majority of this activity, with 440 publicly traded companies employing 136,000 people and generating \$112 billion in revenue, plus thousands of startups that are on the leading edge of innovation.¹² Biopharmaceuticals are a leading component of biotechnology growth, and China is working to become a major player in the segment.

Estimating the performance of the biotechnology industry in China is difficult, as most sources cite Chinese officials who may provide inflated numbers. A reliable estimate of the entire Chinese biotech industry could not be found, but some sources provide assessments of the major segments within biotechnology. China's biologics market, comprised largely of revenues from antibody and protein therapeutics, was estimated at 30 to 40 billion yuan (\$4.7 to \$6.2 billion) in 2016, up from 18 billion yuan (\$2.8 billion) in 2013.¹³ China's agricultural biotechnology segment was estimated at around \$8.1 billion in 2013.¹⁴ Note, however, that agricultural biotechnology markets are typically measured by the sale of GM crops (mostly cotton in China) and thus are not necessarily indicators of the biotechnology activity of producing GM seed or other agricultural biotechnology products. The net increase in profits for Chinese farms generated by cultivating GM crops, as opposed to traditional varieties of the same crops, was estimated at \$1 billion in 2015.¹⁵ Data on the industrial biotechnology market are limited, so a uniform value for the size of this sector could not be identified. Generally, the lack of high-quality data appears to stem from a varying definition of the scope of this sector across sources and from a large number of small but rapidly-changing participant companies (due to the nascence of these fields) that makes comprehensive tracking and data compilation difficult. Overall, these rough numbers suggest the Chinese biotechnology market is less than a tenth the size of US biotechnology.

China's current standing in the global biotechnology industry represents significant recent growth; China rose from the ninth-largest biomedical sector in the world in 2006 to the third-largest in 2010 (the period of the 11th Five-Year Plan [FYP]).¹⁶ Since then, the output value of the biological industry has increased by

¹⁰ Grand View Research, *Biotechnology Market Analysis By Application (Health, Food & Agriculture, Natural Resources & Environment, Industrial Processing Bioinformatics), By Technology, And Segment Forecasts, 2018 - 2025*.

¹¹ Ernst & Young Global Life Sciences, *Beyond borders: Biotechnology report 2017 – Staying the course*.

¹² Ibid.

¹³ Richard Yeh et al. *China: Healthcare: Biotechnology: Biologics: Balancing quality and affordability; Fosun Pharma up to Buy*. Goldman Sachs Global Investment Research, 2018. ; R&D-based Pharmaceutical Association Committee. *Building a World-Class Innovative Therapeutic Biologics Industry in China* Beijing: China Association of Enterprises with Foreign Investment, 2013. ; Throughout the document, yuan to USD conversions use the 2018 YTD average conversion of 6.43 yuan per USD as of August 6, 2018 as given by OFX Group (<https://www.ofx.com/en-us/forex-news/historical-exchange-rates/yearly-average-rates/>); Unless otherwise specified, all dollar denominated values refer to USD.

¹⁴ Duu-Hwa Lee, "Bio-based economies in Asia: Economic analysis of development of bio-based industry in China, India, Japan, Korea, Malaysia and Taiwan," *International Journal of Hydrogen Energy* 41, no. 7 (2016): 4333-46.

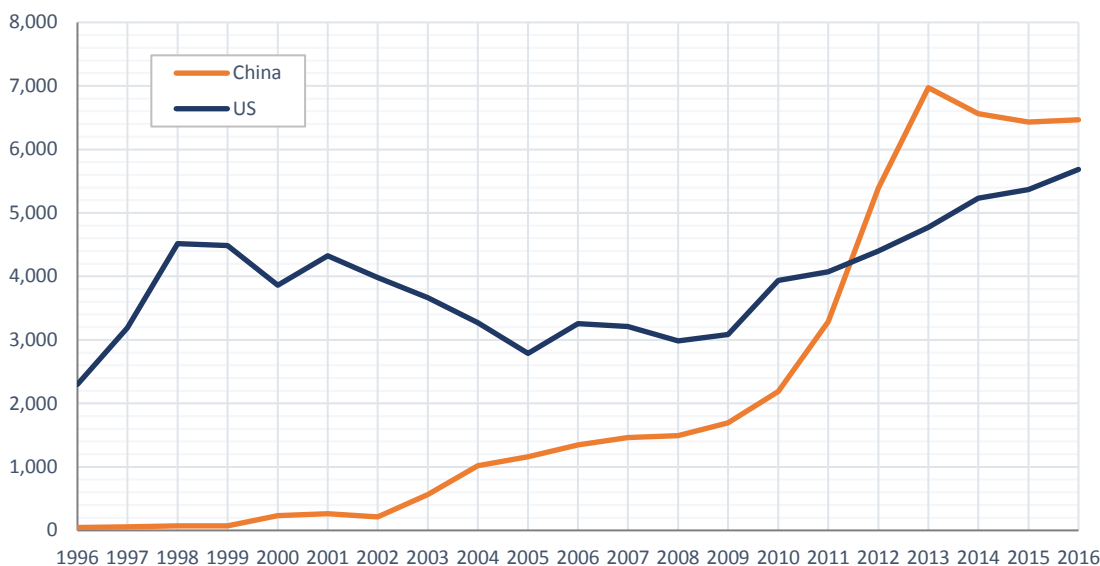
¹⁵ Graham Brookes and Peter Barfoot. *GM crops: global socio-economic and environmental impacts 1996-2015*: PG Economics Ltd, UK, 2017.

¹⁶ Wang Yaping, "Biopharmaceutical Opportunity: Enhancing International Competitiveness by Innovation and Features," *China Economic Herald* May 22, 2012, www.ceh.com.cn/ceh/jryw/2012/5/22/114078.shtml

an average annual growth rate of 23 percent, according to Chinese officials.¹⁷ During the 12th FYP (2011-2015), the output value maintained an average annual growth rate of over 15 percent.¹⁸ As a proportion of total Chinese GDP, biotechnology has increased from 1.3 percent 30 years ago to 4.6 percent in 2014.¹⁹ By comparison, the US derives around 2 percent of its GDP from biotechnology (as estimated in 2012).²⁰ The number of biotechnology patents granted in China rose from over 1,000 (12 percent of global total) in 2006 to more than 6,000 (27 percent of global total) in 2016, surpassing the US in 2012 (Figure 1-1).²¹

Figure 1-1. Annual Biotechnology Patents Granted in the US and China, 1996-2016

Number of Patents



Source: World Intellectual Property Organization.

Another way to describe the biotechnology industry is through expenditures on R&D, from government funds as well as private companies, universities, and non-profits. While specific biotechnology numbers are not available, a look at overall science and engineering research may provide some insight into Chinese innovation. In 2015, the US spent nearly \$500 billion on science and engineering R&D, while China spent almost \$410 billion, enough to surpass the EU for second worldwide.²² US expenditures represent 2.7 percent of GDP, and China's 2.0 percent.²³

Chinese academic research in biotechnology is also prominent. From 2007-2017, the number of biotechnology research publications from Chinese institutions increased year-to-year by an average of 20 percent. These trends closely mirror those of researchers from the US and the rest of the world. Over the same period, the US share of global biotechnology publications was consistently around 33 percent versus China's share of 15 percent, demonstrating that biotechnology research is growing at similar rates in China, the US, and globally (Figure 1-2)

¹⁷ Department of Social Development Science and Technology of the People's Republic of China and China Biotechnology Development Center. *2015 China Biotechnology and Industry Development Report*. Science Press, 2015.

¹⁸ National Development and Reform Commission of the People's Republic of China. *'13th Five-Year' Bioindustry Development Plan 2016*. [Chinese Language Source]

¹⁹ Department of Social Development Science and Technology of the People's Republic of China and China Biotechnology Development Center, *2015 China Biotechnology and Industry Development Report*.

²⁰ Robert Carlson. *Biodefense Net Assessment: Causes and Consequences of Bioeconomic Proliferation: Implications for U.S. Physical and Economic Security* Washington, D.C.: Department of Homeland Security, 2012.

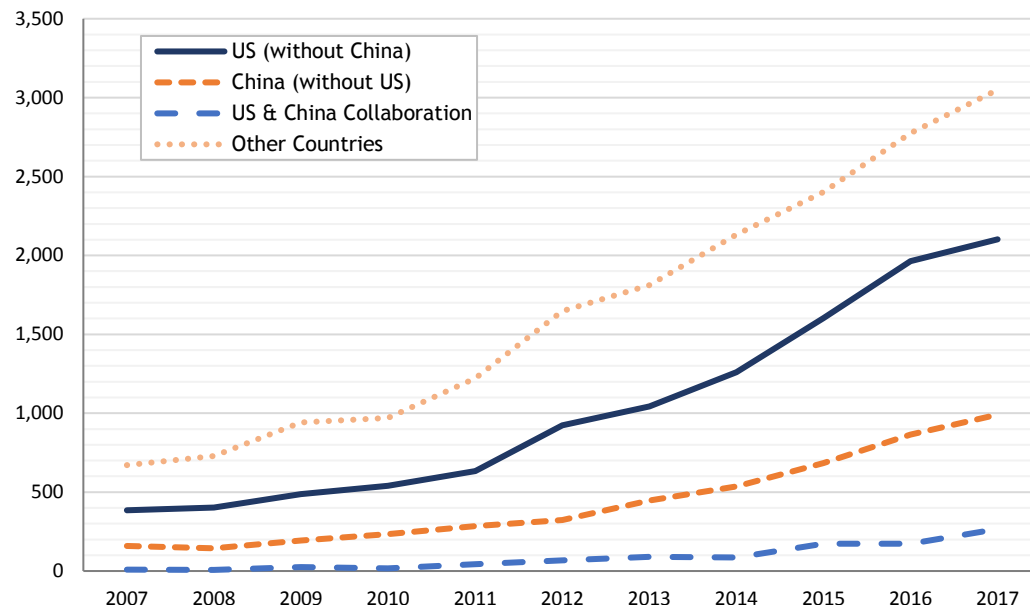
²¹ "WIPO IP Statistics Data Center," World Intellectual Property Organization, updated May 2018, <https://www3.wipo.int/ipstats/index.htm>

²² National Science Board. *Science and Engineering Indicators 2018*. [Figure 4-6]

²³ Ibid. [Figure 4-7]

Figure 1-2. Annual Biotechnology Publications by Country, 2000-2017

Number of Publications

Source: Scopus.²⁴

1.1.2. Biologics (Biopharmaceuticals)

1.1.2.1. Biologics Market Overview

Biologics, which make up 12 percent of total hospital prescription drug sales worldwide, are growing as the predominant treatment for maladies such as cancer and autoimmune disorders. The trend toward biologics is reflected within China as well, although in China biologics have not yet reached the same level of prescription drug market penetration. According to a Goldman Sachs estimate, the current Chinese biologics market constitutes 5 percent of total hospital prescription drug sales for a total of 30-40 billion yuan (\$4.7-6.2 billion) in 2016.²⁵ Estimates vary considerably, though, with other sources placing the size of China's biologics industry from 18 billion yuan (\$2.8 billion) to 152.7 billion yuan (\$23.7 billion).²⁶ Protein therapeutics, often used for cancer and autoimmune disease therapy, are a growing category within Chinese biologics. Since 2005, these products rose from 14 percent to 43 percent of China's biologics market share. Insulin products, the second largest product category today, have carried a steady 21-23 percent market share over that span. Overall, the number of medical biologics produced in China is increasing; investigational new drug (IND) filings (i.e., applications for clinical trials) for biologics have increased from fewer than 10 per year before 2013 to 30-40 in the past few years.²⁷

China has a large potential market for biologics and other pharmaceuticals, driven by an aging population and factors such as pollution, greater healthcare awareness, and increasing healthcare spending.²⁸

²⁴ English language search performed in Scopus for keywords: "CAR-T" OR ("therapeutic antibodies") OR (CRISPR AND editing OR engineering) OR (synthetic biology) OR "metabolic engineering" OR (genomics AND "precision medicine" OR "personalized medicine") OR agrobacterium OR (CRISPR AND plants)

²⁵ Yeh et al., *China: Healthcare: Biotechnology: Biologics: Balancing quality and affordability; Fosun Pharma up to Buy.*

²⁶ Frost & Sullivan, "Industry Overview," in *Post Hearing Information Pack of WuXi Biologics (Cayman) Inc.* (2017).; R&D-based Pharmaceutical Association Committee, *Building a World-Class Innovative Therapeutic Biologics Industry in China.*

²⁷ Yeh et al., *China: Healthcare: Biotechnology: Biologics: Balancing quality and affordability; Fosun Pharma up to Buy.*

²⁸ Deloitte China Life Sciences and Health Care. *The next phase: Opportunities in China's pharmaceuticals market Hong Kong: Deloitte Touche Tohmatsu Limited, 2011.*; R&D-based Pharmaceutical Association Committee, *Building a World-Class Innovative Therapeutic Biologics Industry in China.*

(While total healthcare expenditure in China is high and growing, per capita spending is low relative to other countries.²⁹) China's biologics industry is still emerging but is growing quickly in part due to government R&D spending.³⁰ China's slow review timelines and limited capacity has in the past caused challenges in drug approvals for both foreign and domestic applications. But the country has initiated regulatory reforms in recent years to address these challenges.³¹ The Chinese government has also made efforts to bring talent to China and increase spending on life sciences; while these efforts have not fully translated into biologics innovation, they do provide a basis for future innovation.³² In addition, China has established an industrial foundation for lower-value biologics products, especially biosimilars and biobetters (i.e., generics and follow-ons; see Section 1.1.2.3 for more). With an initial focus on biosimilars, companies develop key capabilities to support development and commercialization of future products, including biologics manufacturing and clinical development capacity. This existing capacity enables China to more rapidly develop and manufacture innovative biologics once the companion R&D and innovation pipelines are established.

1.1.2.2. Regulatory Environment

Historically, drug approval in China has been difficult and time-consuming, due to both extensive requirements to submit a new drug application and a slow and backlogged review process. The validation and characterization studies required by the China Food and Drug Administration (CFDA) for a new drug application package can take over a year to assemble. Some requirements are more stringent than in other countries, including a minimum six-month real-time study on the stability of the material (the US Food and Drug Administration (FDA) requires three months) and characterization of three production lots of clinical-grade material (the US requires one lot).³³ Until recently, drugs (including biologics) marketed outside of China have required full clinical trial data generated in China in order to be approved. Multinational corporations, even ones with Chinese ownership, needed to run a separate set of trials for approval to market the drug within China; Chinese companies also could not make generic drugs without performing clinical trials. In the past few years, however, China has reformed its regulatory process to make approval of imported and new drugs less onerous. In February 2016, CFDA created a new drug classification scheme that includes priority review status for certain innovative drugs, reducing review times to six months. (Priority reviews include innovative drugs not approved anywhere worldwide; innovative drugs where the manufacturing site will be transferred to China; global clinical trial applications in parallel with the US or EU; innovative drugs for HIV/AIDS, viral hepatitis, and rare diseases; and newly launched generic drugs.) In March 2017, China further loosened restrictions by allowing Chinese-produced generics as well as imported innovator drugs to apply for approval without the need for full clinical trials performed within China.³⁴

Post-application review of drugs in China is a slow process that can take 12-18 months, a significant portion of which is due to a backlog of application reviews.³⁵ In 2015, there was approximately one reviewer per 100 drug applications in the Center for Drug Evaluation (CDE), the reviewing body under the CFDA. Fortunately, China is increasing the number of reviewers to cut into the backlog of approvals. In 2016, 600 reviewers were added to the 70 previously in place, with more hiring to follow.³⁶

²⁹ CITIC Capital. *China Healthcare Market and Key Recent Policy Updates* Hong Kong: CITIC Capital, 2016.

³⁰ "China forecasted as the fastest growing biologics market over the next decade with Chinese NCEs within 5-years," BioPharma Dive, updated July 1, 2016, <https://www.biopharmadive.com/press-release/20160701-china-forecasted-as-the-fastest-growing-biologics-market-over-the-next-deca/>; "China: Innovation, Driven by the Government," Credit Suisse, updated March 23, 2017, <https://www.credit-suisse.com/microsites/conferences/aic/en/blog/china-innovation-driven-by-the-government.html>; World Health Organization. *China policies to promote local production of pharmaceutical products and protect public health* Geneva: World Health Organization, 2017.

³¹ Bill Wang and Alistair Davidson, "An overview of major reforms in China's regulatory environment," *Regulatory Rapporteur* 14, no. 7 (2017): 5-9.

³² R&D-based Pharmaceutical Association Committee, *Building a World-Class Innovative Therapeutic Biologics Industry in China*.

³³ Andy Tsun et al., "The Chinese Biologics Drug Market: demand and execution," *Drug Discovery World* Spring(2015).

³⁴ Wang and Davidson, "An overview of major reforms in China's regulatory environment," 5-9.

³⁵ Tsun et al., "The Chinese Biologics Drug Market: demand and execution."

³⁶ Wang and Davidson, "An overview of major reforms in China's regulatory environment," 5-9; *ibid.*

In April 2018, the CFDA proposed a rule that gives up to 12 years of data exclusivity to innovator biologics, which would create a significant market incentive for Chinese biopharmaceutical firms, and brings China's protection of drug application on par with the US and EU. The US provides up to 12 years of data exclusivity,³⁷ and the EU provides eight plus two to three more years of continued market exclusivity once the data exclusivity expires.³⁸ Data exclusivity refers to the protection of clinical trial data that prevents generic drug manufacturers from relying on these data in their own applications. Because clinical trials are exceptionally expensive, data exclusivity serves as a form of market protection for developers of innovative new drugs in addition to those offered by patent protection.³⁹ Before China's new policy, innovative drugs (including biologics) were only given six years of data exclusivity.⁴⁰

Notably, the CFDA's proposed rule would allow for the maximum protection period for biologics only if they are submitted with Chinese clinical trial data and submitted for approval first in China before other countries.⁴¹ For drugs first approved outside of China but using data from Chinese trials, the market exclusivity is only one to five years, depending on the time between foreign approval and filing in China (if the difference is more than six years, China provides no exclusivity). Drugs first approved outside of China will receive only 25 percent of the maximum data exclusivity (i.e., three years for biologics) if they use no data from Chinese trials and 50 percent (i.e., six years for biologics) if using outside data supplemented with Chinese data. The comparable US and EU regulations appear to have no such bias in treatment. By favoring Chinese data and applications, the CFDA rules would, in effect, provide support and protection to Chinese companies, as well as encourage foreign companies to seek approval for their products in China first.

The growth of the Chinese pharmaceutical and biopharmaceutical industry has been hampered by lapses in product quality, such as product contamination and consistent potency. To help address these issues and become more competitive on the global stage, China is now aligning their standards with the international community. In 2017, China joined the International Council for Harmonization (ICH), which requires members to implement a basic set of regulatory requirements for the manufacture of pharmaceuticals, for the conduct of clinical trials, and for stability testing of pharmaceutical products.⁴² Though the Chinese government has been tightening quality control regulations in the pharmaceutical and biopharmaceutical industry in the past five years, effective enforcement and implementation of these regulations have been lacking. The system suffers from problems such as inefficient approval process and other administrative procedures, lack of clarity in certain regulatory documents, and obscure definition of accountability in others.⁴³ As a result, poor quality control persists as exemplified by the July 2018 instance in which vaccine maker Changsheng Biotech was found guilty of forging data on rabies vaccine products that were not up to Chinese standards.⁴⁴

³⁷ There is some debate about the extent to which the US provides data exclusivity for innovator biologics; the FDA has argued the law provides for both data and market exclusivity for the first four years and only market exclusivity afterward, but contemporary sources still interchangeably refer to the 12-year period as market and data exclusivity.

³⁸ Pharmacy Choice Staff, "CFDA proposes 12-year data exclusivity for innovative biologics," *Pharmacy Choice* April 30, 2018, https://www.pharmacychoice.com/news/article.cfm?Article_ID=1996990; E. F. M. 't Hoen, P. Boulet, and B. K. Baker, "Data exclusivity exceptions and compulsory licensing to promote generic medicines in the European Union: A proposal for greater coherence in European pharmaceutical legislation," *J Pharm Policy Pract* 10(2017): 19.; European Parliament, "Regulation (EC) No 726/2004," (2004).

³⁹ Jacques Gorlin, "Encouragement of new clinical drug development: the role of data exclusivity," *International Federation of Pharmaceutical Manufacturers Associations (IFPMA)*(2000), http://www.who.int/intellectualproperty/topics/ip/en/DataExclusivity_2000.pdf

⁴⁰ Ropes & Grey, "The China Drug Administration Proposes a Working Procedure for Pharmaceutical Study Data Protection," <https://www.ropesgray.com/en/newsroom/alerts/2018/05/The-China-Drug-Administration-Proposes-a-Working-Procedure-for-Pharmaceutical-Study-Data-Protection>

⁴¹ Ibid.

⁴² Theresa M. Mullin, "China Joins ICH in Pursuit of Global Harmonization of Drug Development Standards," *FDA Voice* August 9, 2017, <https://blogs.fda.gov/fdavoices/index.php/2017/08/china-joins-ich-in-pursuit-of-global-harmonization-of-drug-development-standards/>

⁴³ Shang Yang, "大破大立！医药新政策你必须懂的五个关键词," *EO Intelligence* 2018, <https://m.iyiou.com/intelligence/insight68595> [Chinese Language Source]

⁴⁴ Andy Extance, "Vaccine Scandal and Heart Drug Recall show China's Pharma Struggles," *Chemistry World*(2018), <https://www.chemistryworld.com/news/vaccine-scandal-and-heart-drug-recall-show-chinas-pharma-struggles/3009330.article;>

1.1.2.3. Biosimilars

The biologics produced in China are mostly biosimilars, meaning a nearly identical copy of an original biopharmaceutical product that is manufactured by a different company. Biosimilars are officially approved versions of original innovator biopharmaceutical products, and can be manufactured when the original product's patent expires. While akin to generics of traditional pharmaceuticals, biosimilars are significantly more advanced and technologically difficult to produce. Biopharmaceuticals are manufactured using cell lines that are specifically engineered—e.g., by insertion of new genetic material—to produce a molecule of interest. Because companies protect these cell lines once created, attempts to reproduce the final biologic product require recreating the production cell lines anew, an R&D activity that could take six to nine months (note, however, that those looking to develop biosimilars are starting with a proven end goal, sparing them the years of research to identify potential drug targets that go into developing novel biologics). Once the cell line is created, the manufacturing process itself is highly complex and technical, requiring not only scale-up of cellular production but also purification of the desired product from a complex matrix of media, cells, and cellular products. Thus, while China may not be producing many innovative, new therapeutics, their robust biosimilars industry demonstrates that they possess the necessary high-tech talent and resources to produce quality biologics.

To date, Chinese companies are responsible for the development of approximately 250 biosimilars.⁴⁵ Most companies have few biosimilars in their pipelines; around 60 Chinese companies account for approximately 120 biosimilars plus 50 novel biologics.⁴⁶ North America has developed the most biosimilars (over 600) with Europe a close second (around 470).⁴⁷ The majority of biosimilars worldwide are still in pre-clinical development, however, with very few marketed. Two original biologics that are frequently the target of biosimilar products in China are the monoclonal antibody drugs Humira (used as treatment for rheumatoid arthritis, Crohn's, and other autoimmune diseases) and Avastin (for several types of cancer including colorectal and lung cancer), both products developed by US biopharmaceutical companies. As of the end of 2017, 19 Chinese biologics companies had at least three therapeutic candidates at or past the stage of IND filing.⁴⁸ Among these companies are GenorBio, Qilu Pharmaceutical, Fosun Pharma, Hengrui, 3SBio, Innovent Biologics, Hisun pharma, and Zhangjiang Biotech; two of these companies—Hisun pharma and Zhangjiang Biotech—are partially state-owned.⁴⁹ Chinese companies with relatively high numbers of biologic candidates in the pipeline tend to produce a mix of biosimilars and new biologics or biobetters (e.g., new antibodies against an established oncology target). Many of these biologic products are monoclonal antibodies, antibody-based drugs (such as Fc-fusion proteins and antibody-drug conjugates), and recombinant human proteins. Antibody therapeutics commonly target cancer and autoimmune disease.

Fosun Pharma has a robust pipeline, with several antibody biosimilars in late-stage clinical development.⁵⁰ It has also engaged in a joint venture with Kite Pharma, a US-based Chimeric Antigen Receptor T-Cell (CAR-T) leader, to manufacture and commercialize Yescarta, Kite's US FDA-approved CAR-T treatment for lymphoma, in China.⁵¹ (See Section 1.1.2.5 for more details about China's CAR-T industry.) Other notable companies include BeiGene, which raised \$158 million in its 2016 US initial public offering (IPO) and has a clinical pipeline with several candidate cancer treatments including small molecule drugs, a monoclonal antibody, and some combination therapies.⁵²

⁴⁵ "Biosimilars/Biobetters Pipeline Directory," <http://www.biosimilarspipeline.com>

⁴⁶ Yeh et al., *China: Healthcare: Biotechnology: Biologics: Balancing quality and affordability; Fosun Pharma up to Buy.*

⁴⁷ "Biosimilars/Biobetters Pipeline Directory," <http://www.biosimilarspipeline.com>

⁴⁸ *China: Healthcare: Biotechnology: Biologics: Balancing quality and affordability; Fosun Pharma up to Buy.*

⁴⁹ Hisun Pharma is 40 percent state-owned, and Zhangjiang Biotech is 70 percent state-owned.

⁵⁰ Yeh et al., *China: Healthcare: Biotechnology: Biologics: Balancing quality and affordability; Fosun Pharma up to Buy.*

⁵¹ "Fosun Kite Initiates the Manufacturing of FDA-approved CAR-T Product Yescarta in China to Follow Chinese Regulatory Path," Fosun International, updated December 5, 2017, <https://www.fosun.com/language/en/p/23942.html>

⁵² Reuters, "BeiGene raises \$158.4 mln in second U.S. IPO to price in 2016," *Reuters* February 2, 2016, <https://www.reuters.com/article/beigene-ipo-idUSL2N151049>; "Pipeline Overview," BeiGene, updated July 17, 2018, www.beigene.com/pipeline/clinical-candidates/overview/

Regulation of Biosimilars

Generally, obtaining market approval for biosimilars involves demonstrating that the product is not significantly different from an approved innovator biologic (e.g., in physical and chemical properties, potency, and purity). Once similarity is demonstrated, approval typically requires reduced pre-clinical and clinical studies given that the originator product has already been shown to be effective. The biosimilar regulations of the EU are considered the most comprehensive and sophisticated and take a risk-based approach to determining the extent of testing and clinical data needed for a biosimilar application.⁵³ Several other countries, including Australia in 2007 and the US in 2012 have released comparable biosimilars regulations since then.

In 2015, the CDE released new guidelines that provide a set of technical review principles for biosimilars that are separate for innovator biologics.⁵⁴ Prior to these guidelines, biosimilars approvals in China were handled on a case-by-case basis, causing uncertainty among biosimilar manufacturers and resulting in approval delays. The new CDE guidelines, like regulations in the US and EU, provide a definition for biosimilars, specify which products are acceptable as reference products, and reduce pre-clinical and clinical data requirements compared to innovator biologics. Unlike their foreign counterparts, however, Chinese regulations do not create a separate approval pathway from innovator biologics or provide market exclusivity for first-to-market biosimilars. By updating their biologics review process, China has become more aligned with major biotechnology players like the US and EU, paving the way for further growth of the Chinese biosimilars market.⁵⁵ Unlike China's innovator biologics regulations, the new biosimilars guidelines do not create additional practices that favor Chinese companies and exclude foreign ones

1.1.2.4. Contract Research and Manufacturing

Contract Research Organizations

Contract research organizations (CROs) support pharmaceutical, biologics, and medical device companies by providing outsourced services for preclinical or clinical development. CROs can perform preclinical studies for a drug candidate, such as safety and efficacy trials and pharmacodynamics studies, as well as conduct Phase I-IV clinical trials. CROs play a prominent role in drug development worldwide, with over half of all pharmaceutical companies using them. Percentages of the addressable market (in USD) outsourced to CROs include 25 percent of discovery, 30 percent of preclinical development, and 41 percent of clinical development.⁵⁶ The global CRO industry had an estimated market size of \$31.7 billion in 2016, with China's CRO segment at 46.2 billion yuan (\$7.2 billion), and were expected to grow rapidly over the subsequent five years.⁵⁷ In 2017, there were more than 1,100 CROs worldwide, around 400 of them in China.⁵⁸ While China has a sizeable CRO industry, most of the world's top CROs are headquartered in the US. Detailed estimates of US market share are difficult to acquire, due to the large number of CROs globally, and frequent mergers and acquisitions (M&A). As of 2016, the largest CROs headquartered in the US were estimated to represent 48 percent of the global market.⁵⁹ Another source

⁵³ Nick Beckett and Jane Lin, "A comparison of European and Chinese regulation of biosimilar products," *Lexology*(2015), <https://www.lexology.com/library/detail.aspx?g=2070d1ed-8ff6-46eb-a18d-25e74ee7e8a4>

⁵⁴ Center for Drug Evaluation, "Technical Guideline for the Research, Development and Evaluation of Biosimilars," (2015).

⁵⁵ Joan Boren and Costantino Congiatu, "Challenges in the global clinical development of biosimilar products," *Regulatory Rapporteur* 12, no. 5 (2015): 22-26.; Katherine Wang, *Biosimilars are Regulated Differently in China*: PharmaDJ, 2015.

⁵⁶ Eric Wilson, Robert Willoughby, and Mark Wallach. *CRO Industry Primer*. Credit Suisse Securities Research & Analytics, 2016.

⁵⁷ Research and Markets, "China Contract Research Organization (CRO) Industry Report 2017," *Globe Newswire* October 23, 2017, <https://globenewswire.com/news-release/2017/10/23/1151370/0/en/China-Contract-Research-Organization-CRO-Industry-Report-2017.html>

⁵⁸ Natalie Chiu. *Contract Research Organization Market*: GF Securities (Hong Kong) Brokerage LTD, 2017. ; PR Newswire, "Contract Research Organizations Global Market Opportunities And Strategies To 2021," (2018), <https://www.prnewswire.com/news-releases/contract-research-organizations-global-market-opportunities-and-strategies-to-2021-300696819.html>

⁵⁹ Wilson, Willoughby, and Wallach, *CRO Industry Primer*.

estimated the North American market to be 45 percent of the global total in 2016-2017.⁶⁰ (All figures reflect CROs as a whole and are not specific to biotechnology services.)

Chinese preclinical CROs have traditionally been chosen by international clients for providing lower-cost services—around 25-40 percent lower than in western countries.⁶¹ Outsourcing to CROs also presents a way for multi-national corporations to utilize China's maturing R&D capabilities without many of the difficulties that come with other business relationships such as joint ventures; CRO contracts have fewer regulatory hurdles than joint ventures and can help ease some wariness local companies may have of foreign firms looking for partnerships.⁶² Furthermore, clinical outsourcing is seen as an effective way for drugs to gain early market access in China. CROs can help foster relationships with government officials, investigators, and local vendors, which can help new drugs gain approval and enter the market faster.⁶³

In addition to these factors, the Chinese CRO industry has been building its ability to add value, with companies constructing more integrated services chains or developing niche expertise.⁶⁴ As a result, Chinese CROs have also been receiving increased business from domestic biotech and pharmaceutical customers.⁶⁵ Chinese CROs have also been making strides in quality improvement, as more are adopting international R&D standards—including Good Laboratory Practice (GLP), Good Manufacturing Practice (GMP), and Good Clinical Practice (GCP)—and aligning to FDA and European Medicines Agency quality standards.⁶⁶

China's WuXi AppTec is a leading global CRO, and biologics services make up 12 percent of its \$800 million annual sales (2015 estimate).⁶⁷ In 2017, the company's biologics services segment, WuXi Biologics, raised over \$500 million in its IPO in Hong Kong.⁶⁸ WuXi Biologics offers discovery, development, and manufacturing services for clients in the biologics space.⁶⁹

Biologics Manufacturing

In addition to outsourcing their preclinical and clinical studies, pharmaceutical and biopharmaceutical companies often look to other companies for production of their products. Contract manufacturing organizations (CMOs) provide services that include formulation, small-scale production for preclinical or clinical studies, scale-up, and large-scale production of marketed drugs.

The CMO market has grown rapidly in China since 2016, driven by Chinese regulatory changes that occurred that year.⁷⁰ Prior to 2016, domestic drug developers were prohibited from using contract

⁶⁰ "Surveying The Clinical CRO Market & Outsourcing Landscape," Mathini Ilancheran, updated July 6, 2017, <https://www.clinicalleader.com/doc/surveying-the-clinical-cro-market-outsourcing-landscape-0001>

⁶¹ Chiu, *Contract Research Organization Market*.

⁶² Yun-Zhen Shi, Hao Hu, and Chunming Wang, "Contract Research Organizations (CROs) in China: integrating Chinese research and development capabilities for global drug innovation," *Globalization and Health* 10(2014): 78.

⁶³ Chiu, *Contract Research Organization Market*.

⁶⁴ Christine Xia and Ajay Gautam, "Biopharma CRO industry in China: landscape and opportunities," *Drug Discovery Today* 20, no. 7 (2015): 794-98.; Shi, Hu, and Wang, "Contract Research Organizations (CROs) in China: integrating Chinese research and development capabilities for global drug innovation," 78.; Steve Yang, "The Rise Of R&D Capability And Technology Platforms In China," *Forbes* December 2, 2014, <https://www.forbes.com/sites/medidata/2014/12/02/the-rise-of-rd-capability-and-technology-platforms-in-china/#62cab0773267>

⁶⁵ Jean-François Tremblay, "Why China's contract research firms are doing more business at home," *Chemical & Engineering News* 94, no. 44 (2016): 22-25.

⁶⁶ Shi, Hu, and Wang, "Contract Research Organizations (CROs) in China: integrating Chinese research and development capabilities for global drug innovation," 78.

⁶⁷ Jean-François Tremblay, "C&EN profiles WuXi AppTec, Chinese contract research giant," *Chemical & Engineering News* 94, no. 11 (2016): 21-24.

⁶⁸ Angus Liu, "WuXi Biologics prices shares at top end, aims for \$510M IPO: Bloomberg," *FierceBiotech* June 7, 2017, <https://www.fiercebiotech.com/cro/wuxi-biologics-prices-share-at-top-end-aims-for-510m-ipo-bloomberg>

⁶⁹ "Wuxi Biologics IPO in Hong Kong brings in \$511m," BioPharma-Reporter.com, <https://www.biopharma-reporter.com/Article/2017/06/16/Wuxi-Biologics-IPO-in-Hong-Kong-brings-in-511m>

⁷⁰ Vicky Qing Xia and Leo Cai Yang, *Directory of Top 60 Biopharmaceutical Manufacturers in China: A comprehensive industry review: Profiles of established, and rapidly growing, organizations involved in biomanufacturing.*, 2 ed. (Rockville, MD: BioPlan Associates, 2017), Industry Review.

manufacturing services, limiting CMOs to only serving foreign customers and leaving the CMO market underdeveloped (though a few larger companies, such as WuXi Biologics, could gain a foothold). In 2016, however, China introduced the Marketing Authorization Holder (MAH) system, a regulatory change that enabled domestic biologics developers to make use of CMO services, quickly expanding the CMO market.⁷¹ As a result, large projects have emerged in recent years: in 2015, WuXi Biologics built a \$150 million biologics manufacturing facility with 30,000L capacity, and in 2017, Boehringer Ingelheim (German) opened a \$77 million biologics CMO plant in Shanghai.⁷²

China-based facilities owned by multinational companies have been in existence before introduction of the MAH reforms; for instance, Sanofi and GlaxoSmithKline (GSK) have operated influenza vaccine production facilities out of Shenzhen.⁷³ Sanofi's first doses were produced during the 2014/2015 flu season.⁷⁴ GSK's efforts began with a joint venture with Shenzhen Neptunus in 2009, and GSK later acquired the remaining 51 percent equity stake in 2011 to gain full ownership.⁷⁵ In 2016, Pfizer announced plans for a \$350 million biotechnology center in the Hangzhou Economic Development Area to produce biosimilars for Chinese and global patients.⁷⁶

Based on 2016 estimates, China's biopharmaceutical manufacturing capacity reached at least 1.6 million liters, compared to over 18 million liters capacity worldwide.⁷⁷ In 2017, capacity expanded by over 10 percent, and this expansion trend is expected to continue.⁷⁸ Today, China ranks third globally behind the US and EU in number of production facilities and capacity.⁷⁹ As domestic biologics companies (especially producers of mAb therapeutics) develop their R&D and drug pipelines, they simultaneously build their production and manufacturing capacities. CMOs have grown rapidly since regulatory reforms, with new companies arising and existing companies expanding their production capacities.⁸⁰

The primary value Chinese CMOs offer is low cost manufacturing of products, however quality remains an issue for many manufacturers.⁸¹ With the growth of the Chinese CMO industry, the FDA has increased its inspections of Chinese facilities, which has resulted in numerous warning letters. In 2016-2017, Chinese

⁷¹ "Contract BioManufacturing in China: Creating a New Segment," *Contract Pharma* April 10, 2018, https://www.contractpharma.com/issues/2018-04-01/view_features/contract-biomanufacturing-in-china-creating-a-new-segment/49796; *Directory of Top 60 Biopharmaceutical Manufacturers in China: A comprehensive industry review: Profiles of established, and rapidly growing, organizations involved in biomanufacturing.*

⁷² "WuXi Biologics Initiated cGMP Manufacturing in the World's Largest Biologics Manufacturing Facility Using Only Single-Use Bioreactors," WuXi Biologics, updated December 6, 2017, <https://www.prnewswire.com/news-releases/wuxi-biologics-initiated-cgmp-manufacturing-in-the-worlds-largest-biologics-manufacturing-facility-using-only-single-use-bioreactors-300567515.html>; Eric Palmer, "Boehringer Ingelheim's CMO operations pay off even as new production comes online," *FiercePharma* August 2, 2017, <https://www.fiercepharma.com/manufacturing/boehringer-ingelheim-s-cmo-operations-pay-off-even-as-new-production-comes-online>

⁷³ FiercePharma admin, "Sanofi to build vaccine plant in China," *ibid.* (2007), <https://www.fiercepharma.com/pharma/sanofi-to-build-vaccine-plant-china/>; "GSK to purchase Shenzhen Neptunus stake in previously formed joint venture for influenza vaccines in China," GlaxoSmithKline, updated June 14, 2011, <https://www.gsk.com/en-gb/media/press-releases/gsk-to-purchase-shenzhen-neptunus-stake-in-previously-formed-joint-venture-for-influenza-vaccines-in-china/>

⁷⁴ "Influenza Vaccine Production in China," International Federation of Pharmaceutical Manufacturers & Associations (IFPMA), <http://partnerships.ifpma.org/partnership/influenza-vaccine-production-in-china>

⁷⁵ "GSK expands presence in China through strategic cooperation to form a joint venture on paediatric vaccines," GlaxoSmithKline (GSK), updated October 5, 2009, <https://www.gsk.com/en-gb/media/press-releases/gsk-expands-presence-in-china-through-strategic-cooperation-to-form-a-joint-venture-on-paediatric-vaccines/>; GlaxoSmithKline, "GSK to purchase Shenzhen Neptunus stake in previously formed joint venture for influenza vaccines in China," <https://www.gsk.com/en-gb/media/press-releases/gsk-to-purchase-shenzhen-neptunus-stake-in-previously-formed-joint-venture-for-influenza-vaccines-in-china/>

⁷⁶ "Pfizer Advances Biosimilars Leadership with Investment in a New World-Class Global Biotechnology Center in China," Pfizer, updated June 27, 2016, <http://press.pfizer.com/press-release/pfizer-advances-biosimilars-leadership-investment-new-world-class-global-biotechnology>

⁷⁷ Eric S. Langer, "Biopharmaceutical Manufacturing Growing Rapidly in China," *Genetic Engineering & Biotechnology News* 36, no. 21 (2016).

⁷⁸ Vicky Qing Xia and Leo Cai Yang, "Demand for Capacity Drives China's Biomanufacturing Expansion," *BioProcess International* June 20, 2018, <http://www.bioprocessintl.com/business/bioregions/demand-for-capacity-drives-chinas-biomanufacturing-expansion/>

⁷⁹ "Top1000Bio," BioPlan Associates, <http://top1000bio.com/>

⁸⁰ Xia and Yang, "Demand for Capacity Drives China's Biomanufacturing Expansion," <http://www.bioprocessintl.com/business/bioregions/demand-for-capacity-drives-chinas-biomanufacturing-expansion/>

⁸¹ "Contract BioManufacturing in China: Creating a New Segment," https://www.contractpharma.com/issues/2018-04-01/view_features/contract-biomanufacturing-in-china-creating-a-new-segment/49796

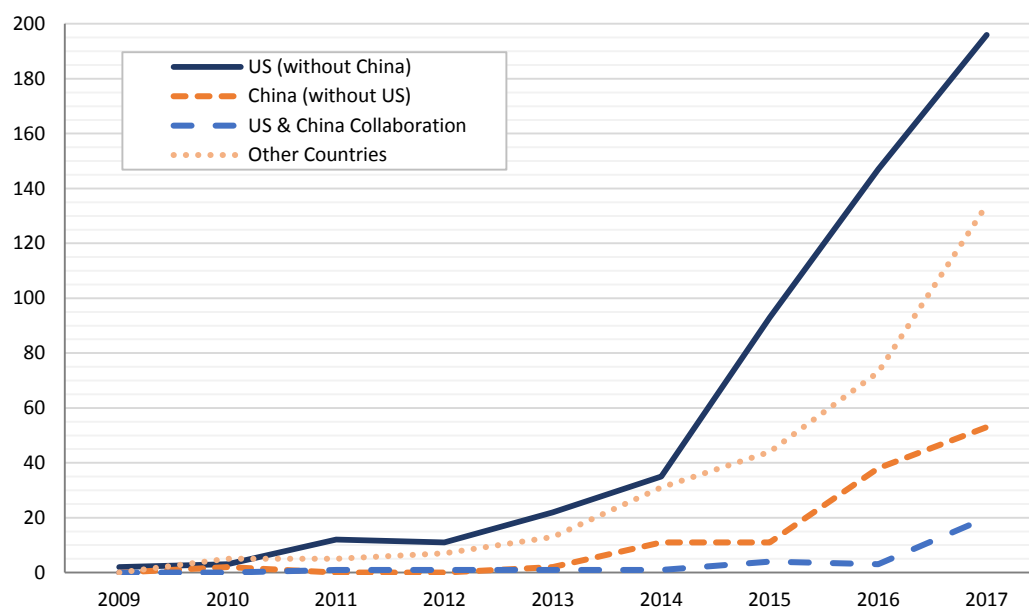
manufacturers averaged 16 FDA warning letters per year, more than one third of all warning letters sent in those two years.⁸²

1.1.2.5. Innovative Technologies

While much of the Chinese biologics industry consists of CROs, CMOs, and producers of biosimilars, Chinese scientists have shown world-leading innovation in two areas: CAR-T cell therapy and Clustered Regularly Interspaced Short Palindromic Repeats (CRISPR)-editing of cells for cancer treatment. Research publications by authors from Chinese institutions in both of these areas have increased since the advent of the technologies (Figure 1-3 and Figure 1-4)⁸³ and Chinese authors make up a larger portion of global publications on CAR-T and CRISPR than on other technologies. More significant are the advances China has made in successful medical applications of these technologies, which may not necessarily be reflected in the scientific research literature.

Figure 1-3. Annual Publications on CAR-T by Country, 2009-2017

Number of Publications



Source: Scopus.⁸⁴

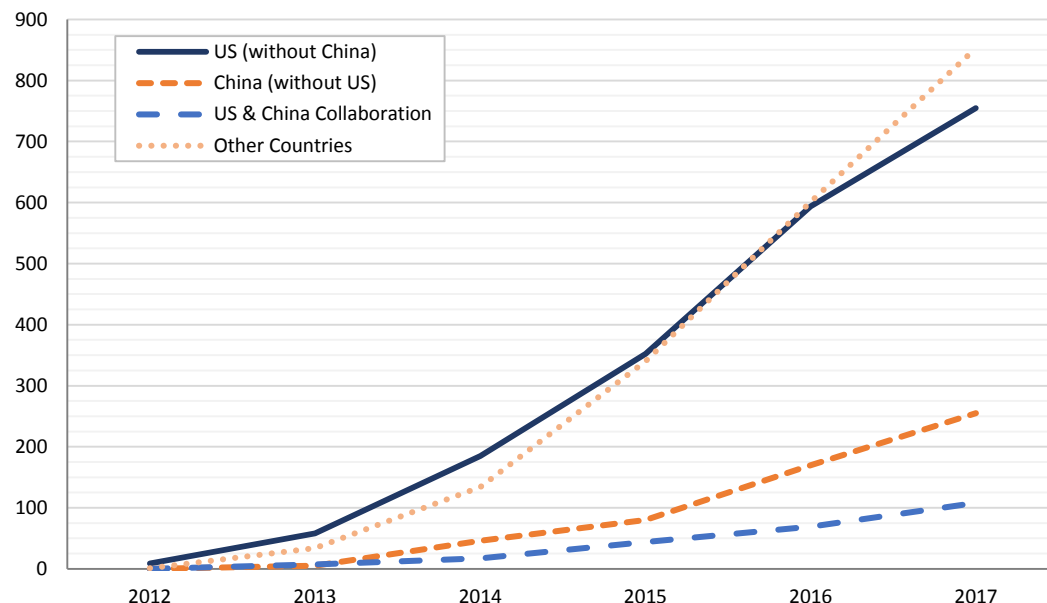
⁸² Ned Pagliarulo, "Wuxi preps for biologics manufacturing surge in China," (2017), <https://www.biopharmadive.com/news/wuxi-preps-for-biologics-manufacturing-surge-in-china/512526>

⁸³ In Figures 1-2 and 1-3, publications are counted by the nations of the authoring institutions. The categories of "US" and "China" constitute all articles with authorship from the respective country, regardless of co-authorship from other, non-US and non-China countries. The "US & China" category is individual publications with co-authors from both US and Chinese institutions, regardless of additional country co-authorship.

⁸⁴ English language search performed in Scopus for keyword: "CAR-T"

Figure 1-4. Annual Publications on CRISPR by Country, 2012-2017

Number of Publications

Source: Scopus.⁸⁵

CAR-T

Chimeric antigen receptor T-cell therapy is a procedure where a patient's immune cells (T-cells) are collected, modified in the laboratory to target cancer cells, and re-introduced into the body.⁸⁶ It is a form of cancer immunotherapy that is being applied more and more frequently around the world. Along with the US, China is leading the world in clinical applications of this technology. The US and China hold the highest numbers of CAR-T clinical trials, with different sources placing either the US or China in the leading spot, though the two are neck-and-neck.⁸⁷ (The variance is caused by differences in methodologies for identifying trials and the dates when the surveys were taken.) According to Goldman Sachs data, as of February 2018, a survey that appeared to use a more rigorous methodology than some others, there have been 153 CAR-T trials in China, a close second to the US (164 trials), and overtaking Europe (73) and the rest of the world (56).⁸⁸

One of the well-known CAR-T companies in China is Legend Biotech, a subsidiary of the US company Genscript, which has developed a CAR-T product for multiple myeloma and reports high remission rates in early clinical trials.⁸⁹ This CAR-T therapeutic is the first to be accepted for review by the CFDA.⁹⁰ Legend has entered into a collaboration and licensing agreement with US-based Janssen (a Johnson &

⁸⁵ English language search performed in Scopus for keyword: CRISPR AND (editing OR engineering)

⁸⁶ C. H. June et al., "CAR T cell immunotherapy for human cancer," *Science* 359, no. 6382 (2018): 1361-65.

⁸⁷ David Crow, Tom Hancock, and Wang Xueqiao, "Healthcare: Cancer breakthrough leads China's biotech boom," *Financial Times* (2018), <https://www.ft.com/content/30b5a944-3b57-11e8-b9f9-de94fa33a81e>; John Carroll, "As gene editing explodes, a new report from Goldman says Chinese groups are seizing the lead on CRISPR and CAR-T studies," *Endpoints News* (2018), <https://endpts.com/as-gene-editing-explodes-a-new-report-from-goldman-says-chinese-groups-are-seizing-the-lead-on-crispr-and-car-t-studies/>

⁸⁸ "As gene editing explodes, a new report from Goldman says Chinese groups are seizing the lead on CRISPR and CAR-T studies", <https://endpts.com/as-gene-editing-explodes-a-new-report-from-goldman-says-chinese-groups-are-seizing-the-lead-on-crispr-and-car-t-studies/>

⁸⁹ Angus Liu, "ASCO dark horse Nanjing Legend Biotech shines with promising CAR-T data," *FierceBiotech* June 5, 2017, <https://www.fiercebiotech.com/biotech/asco-dark-horse-nanjing-legend-biotech-shines-promising-car-t-data>

⁹⁰ "Janssen Enters Worldwide Collaboration and License Agreement with Chinese Company Legend Biotech to Develop Investigational CAR-T Anti-Cancer Therapy," Johnson & Johnson, updated December 21, 2017, <https://www.jnj.com/media-center/press-releases/janssen-enters-worldwide-collaboration-and-license-agreement-with-chinese-company-legend-biotech-to-develop-investigational-car-t-anti-cancer-therapy>

Johnson company), in which the companies will collaborate on the development and manufacturing of this therapeutic.⁹¹ The agreement includes a \$350 million upfront payment from Janssen to Legend for a Janssen license to the technology and, after joint development of the therapeutic, 70 percent of profits from sales in China and half of profits from the rest of the world.⁹² Chinese CAR-T company CARsgen Therapeutics has initiated several clinical trials for solid tumors as well as leukemia and multiple myeloma and received a \$60 million funding round in early 2018;⁹³ CARsgen has reported results from its phase I trial of a CAR-T therapy for hepatocellular carcinoma (i.e., liver cancer), with plans to initiate further efficacy studies.⁹⁴ Another player is JW Therapeutics, an initial equal-ownership joint venture of Juno Therapeutics (US) and WuXi AppTec (Chinese), drawing from Juno's CAR-T technology and WuXi's manufacturing capabilities and knowledge of the Chinese market.⁹⁵ JW Therapeutics subsequently raised \$90 million in a Chinese-backed series A round in early 2018, and their CAR-T therapy for B-cell malignancies is in the clinical phase, with an IND filing accepted by the CFDA.⁹⁶

One reason for China's leading implementation of CAR-T is their ability to provide high-tech manufacturing at cheaper prices than the rest of the world. Price is a major factor in CAR-T treatment because it involves custom modification of a patient's cells; drug costs alone can range as high as \$475,000 per person in the US, with costs to perform the procedure doubling the price tag.⁹⁷

Another significant factor in China's uptake of CAR-T is a favorable regulatory environment. Because the Chinese government categorized the procedure as a medical technology rather than a drug, approval to conduct CAR-T trials did not need to go through CFDA's lengthy drug review process and instead requires only a review by the hospital's ethics committee (commercialization still requires CFDA approval). In the US, CAR-T trials need to go through the standard IND application process. Additionally, in the US, patients are eligible for CAR-T only after all other available treatments have failed. But in China, patients can turn to CAR-T after failing only the first-line chemotherapy drugs.⁹⁸

CRISPR

CRISPR is a genome editing technology that is changing the research and medical technology landscape. CRISPR provides new capacities to precisely edit DNA, enabling scientists to add, modify, or remove features and functions of organisms as diverse as bacteria, insects and mammals. Because of its

⁹¹ John Carroll, "J&J wows with a \$350M cash deal to partner on CAR-T with Legend, a one-time unknown until its star turn at ASCO," *Endpoints News*(2017), <https://endpts.com/jj-wows-with-a-350m-cash-deal-to-partner-on-car-t-with-legend-a-one-time-unknown-until-its-star-turn-at-asco/>

⁹² Johnson & Johnson, "Janssen Enters Worldwide Collaboration and License Agreement with Chinese Company Legend Biotech to Develop Investigational CAR-T Anti-Cancer Therapy," <https://www.jnj.com/media-center/press-releases/janssen-enters-worldwide-collaboration-and-license-agreement-with-chinese-company-legend-biotech-to-develop-investigational-car-t-anti-cancer-therapy>

⁹³ "CARsgen Completed \$60 Million Pre-C Financing Framework Agreements," CARsgen Therapeutics, updated March 2, 2018, <https://www.prnewswire.com/news-releases/carsgen-completed-60-million-pre-c-financing-framework-agreements-300607289.html>

⁹⁴ The application of CAR-T for treatment of solid tumors is more challenging than for liquid malignancies like lymphoma, due to challenges inherent in getting engineered cells to reach the solid tumor versus the easier task of reaching cancerous cells in liquid malignancies. In addition, treatment of solid tumors requires overcoming challenges with engineered cell survival in the tumor microenvironment, which is often physiologically different than healthy tissue. "CARsgen Presents Phase I Results of CAR-GPC3 T HCC Trial at ASCO 2017 Annual Meeting," updated June 5, 2017, <https://www.prnewswire.com/news-releases/carsgen-presents-phase-i-results-of-car-gpc3-t-hcc-trial-at-asco-2017-annual-meeting-300468422.html>; Maria Michela D'Aloia et al., "CAR-T cells: the long and winding road to solid tumors," *Cell Death & Disease* 9, no. 3 (2018): 282.

⁹⁵ "Juno Therapeutics and WuXi AppTec Announce New Company to Develop Novel Cell-Based Cancer Immunotherapies in China," PR Newswire, updated April 7, 2016, <https://www.prnewswire.com/news-releases/juno-therapeutics-and-wuxi-apptec-announce-new-company-to-develop-novel-cell-based-cancer-immunotherapies-in-china-300247765.html>; Ben Adams, "JW Therapeutics, a China CAR-T biotech formed by Juno and WuXi, gains \$90M series A," *FierceBiotech*(2018), <https://www.fiercebiotech.com/biotech/juno-wuxi-car-t-china-biotech-jw-therapeutics-gains-90m-series-a>

⁹⁶ Mark Terry, "Juno Therapeutics Spinout Raises \$90M," *BioSpace* March 8, 2018, <https://www.biospace.com/article/juno-therapeutics-spinout-raises-90m/>

⁹⁷ Nick Mulcahy, "What's the Total Cost of One CAR T-Cell Treatment?," *Medscape*(2018), <https://www.medscape.com/viewarticle/895735>

⁹⁸ Crow, Hancock, and Xueqiao, "Healthcare: Cancer breakthrough leads China's biotech boom". <https://www.ft.com/content/30b5a944-3b57-11e8-b9f9-de94fa33a81e>

flexibility, lower cost, and relative simplicity compared to other genetic manipulation techniques, CRISPR is being rapidly adopted for all sorts of genetic work, including treatment of genetic diseases like cancer. In October 2016, a group at Sichuan University became the first to use CRISPR in a clinical trial to treat humans (the trial was one to treat aggressive lung cancer).⁹⁹ The study appears to be still ongoing, so its success or failure has yet to be determined.¹⁰⁰ Genetic targeting of disease therapies is in its infancy compared to other techniques using drugs or antibodies, and even with the advent of CRISPR gene editing, there are few trials using the technology. As of the end of February 2018, there were nine registered clinical studies to test CRISPR-edited cells to treat cancer and HIV in China, treating over 80 patients; only one such trial exists in the US.¹⁰¹ As with CAR-T, China is benefitting from a laxer regulatory environment to move ahead of the US in CRISPR-based therapies. There are no regulations in China prohibiting genetic manipulation of humans, and several trials are under way. Meanwhile, in the US, regulators have taken a more cautious approach with stringent safety demands before approving trials, and to date no trials have started yet here.¹⁰²

1.1.3. Genomics, Molecular Diagnostics, and Precision Medicine

The emergence of high-throughput (often called next-generation) DNA sequencing in the mid-2000s is a breakthrough that has enabled many different scientific and medical advances including genomics (the study of the entirety of an individual's DNA sequence information—the genome), molecular diagnostics (the use of DNA or RNA sequences to diagnose a disease or condition), and precision medicine (the use of genetic information to tailor the treatment of an illness to the individual). Companies operating in this space constitute a significant, growing segment within China's biotechnology sector, supported by China's abundant DNA sequencing capacity. While private investment has contributed to much of this growth, state support of Chinese companies has also been an important factor.

Sequencing colossus BGI, previously known as the Beijing Genomics Institute, is China's top genomics player. Founded in 1999, BGI was responsible for sequencing one percent of the human genome in China's contribution to the Human Genome Project and subsequently continued to contribute to high-profile research projects.¹⁰³ In recent years, in what appears to be a market-driven change, the company shifted from mainly sequencing for basic research and pharmaceutical purposes to more reproductive-health services, specifically in-vitro fertilization embryo, prenatal, and newborn testing; reproductive-health screening made up 55 percent of BGI's income in 2016.¹⁰⁴ The company (specifically, a BGI Group arm called BGI Genomics) went public in 2017 on the Shenzhen Stock Exchange, raising 547 million yuan (\$85 million).¹⁰⁵ BGI has received state support, including a ten-year, \$1.5 billion loan from China Development Bank in 2010, which enabled it to purchase 128 HiSeq 2000 sequencers.¹⁰⁶ BGI is a world leader in sequencing, and has at times had the world's largest capacity (in terms of amount of DNA sequence produced), often vying for the top spot with US-based Illumina.¹⁰⁷ BGI has engaged in research

⁹⁹ David Cyranoski, "CRISPR gene-editing tested in a person for the first time," *Nature* 539, no. 7630 (2016): 479.

¹⁰⁰ "PD-1 Knockout Engineered T Cells for Metastatic Non-small Cell Lung Cancer (ClinicalTrials.gov Identifier: NCT02793856)," You Lu via ClinicalTrials.gov, updated December 27, 2017, <https://www.clinicaltrials.gov/ct2/show/NCT02793856>

¹⁰¹ Carroll, "As gene editing explodes, a new report from Goldman says Chinese groups are seizing the lead on CRISPR and CAR-T studies". <https://endpts.com/as-gene-editing-explodes-a-new-report-from-goldman-says-chinese-groups-are-seizing-the-lead-on-crispr-and-car-t-studies/>

¹⁰² Preetika Rana, Amy Dockser Marcus, and Wenxin Fan, "China, Unhampered by Rules, Races Ahead in Gene-Editing Trials," *Wall Street Journal* January 21, 2018, <https://www.wsj.com/articles/china-unhampered-by-rules-races-ahead-in-gene-editing-trials-1516562360>; Bailey Lipschultz and Rebecca Spalding, "Gene-Therapy Company Crispr Drops as FDA Puts Trial on Hold," *Bloomberg* May 30, 2018, <https://www.bloomberg.com/news/articles/2018-05-30/gene-therapy-company-crispr-drops-after-fda-puts-hold-on-trial>; Emily Mullin, "CRISPR in 2018: Coming to a Human Near You," *MIT Technology Review* December 18, 2017, <https://www.technologyreview.com/s/609722/crispr-in-2018-coming-to-a-human-near-you/>

¹⁰³ David Cyranoski, "China's genomics giant to make stock-market debut," *Nature* 546, no. 7659 (2017): 461.

¹⁰⁴ "Reproductive Health," BGI, <https://www.bgi.com/us/research-areas/reproductive-health/>; Cyranoski, "China's genomics giant to make stock-market debut," 461.; *ibid.*

¹⁰⁵ "BGI Genomics Raises \$81M in IPO," *Genetic Engineering & Biotechnology News*(2017), <https://www.genengnews.com/gen-news-highlights/bgi-genomics-raises-81m-in-ipo/81254663>

¹⁰⁶ Shu-Ching Jean Chen, "Genomic Dreams Coming True In China," *Forbes*(2013), <https://www.forbes.com/sites/forbesasia/2013/08/28/genomic-dreams-coming-true-in-china/>

¹⁰⁷ *Ibid.*

partnerships with US institutions (see Section 5.3.1) and benefited from its acquisition of the US sequencing company Complete Genomics (see Section 3.4.3 for more on this transaction).

Other top genomics companies in China include WuXi NextCODE, Novogene, and CloudHealth Genomics.¹⁰⁸ WuXi NextCODE arose from the acquisition of US-based NextCODE Health by WuXi PharmaTech (discussed in Section 5.3.1). The company provides an online database and platform for genomics data as well as sequencing services;¹⁰⁹ further, it boasts the first sequencing facility in China to be accredited by the College of American Pathologists (CAP), certified through Clinical Laboratory Improvement Amendments (CLIA), and licensed by the State of California to perform testing (see Section 5.3.3 for more on the importance of CLIA certification and CAP accreditation).¹¹⁰ Novogene is another major provider of genomics and bioinformatics services with vast sequencing capacity.¹¹¹

In the field of molecular diagnostics, many companies are interested in liquid biopsy for cancer diagnostics. One such company is HaploX Biotechnology, which raised a \$32 million funding round that it intends to use for two major sequencing projects in the areas of lung cancer and colorectal cancer.¹¹² Singlera Genomics, which is developing proprietary technology for analysis of circulating tumor DNA, closed a \$60 million series A round in early 2018.¹¹³ This area of molecular diagnostics is intertwined with genomics, with many companies concurrently developing genomic sequencing capabilities and liquid biopsy tests.¹¹⁴ Another notable application of genetic sequencing is non-invasive prenatal testing, offered by companies including Berry Genomics and Annoroad Genomics.¹¹⁵

Hospitals, pharmaceutical companies and biotech research institutes need efficient and cost-effective genomics services, giving China huge market potential for genomics technologies and sequencing services. Market growth in China's molecular diagnostics industry is over 20 percent, compared to a global growth rate of 11 percent. However, the Chinese molecular diagnostics industry only makes up two percent of the global market.¹¹⁶ China's molecular diagnostics market is expected to reach more than \$1.5 billion by 2022 (though virology tests make up a larger portion of this number than do oncology testing or genetic disease testing, which are more relevant to genomics).¹¹⁷ Worldwide, genomics and molecular diagnostics are also large and growing fields. Various estimates have placed the global DNA sequencing market in 2016-2017 at \$5.2 billion to \$7.9 billion, with an expected compound annual growth rate of 17.6-19.6 percent over the next several years.¹¹⁸

¹⁰⁸ Yiting Sun, "China Doubles Down on the Double Helix," *Neo.life* November 2, 2017, <https://medium.com/needotlife/cloudhealth-the-booming-genomics-industry-in-china-2e5476f469b0>

¹⁰⁹ Sarah Buhr, "WuXi NextCODE aims for the genomics database 'gold standard' with new \$240 million," *TechCrunch*(2017), <https://techcrunch.com/2017/09/07/wuxi-nextcode-aims-for-the-genomics-database-gold-standard-with-new-240-million/>

¹¹⁰ "WuXi NextCODE Becomes the First and Only CAP, CLIA, and California Accredited Sequencing Laboratory in China," WuXi NextCODE, updated February 23, 2016, <https://www.prnewswire.com/news-releases/wuxi-nextcode-becomes-the-first-and-only-cap-clia-and-california-accredited-sequencing-laboratory-in-china-300224420.html>

¹¹¹ "About Novogene," Beijing Novogene Technology Co. Ltd., <https://en.novogene.com/about/about-novogene/>

¹¹² GenomeWeb, "Chinese Firm HaploX Biotechnology Raises \$32M in Financing," *GenomeWeb*(2018), <https://www.genomeweb.com/informatics/chinese-firm-haplox-biotechnology-raises-32m-financing>

¹¹³ "Singlera Genomics Raises \$60 Million in Series A+ Financing," Singlera Genomics, updated March 27, 2018, <https://www.prnewswire.com/news-releases/singlera-genomics-raises-60-million-in-series-a-financing-300619990.html>

¹¹⁴ Sun, "China Doubles Down on the Double Helix," <https://medium.com/needotlife/cloudhealth-the-booming-genomics-industry-in-china-2e5476f469b0>

¹¹⁵ "Press Release: Berry Genomics NextSeq CN500 Instrument and Non-Invasive Prenatal Testing Reagent Kit Receives Chinese FDA Premarket Clearance," Illumina, updated March 31, 2015, <https://www.illumina.com/company/news-center/press-releases/press-release-details.html?newsid=2030982>; GenomeWeb, "Chinese Genomics Firm Annoroad Raises \$105M," (2017), <https://www.genomeweb.com/business-policy-funding/chinese-genomics-firm-annoroad-raises-105m>

¹¹⁶ China Industry Research. *China's molecular diagnostic industry development status analysis and market prospects report (2018-2025)* Beijing: China Industry Research Network, 2018. [Chinese Language Source]

¹¹⁷ "China Molecular Diagnostics Market, 2022: Market is Expected to Be More Than USD 1.5 Billion by the Year 2022," Research and Markets, updated September 22, 2017, <https://www.prnewswire.com/news-releases/china-molecular-diagnostics-market-2022-market-is-expected-to-be-more-than-usd-15-billion-by-the-year-2022-300524350.html>

¹¹⁸ Onkar Sumant and Sohail Shaikh. *DNA Sequencing Market - Global Opportunity Analysis and Industry Forecast, 2017 - 2023*: Allied Market Research, 2017. ; Inkwood Research. *Global DNA Sequencing Market Forecast 2018-2026*. Inkwood Research, 2018.

CFDA approval of sequencing tests for diagnostic purposes can be a complicated process, but the agency has implemented fast-tracking for genomic cancer tests. Beyond these headways in the clinical market, genome sequencing has gained popularity in the consumer market, and sequence-based risk assessments can be provided without the same restrictions as diagnostic testing.¹¹⁹

Precision medicine entails the use of genetic and other information to tailor the treatment of an illness to the individual, compared to classical medicine where treatment is by and large the same for all. For an increasing number of conditions and treatments, knowledge of specific gene sequences from an individual provides information about which treatment strategy will be most effective in that individual, whether that strategy involves selection of a specific drug or combination of drugs or tailoring of drug dosage. Given the need for knowledge of personal genomic sequences in precision medicine, companies often span the space between molecular diagnostic or genomics and personalized medicine. For example, CloudHealth Genomics is a genome sequencing company and has demonstrated interest in genomics-based precision medicine with initiatives like their collaboration with the Mongolian Health Initiative that aims to use precision medicine to fight nutrition-related diseases.¹²⁰ Precision medicine has seen significant state support in China; in March 2016, China launched the China Precision Medicine Initiative, with plans to invest 60 billion yuan (\$9.3 billion) over 15 years and invest in various projects in genome sequencing and clinical data acquisition.¹²¹ This announcement came out a year after the US launched its own \$215 million Precision Medicine Initiative.

China's interest in genomic data is discussed in greater detail in Section 5.1.1.

1.1.4. Agricultural Biotechnology

The term agricultural biotechnology describes a broad range of technologies used to enhance or protect plants and animals and includes animal vaccines, plant modification techniques such as genetic marker-assisted breeding, and genetic engineering of agricultural species (both plant and animal). A major segment of agricultural biotech is genetic modification of crops, which is used to increase productivity through conferring insect resistance, herbicide tolerance, virus resistance, drought tolerance, and other traits. The value of GM crop production in China has been estimated at around \$8.1 billion in 2013.¹²² Like the US, whose \$128 billion GM crop industry makes up 40 percent of its biotechnology industry, proceeds from GM crop production is a large portion of China's bioeconomy. Note, however, that these figures represent the sale of GM crops (as do most available estimates of countries' GM crop industries), not the biotechnology activity of producing GM seed. While estimates are not available at that level of detail, one estimate puts the net increase in profits for Chinese farms due to cultivating GM crops, rather than traditional varieties of the same crops, at \$18.65 billion cumulatively from 1997-2015, including \$1 billion in 2015 alone.¹²³

China views GM crops as a way to bolster food security and improve the performance of their agricultural sector.¹²⁴ China's Ministry of Agriculture (MOA) has produced a roadmap to commercialization of GM

¹¹⁹ Monica Heger, "China's Genomic Testing Driven by Government and Private Investment, Consumer Acceptance," *GenomeWeb* (2018), <https://www.genomeweb.com/molecular-diagnostics/chinas-genomic-testing-driven-government-and-private-investment-consumer>

¹²⁰ "The Launch of CloudHealth Genomics One Belt, One Road Initiative, a Precision Medicine Collaboration with the Mongolian Health Initiative," CloudHealth Genomics, <http://www.marketwired.com/press-release/launch-cloudhealth-genomics-one-belt-one-road-initiative-precision-medicine-collaboration-2221147.htm>

¹²¹ David Cyranoski, "China embraces precision medicine on a massive scale," *Nature* 529, no. 7584 (2016): 9-10.; Bien Perez, "China's 'precision medicine' initiative gets lift from latest genomics company funding," *South China Morning Post* May 2, 2017, <https://www.scmp.com/tech/china-tech/article/2092362/chinas-precision-medicine-initiative-gets-lift-latest-genomics>

¹²² Lee, "Bio-based economies in Asia: Economic analysis of development of bio-based industry in China, India, Japan, Korea, Malaysia and Taiwan," 4333-46.; R&D-based Pharmaceutical Association Committee, *Building a World-Class Innovative Therapeutic Biologics Industry in China*.

¹²³ Brookes and Barfoot, *GM crops: global socio-economic and environmental impacts 1996-2015*.

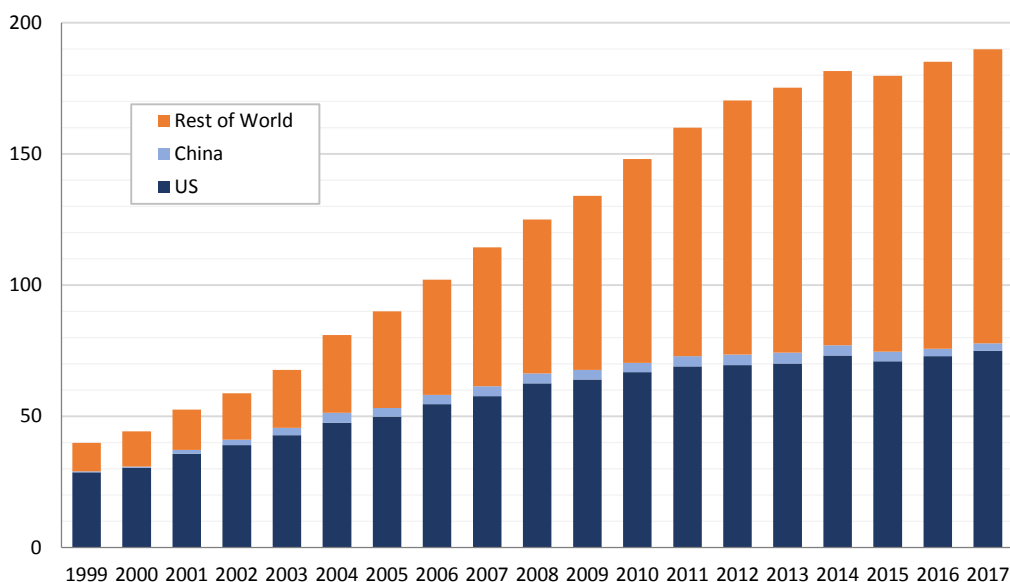
¹²⁴ Kai Cui and Sharon P. Shoemaker, "A look at food security in China," *npj Science of Food* 2, no. 1 (2018): 4.; Dominique Patton, "China approves fewer GMO crop imports, hampering trade: U.S. industry group," *Reuters* March 21 2017, <https://www.reuters.com/article/us-china-agriculture-usa/china-approves-fewer-gmo-crop-imports-hampering-trade-u-s-industry-group-idUSKBN16S0UL>

crops and initiated public outreach and education efforts, aiming to first develop non-food cash crops (such as cotton), then indirect food crops (e.g., those processed into oil or used for animal feed), and finally food crops.¹²⁵ However, the plan lacks detail on the GM plant varieties slated for development and the timing and order of commercialization, and little progress has been made.

China currently cultivates only two GM crops: cotton and papaya. Both are primarily produced for export; China is one of the largest producers of GM cotton in the world, and GM cotton makes up 95 percent of all cotton growing areas.¹²⁶ Out of 189.8 million hectares of biotech crops planted worldwide in 2017, 2.9 million hectares were grown in China (eighth largest); the top country for biotech crops by area was the US with 75.0 million hectares.¹²⁷ While countries like the US and Brazil have continued to increase their acreage of GM crops, China has maintained steady in its relatively meager production (Figure 1-5).¹²⁸ Four other GM products have been approved for cultivation in China since 1997—tomato, sweet pepper, petunia, and poplar—but are not currently grown due to commercial cultivation difficulties.¹²⁹

Figure 1-5. GM Crop Plantings for US, China, and Rest of World, 1999-2017

GM crop area (millions of hectares)



Source: Adapted from ISAAA annual reports.

Chinese farmers do not cultivate GM varieties of corn and soybeans, the most common biotech crops, despite growing large amounts of these crops. Worldwide, more than 30 percent of corn and 50 percent of soybeans cultivated are GM varieties yet no GM varieties of these crops are grown in China.¹³⁰ Instead, China is a major producer of the non-GM varieties, planting 39 million hectares of non-GM corn (compared to US farmers that planted just over two million hectares of non-GM corn and nearly 32 million

¹²⁵ Ministry of Agriculture and Rural Affairs of the People's Republic of China, "MOA holds press conference on GMO," http://english.agri.gov.cn/news/dqnf/201604/t20160414_168130.htm

¹²⁶ Foreign Agricultural Service Staff. *China: Agricultural Biotechnology Annual* Washington, D.C.: United States Department of Agriculture, 2017.

¹²⁷ The International Service for the Acquisition of Agri-biotech Applications. *Global Status of Commercialized Biotech/GM Crops: 2017* Ithaca, NY: The International Service for the Acquisition of Agri-biotech Applications, 2017.

¹²⁸ Sygenta Crop Protection AG. *Our industry 2016* Basel: Sygenta Crop Protection AG, 2016.

¹²⁹ Foreign Agricultural Service Staff, *China: Agricultural Biotechnology Annual*.

¹³⁰ The International Service for the Acquisition of Agri-biotech Applications, *Global Status of Commercialized Biotech/GM Crops: 2017*.

hectares of GM corn) and more than six million hectares of non-GM soybeans (compared to US farmers that planted two million hectares of non-GM soybeans and 32 million hectares of GM soybeans).¹³¹

One hindrance to growth of the domestic agricultural biotechnology market in China is the lack of public acceptance of GM crops, particularly for food. A survey of Chinese consumers found that just 12 percent held a positive view of GM food, with 41 percent and 47 percent having neutral and negative views, respectively.¹³² China does not have a statutory prohibition on use of GM crops in food, but to date has not approved of any such uses for either domestically produced or imported products. Despite being the world's largest importer of GM crops—including soybeans and corn—no imports have been approved for use directly in food. Instead, imported GM crops consists of those not for food use (e.g., cotton) or for indirect use in food via further processing into vegetable oil or animal feed (e.g., soybeans and corn).¹³³

Although uptake of GM crops remains slow, the Chinese government has been pushing for research into and commercialization of GM crops. China has invested heavily in GM seed development, including 24 billion yuan (\$3.7 billion) through the Key Scientific and Technological Grant of China for Breeding New Biotech Varieties and the Long-Term and Mid-Term National Development Plan for Science and Technology, which includes 585 biotech breeding projects to develop new traits such as insect, disease, and stress resistance in animals and crops.¹³⁴ The Chinese Academy of Science's State Key Laboratory of Plant Cell and Chromosome Engineering is a premier research institute that focuses on molecular research of agricultural products such as wheat, corn, rice, and soybeans, including "creating novel germplasms via chromosome engineering and breeding new varieties by molecular design."

Analysis of the scientific literature shows that China is very active in research in this field. A targeted analysis of 52 studies in which the gene editing technique CRISPR was used for trait improvement in crops found twice as many published articles coming from China than the US, contributing 42 percent and 19 percent of the articles, respectively.¹³⁵ Our own bibliometric analysis, which captured all articles resulting from keyword searches pertaining to plant engineering and CRISPR but did not screen studies specifically for those producing trait improvement, showed that China has a substantial and growing position in total articles produced, at approximately the same rate as the US (Figure 1-6).¹³⁶ Overall, US publications on this topic appear to be of slightly higher quality than those from China as judged by the number of times they are cited in other peer-reviewed journals; US publications had an average of 44 citations per paper over the assessed period (2013-2017), compared to an average of 32 citations per paper from China. Though US papers have a higher number of citations, the difference is slight, highlighting Chinese competitiveness with the US in this area of research.

A similar analysis of studies using *Agrobacterium*, a more traditional, bacterial vector for creating transgenic plants, revealed a slow but steady increase in publications from China, surpassing the US around 2010 (

Figure 1-7). For these publications, those with US authorship have had a significantly higher scientific impact, with an average of 25 citations per paper over the assessed period (2004-2017), compared to an average of 11 citations per paper from China, more than a two-fold difference.

¹³¹ Ibid.; *Global Status of Commercialized Biotech/GM Crops: 2016* Ithaca, NY: The International Service for the Acquisition of Agri-Biotech Applications, 2016. ; US Department of Agriculture, National Agricultural Statistics Service, "Acreage," 2018, <http://usda.mannlib.cornell.edu/usda/current/Acre/Acre-06-29-2018.pdf>

¹³² Kai Cui and Sharon P. Shoemaker, "Public perception of genetically-modified (GM) food: A Nationwide Chinese Consumer Study," *npj Science of Food* 2, no. 1 (2018): 10.

¹³³ Foreign Agricultural Service Staff, *China: Agricultural Biotechnology Annual*.

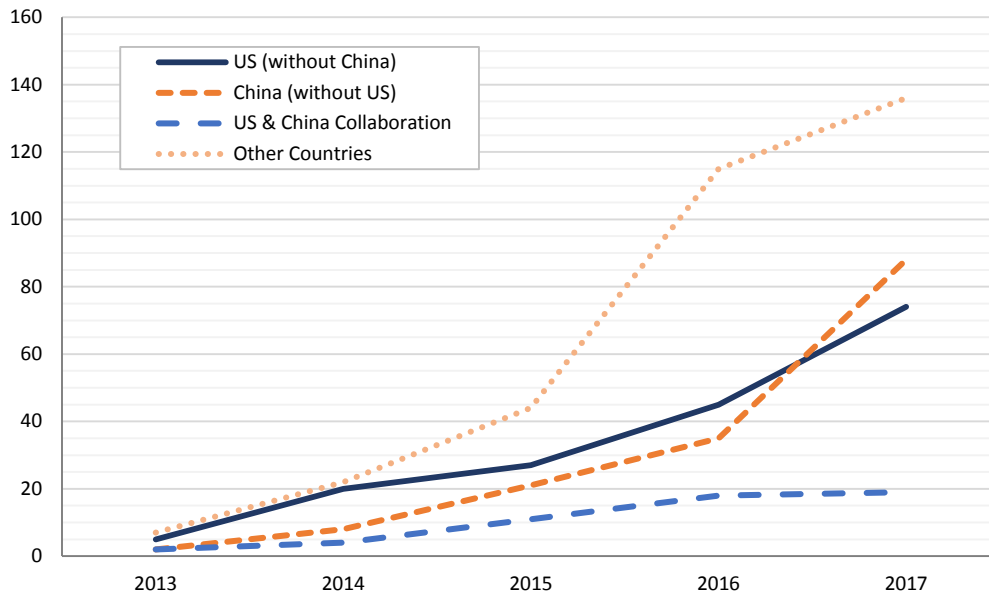
¹³⁴ Ibid.

¹³⁵ Agnès Ricroch, Pauline Clairand, and Wendy Harwood, "Use of CRISPR systems in plant genome editing: toward new opportunities in agriculture," *Emerging Topics in Life Sciences* 1, no. 2 (2017): 169-82.

¹³⁶ In Figures 1-5 and 1-6, publications are counted by the nations of the authoring institutions. The categories of "US" and "China" constitute all articles with authorship from one of the respective countries but not the other, regardless of co-authorship from other, non-US and non-China countries. The "US & China" category is individual publications with co-authors from both US and Chinese institutions, regardless of additional country co-authorship.

Figure 1-6. Annual Publications on CRISPR in Plants by Country, 2013-2017

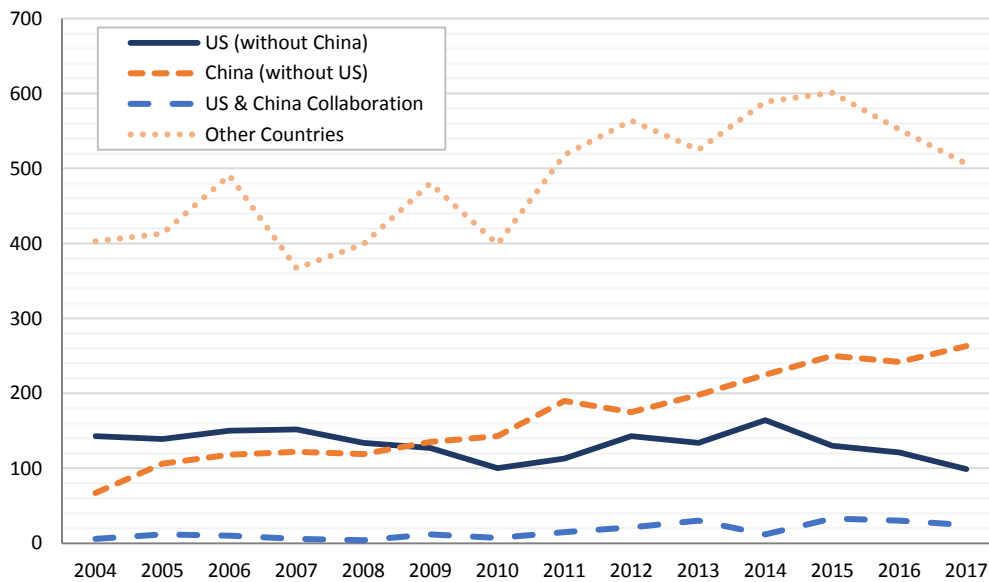
Number of Publications



Source: Scopus.¹³⁷

Figure 1-7. Annual Publications on Transgenic Plants by Country, 2004-2017

Number of Publications



Source: Scopus.¹³⁸

A major milestone in advancement of China's agricultural biotechnology industry was the 2017 acquisition of Swiss crop engineering firm Syngenta by the state-owned ChemChina for \$43 billion (China's biggest

¹³⁷ English language search performed in Scopus for keyword: CRISPR AND plants.

¹³⁸ English language search performed in Scopus for keyword: agrobacterium (a plant transfection method)

foreign corporate acquisition).¹³⁹ The deal is part of a larger food security strategy to be self-sufficient in food production, and enables China to reduce reliance on foreign GM crops, better position itself to compete with other multinationals, and gain financial and political incentives to push wider adoption of GM organisms in China and globally (see Box 1). This acquisition may lead to regulatory changes that might increase China's standing as a producer of GM crops.

Box 1. ChemChina Acquisition of Syngenta

In 2017, the state-owned China National Chemical Corporation (ChemChina) completed a \$43 million acquisition of Switzerland-based Syngenta, the largest acquisition or merger ever completed by a Chinese enterprise. The transaction was financed in large part by loans from a consortium of Chinese state-run policy banks, municipal policy banks, private banks, bonds issued to special purpose vehicles backed by state-owned commercial and policy banks, and the state-owned investment holding firm China Reform Holdings.¹⁴⁰ Syngenta was a world leader in advanced insecticides, herbicides, and other crop-protection products and the third largest producer of seeds. The firm had less presence in Asia than in other regions, though Syngenta did establish a biotech research center in Beijing in 2008 and China had imported Syngenta insect-resistant GM corn.¹⁴¹ Prior to the acquisition, ChemChina sold mostly low-profit commodity agrochemicals. Through the acquisition, however, ChemChina gained access to multiple patented GM seed, agriculture, and biotech products cited as targets in China's FYPs. ChemChina also obtained Syngenta's entire US business, including over 4,000 employees, 33 research sites, and 31 production and supply sites.¹⁴² For Syngenta, the deal offered a long-term shareholder and more secure source of funding, as well as greater access to the Chinese government, market, and production capabilities.¹⁴³ Syngenta CEO Erik Fyrwald stressed that Syngenta would remain a Switzerland-based global company while under Chinese ownership, and there is a possibility that ChemChina will take Syngenta public again in the future.¹⁴⁴

The acquisition was primarily motivated by China's desire for increased food security and their desire to use Syngenta's portfolio of top-tier chemicals and patent-protected seeds to improve domestic agricultural output.¹⁴⁵ The acquisition is part of a two-pronged strategy for Chinese food security that involves improving local food production and investing in improvements in food production around the world.¹⁴⁶ Fyrwald stated that the deal would help China achieve food security by improving technology and farm practices in China, where farm productivity is low, and by developing leading-edge technology for agriculture around the world. "Even if there's a big drought or a big flood in China, they want to make sure there's enough food available around the world to import," Fyrwald said.¹⁴⁷ The deal may have also been motivated by the global consolidation of agrochemical companies. When Dow and DuPont announced their merger in 2015, Monsanto was attempting to buy Syngenta, which demanded a higher price than Monsanto's offer. ChemChina agreed to meet Syngenta's price and the acquisition began in 2016. By bringing a leading seed company under a state-owned enterprise, China avoids reliance on foreign GM crops, better positions itself to compete with other multinationals, and gains financial and political incentives to push wider adoption of GM organisms in China and globally.¹⁴⁸

An ongoing dispute between Syngenta and US farmers over the sale of crops to China threatened to interfere with the acquisition. The dispute dates from 2013, when Syngenta sold GM corn seeds in the US without securing approvals from Chinese regulators to import the resulting corn into China. US shipments of the GM

¹³⁹ Geoff Colvin, "Inside China's \$43 Billion Bid for Food Security," *Fortune*(2017), <http://fortune.com/2017/04/21/chemchina-syngenta-acquisition-deal/>

¹⁴⁰ Office of the United States Trade Representative. *Findings of the Investigation into China's Acts, Policies, and Practices Related to Technology Transfer, Intellectual Property, and Innovation Under Section 301 of the Trade Act of 1974*: Executive Office of the President, 2018.

¹⁴¹ Colvin, "Inside China's \$43 Billion Bid for Food Security". <http://fortune.com/2017/04/21/chemchina-syngenta-acquisition-deal/>

¹⁴² Office of the United States Trade Representative, *Findings of the Investigation into China's Acts, Policies, and Practices Related to Technology Transfer, Intellectual Property, and Innovation Under Section 301 of the Trade Act of 1974*.

¹⁴³ Colvin, "Inside China's \$43 Billion Bid for Food Security". <http://fortune.com/2017/04/21/chemchina-syngenta-acquisition-deal/>

¹⁴⁴ Michael Shields, "ChemChina clinches landmark \$43 billion takeover of Syngenta," *Reuters* May 4, 2017, <https://www.reuters.com/article/us-syngenta-ag-m-a-chemchina/chemchina-clinches-landmark-43-billion-takeover-of-syngenta-idUSKBN1810CU>

¹⁴⁵ Ibid.

¹⁴⁶ Colvin, "Inside China's \$43 Billion Bid for Food Security". <http://fortune.com/2017/04/21/chemchina-syngenta-acquisition-deal/>

¹⁴⁷ Ibid.

¹⁴⁸ Ibid.

corn were rejected, and several farmers sued Syngenta for lost profits. While the dispute delayed bonds involved in the Syngenta deal, it did not prevent the acquisition from moving forward.¹⁴⁹

In April 2017, ChemChina won US antitrust approval from the Federal Trade Commission (FTC) on the condition that it divest three pesticide products: paraquat, abamectin and chlorothalonil. Syngenta owned the branded versions of the three products while ChemChina's subsidiary ADAMA sold generic versions in the U.S. The FTC claimed that the merger was likely to cause significant competitive harm in the US markets for these pesticides and required that ChemChina sell all rights and assets of the generic pesticide businesses to AMVAC, a California-based agrochemical company.¹⁵⁰ European Union antitrust approval was granted shortly thereafter, and the acquisition was completed in May 2017.¹⁵¹

1.1.4.1. The Regulatory Landscape for Agricultural Biotechnology

China has substantial regulations on both domestic production and importation of GM crops, which make bringing new crops to market very difficult. For domestic producers, technologies must pass a biosafety evaluation by the National Biosafety Committee to obtain a biosafety certificate from the MOA. The certification process consists of five steps: 1) research, 2) intermediary experiment, 3) environmental release, 4) productive testing, and 5) biosafety certification. Safety is verified with environmental safety field trials and rat feeding studies. After completion of the five stages to obtain a biosafety certificate, approvals for commercial planting generally must be obtained from both the national and provincial governments.¹⁵² Further, foreign investment in production of GM seeds and breeding of GM crops (or livestock) is prohibited by statute, placing additional barriers to innovation and advancement of China's agricultural biotechnology industry. Even in conventional seed production and cultivation of new plant varieties, foreign investment is limited to minority shares in joint ventures with Chinese companies.¹⁵³ Biosafety certificates must also be acquired by foreign seed developers and traders looking to bring GM crops and seeds to China. As part of the approval process, foreign developers must document that the sale and use of the product is allowed in their country.¹⁵⁴ Biosafety certificates for foreign traders are good only for a single shipment, representing a bottleneck in exporting activities that results in significant delays for approvals.¹⁵⁵ The impact of Chinese import approval delays on the US over the past five years are estimated at \$5 billion in output and \$1.8 billion in GDP.¹⁵⁶

1.1.4.2. Other Agriculture-Applicable Biotechnology

China is developing other areas of agriculture-applicable technology, beyond GM crops. Chinese government industrial plans have stated interest in the utilization of molecular biology tools for strategic plant breeding and disease control and in the use of biologically-based pesticides, fertilizers, and feed additives.¹⁵⁷ China has performed extensive research in molecular breeding of important crops such as rice.¹⁵⁸ Molecular breeding techniques include marker-assisted selection, a genetics-driven approach that improves the directedness of conventional breeding but avoids classification as a GM crop.

¹⁴⁹ Lucy Hornsby, "Beijing rules out direct aid on ChemChina's \$44bn Syngenta purchase," *Financial Times*, <https://www.ft.com/content/4a449fc4-a411-11e7-9e4f-7f5e6a7c98a2>

¹⁵⁰ "FTC Requires China National Chemical Corporation and Syngenta AG to Divest U.S. Assets as a Condition of Merger," Federal Trade Commission, updated April 4, 2017, <https://www.ftc.gov/news-events/press-releases/2017/04/ftc-requires-china-national-chemical-corporation-syngenta-ag>

¹⁵¹ Aoife White and David McLaughlin, "ChemChina Gets EU Nod for Syngenta Deal One Day After U.S.," *Bloomberg* April 4, 2017, <https://www.bloomberg.com/news/articles/2017-04-04/chemchina-wins-u-s-approval-for-43-billion-syngenta-takeover-j13z8ty8>

¹⁵² Foreign Agricultural Service Staff, *China: Agricultural Biotechnology Annual*.

¹⁵³ Ministry of Commerce and the National Development and Reform Commission of the People's Republic of China. *Catalogue of Industries for Guiding Foreign Investment (Revision 2017)* Beijing 2017. [Chinese Language Source]

¹⁵⁴ Ministry of Agriculture of the People's Republic of China. *Decree No. 9: Administrative Measures for Safety of Import of Agricultural GMOs* Beijing 2002. [Chinese Language Source]

¹⁵⁵ Jian-ping Kou, Qiao-ling Tang, and Xian-fa Zhang, "Agricultural GMO safety administration in China," *Journal of Integrative Agriculture* 14, no. 11 (2015): 2157-65.

¹⁵⁶ Agribusiness Consulting. *The Impact of Delays in Chinese Approvals of Biotech Crops* Memphis, TN: Informa PLC, 2018.

¹⁵⁷ Bioindustry Development Plan (2012). The State Council of the People's Republic of China,.; National Development and Reform Commission of the People's Republic of China, *'13th Five-Year' Bioindustry Development Plan*.

¹⁵⁸ Y. Rao, Y. Li, and Q. Qian, "Recent progress on molecular breeding of rice in China," *Plant Cell Rep* 33, no. 4 (2014): 551-64.

In addition, China's animal vaccine market is active, with around 100 domestic players. Chinese companies produce vaccines for compulsory and non-compulsory immunizations against epidemic diseases, most commonly for use in hogs and poultry. The size of the animal vaccine market in China was estimated at 14 billion yuan (\$2.2 billion) in 2014, and 25 different vaccines were registered in the country in 2015.¹⁵⁹ These vaccines have commonly been low-quality, using lower-grade raw materials and having limited production oversight, which in turn may impair safety or efficacy; quality issues are due in part to the competitive system for sales that drives down the purchase price of vaccines.¹⁶⁰ Production and consumption of animal vaccines in China remain mostly domestic, though foreign companies supply around 10 percent of China's animal vaccine market, and international companies have invested in manufacturing bases in China.¹⁶¹

1.1.5. Industrial Biotechnology

Industrial biotechnology is the use of living organisms such as bacteria and yeast and cellular components such as enzymes for industrial processing and production of chemicals, biofuels, and other materials.¹⁶² Benefits of industrial biotechnology may include manufacture of new products that could not otherwise be produced at all or at scale, improvement upon traditional industrial processes, and sustainability and reduced environmental impact. Many areas of industrial biotechnology have substantial room for growth and technological advancement. Industrial biotechnology is strong in the US, with revenue over \$140 billion in 2016.¹⁶³

Our definition of biotechnology does not include use of non-biological processes for production from biomass (i.e., matter derived from living organisms, such as plant mass), to include the manufacture of biodiesel by chemical conversion of biomass. Most relevant to our scope are uses of organisms genetically engineered to produce a material of interest (for example, to be able to ferment specific types of biomass for fuel or to produce industrial enzymes). Use of naturally-occurring organisms for fermentation-based production may be relevant to an indirect or lesser degree; for instance, biofuels can be produced by fermentation with unmodified microorganisms. For this study of biotechnology, we are mainly interested in advances in the life sciences, usually involving genetic manipulation.

Tracking of the industrial biotechnology sector is inconsistent, both worldwide and in China, and industry data are limited in comparison to the medical and agricultural biotechnology sectors. Generally, the lack of high-quality data stems from three factors. First, definitions of industrial biotechnology may vary from source to source, making data comparisons and aggregation difficult. Second, due to the range of products and services within this sector, identifying all participants in the sector to generate new data is challenging and time consuming. Lastly, because much of this field is nascent and rapidly evolving, the companies participating are also rapidly changing, making tracking the field more challenging than more established industries.

China has a substantial industrial biotechnology sector, generating large volumes of bio-based products. The country boasts a large fermentation capacity, with an output of 24.3 million tons of bio-fermented

¹⁵⁹ "China Animal Vaccine Industry Report, 2016-2020," <https://www.researchandmarkets.com/reports/3746961>

¹⁶⁰ Hong-hai Xie and Geng-xin Wang, "Strength and Weakness of Animal Vaccine Industry in China," *Asian Agricultural Research* 2, no. 4 (2010): 27-33.

¹⁶¹ "China Animal Vaccine Industry Report, 2016-2020," <https://www.researchandmarkets.com/reports/3746961>

¹⁶² Biopharmaceutical production is sometimes considered part of industrial biotechnology, but in this report, it was included under medical biotechnology.

¹⁶³ "Bioeconomy Dashboard: Economic Metrics," Bioeconomy Capital, updated 2018, <http://www.bioeconomycapital.com/bioeconomy-dashboard/>

products in 2015.¹⁶⁴ Chinese sources have reported that the country produced the world's highest number of industrial biotechnology papers and patents in 2017.¹⁶⁵

Biofuel development is part of China's long-term energy plan to improve reliable access to energy sources and lower environmental impact. Fuel ethanol production was estimated at 3.55 billion liters in 2017, making China's the world's fourth largest producer of fuel ethanol, after the US, Brazil, and the EU. Fuel ethanol production in China is generally used for domestic fuel consumption, and import/export volumes are relatively low. While corn is currently a major feedstock, China is offering subsidies to shift toward cellulosic ethanol production.¹⁶⁶ Several projects funded under the 863 and 973 programs have been related to biofuels, including work on enzymes, processes, and feedstocks.¹⁶⁷

Industrial biotechnology can also be used to produce a wide variety of bio-based chemicals, from commodity to high-value products. Enzyme production is an important application, and approximately 50 Chinese companies were manufacturing enzymes in 2009.¹⁶⁸ China's industrial enzyme output reached 1.1657 million tons in 2014, but the global enzyme industry is dominated by a few large companies; Novozymes (Denmark) and Dupont (US) hold 44 percent and 20 percent of the market, respectively.¹⁶⁹ Other traditional fermentation products, including organic acids, amino acids, starches, and vitamins, have been produced in China for years and these areas of industrial biotechnology are well-developed.¹⁷⁰ For example, lactic acid is one of the major organic acids produced by fermentation in China, with an output over 180,000 tons in 2015.¹⁷¹ Biopolymer production has grown as well.¹⁷²

One of the major contributors to industrial biotechnology in China is the China National Cereals, Oils and Foodstuffs Corporation (COFCO), a state-owned enterprise and agricultural supplier. The COFCO Biochemical division has substantial corn processing capacity and produces a variety of bio-based chemicals as well as a large portion of the fuel ethanol in China.¹⁷³ Another contributor is Cathay Industrial Biotech, a private firm producing fatty acids, biobutanol, and specialty chemicals. Cathay Industrial Biotech has been a leader in China at bringing many of these products to commercial-scale production and has capabilities ranging from molecular biology to fermentation technology.¹⁷⁴

1.1.5.1. Synthetic Biology

Much of today's excitement regarding the role that biotechnology could play in the larger economy is due to the advent of the field of synthetic biology, which promises to add value beyond biopharmaceuticals, medicine and agriculture, because it has the potential to revolutionize processes in materials, information technology (IT), and fuels. Synthetic biology is the discipline entailing the design and construction of new biological systems or redesign of natural systems, with the overall goal of making biology more engineerable.¹⁷⁵ As synthetic biology is an emerging and cutting-edge area of biotechnology, development in this area may serve as an indicator of innovation in biotechnology. Specifically, the

¹⁶⁴ Ruiyan Wang et al., "Bioindustry in China: An overview and perspective," *New Biotechnology* 40(2018): 46-51.

¹⁶⁵ Sun Yusong, "The number of patents and papers in the field of industrial biotechnology in China ranks first in the world," *China Science and Technology Network: STDaily* November 7, 2017, www.stdaily.com/02/difangdongt/2017-11/07/content_593019.shtml [Chinese Language Source]

¹⁶⁶ Foreign Agricultural Service Staff, *China: Agricultural Biotechnology Annual*.

¹⁶⁷ Elizabeth Nesbitt, "Industrial biotechnology in China amidst changing market conditions," *Industrial Biotechnology* 5, no. 4 (2009): 232-36.

¹⁶⁸ *Ibid.*

¹⁶⁹ "Global and China Industrial Enzyme Industry Report, 2014-2017," Reportlinker, updated July 2, 2015, <https://www.prnewswire.com/news-releases/global-and-china-industrial-enzyme-industry-report-2014-2017-300108412.html>

¹⁷⁰ Matthew Chervenak, "Industrial biotechnology in China," *Industrial Biotechnology* 2, no. 3 (2006): 174-76.

¹⁷¹ China Research & Intelligence Co. *Research Report on Lactic Acid and Polylactic Acid (PLA) Industry in China, 2011-2020* Shanghai: China Research & Intelligence Co., 2016.

¹⁷² "Increase on Asian production capacities for bio-based chemicals, building blocks and polymers," Bio-based News, updated January 31, 2017, <http://news.bio-based.eu/increase-on-asian-production-capacities-for-bio-based-chemicals-building-blocks-and-polymers/>

¹⁷³ "COFCO Biochemical," COFCO Group, www.cofco.com/en/BrandProduct/COFCOBiochemical/

¹⁷⁴ "Products," Cathay Industrial Biotech, www.cathaybiotech.com/en/Product.aspx

¹⁷⁵ "What is synthetic biology?," Engineering Biology Research Consortium, <https://www.ebrc.org/what-is-synbio>

synthetic biology field of metabolic engineering, in which organisms are engineered for synthesis of new products using new biological pathways, enables the biological production of chemicals formerly made from plants or animals that were hard to cultivate, or were formerly made from petroleum. For example, an early synthetic biology success was the synthesis in yeast of the anti-malarial drug artemisinin, which was traditionally harvested from a tropical tree, complicating global supply. More recent advances include the industrial-scale production of spider silk, which promises the production of a new generation of ultra-strong, ultra-lightweight natural fibers.¹⁷⁶ Several companies are trying to leverage the tools of synthetic biology to engineer plants, fungi or algae to product gasoline or diesel.

China is interested in developing its synthetic biology capabilities and in the potential of this technology to facilitate economic development. Several organizations, including the Chinese Academy of Sciences (CAS), support synthetic biology research, and 260 million yuan (\$40.4 million) of the annual research budget is allotted to this field.¹⁷⁷ 250 million yuan (\$38.9 million) have been awarded to synthetic biology projects via the 973 program over several years.¹⁷⁸ Dedicated synthetic biology institutes include the CAS Key Laboratory of Synthetic Biology and the Tianjin Institute of Industrial Biotechnology. The CAS Key Laboratory of Synthetic Biology, established in 2008, is focused on basic research and platform technologies for synthetic biology and translation of research to application.¹⁷⁹ The Tianjin Institute of Industrial Biotechnology, a CAS research institute, works on synthetic biology for industrial bioproduction, with space dedicated to industrial enzymes, microbial manufacturing, and bioprocess engineering. This institute has a strong focus on technology transfer and holds cooperative relationships with many commercial enterprises.¹⁸⁰

While synthetic biology is an important emerging field, its nascency and reach across many industries make it difficult to track. It is difficult to discern exactly what role synthetic biology will play in the global biotechnology sector, and China's industry is no exception. In the years to come it will be important to follow development of this segment in China as it compares to the rest of the world.

1.2. China's Plans and Goals for Biotechnology

During the past four decades of economic reform, China has gradually moved from a Soviet-style planned economy toward a more market-oriented approach.¹⁸¹ However, it has not entirely "grown out of the plan" as central and local governments continue to rely on plans and government interventions for the allocation of resources in the economy. In addition to setting high-level development priorities through Five-Year Plans, governments continue to rely on plans to set goals for the development of specific industries and provide guidance for achieving those goals. In recent years, these efforts have increasingly focused on supporting China's transformation to a high-tech nation and fostering the development of specific technologies that were identified as strategic national priorities.¹⁸²

1.2.1. China's Science and Technology Programs

China has long invested in biotechnology, at least as early as the start of the High-Technology Research and Development Plan, which began in 1986. Also known as the 863 Program, this plan has been one of

¹⁷⁶ "Bolt Threads," <https://boltthreads.com/technology/microsilks/>

¹⁷⁷ Committee on Science Technology and Law et al., "Strategies for Advancing Synthetic Biology," in *Positioning Synthetic Biology to Meet the Challenges of the 21st Century: Summary Report of a Six Academies Symposium Series* (Washington, D.C.: National Academies Press, 2013).

¹⁷⁸ "The Rapid Growth of Synthetic Biology in China," Synbiobeta, updated May 24, 2016, <https://synbiobeta.com/rapid-growth-synthetic-biology-china/>

¹⁷⁹ "Key Laboratory of Synthetic Biology, CAS: Introduction," Shanghai Institute of Plant Physiology & Ecology, <http://www.sippe.ac.cn/klb/eindex.asp>

¹⁸⁰ E. J. Schrauwen et al., "Reassortment between Avian H5N1 and human influenza viruses is mainly restricted to the matrix and neuraminidase gene segments," *PLoS One* 8, no. 3 (2013): e59889.

¹⁸¹ Barry Naughton, *Growing Out of the Plan: Chinese Economic Reform, 1978-1993* (Cambridge University Press, 1996).

¹⁸² Tai Ming Cheung et al. *Planning for Innovation: Understanding China's Plans for Technological, Energy, Industrial, and Defense Development*: University of California Institute on Global Conflict and Cooperation, 2016.

China's major science and technology (S&T) programs. The plan specifies several sectors crucial to China's economic and national security, and biotechnology has been included since the program's inception. In recent years, funding for the project has been substantial; from 2009-2013 (the last year with available data), China spent over \$800 million per year on this program. Specific expenditures for biotechnology could not be determined.¹⁸³ The National Plan on Key Basic Research, also known as the 973 Program, is another major research program which started in 1997. Like the 863 Program, this program included specific sectors to fund. However, biotechnology is not specifically included (although health sciences is), and it is unclear how much biotechnology funding has come from the program. In 2013, China spent \$630 million on the 973 Program.¹⁸⁴

In February 2016, the Ministry of Science and Technology created a national key research and development (R&D) plan that encompasses those programs and others under a major program focused on vital fields of research, including agriculture, energy, environment, and health.¹⁸⁵ While the plan signifies a clear support for developing new technologies, no specific projects or amount of funding could be traced to this new plan.

1.2.2. The Strategic Emerging Industries Initiative

In 2010, China's State Council launched the Strategic Emerging Industries (SEI) Initiative, which identifies seven SEIs that the Chinese government feels are crucial to China's economic competitiveness: energy efficient and environmental technologies, next generation IT, biotechnology, high-end equipment manufacturing, new energy, new materials, and new-energy vehicles. Development of these sectors is prioritized, and specific milestones have been declared. For example, the State Council originally set a target for all SEIs to contribute eight percent of GDP by 2015 and 15 percent by 2020.¹⁸⁶ In 2016, the initiative was expanded to nine SEIs with the addition of the digital creative industry and related services.¹⁸⁷ The SEIs have also been incorporated into the 12th and 13th FYPs to facilitate implementation. These policies are discussed more below as they specifically relate to biotechnology.

1.2.3. The 12th and 13th Five-Year Plans

China's FYPs are government doctrines that shape the economic development of the country. While they generally outline broad economic goals, FYPs are often accompanied by a number of more specific development plans that direct their implementation.

The SEIs were included in the 12th FYP, which covers the years 2010-2015. The National Strategic Emerging Industry Development Plan accompanies the FYP and elaborates on specific goals for each of the SEIs. With respect to biotechnology, the Development Plan places a strong focus on the biomedical industry, biomedical engineering, agricultural biotechnology, and bio-manufacturing (i.e., industrial biotechnology). Within each of these fields, the plan puts forth major actions pertaining to the development of new technologies, building innovative capacity, and industrialization. Some notable actions include:

- Establishment of a national gene resource library;
- Implementation of genetic engineering drugs;
- Development of digital medical and telemedicine systems;

¹⁸³ Ibid.; Annual Report of the State Programs of Science and Technology Development (2014). Ministry of Science and Technology of the People's Republic of China.

¹⁸⁴ Annual Report of the State Programs of Science and Technology Development (2014).

¹⁸⁵ Xinhua News Agency, "China inaugurates national R&D plan," (2016), http://www.xinhuanet.com/english/2016-02/16/c_135104108.htm

¹⁸⁶ Decision of the State Council on Accelerating the Cultivation and Development of Strategic Emerging Industries (2010). State Council of the People's Republic of China.

¹⁸⁷ Strategic Emerging Industry Key Products and Services Guidance Catalog (2016). National Development and Reform Commission of the People's Republic of China.

- Implementation of projects to develop genetically modified organisms for cultivation;
- Building an information base for animal and plant genetic resources; and
- Support of advanced bio-manufacturing, including synthetic biology.

Likewise, the Bioindustry Development Plan, released in 2012, highlighted the sectors of biomedical industry for development, including biotechnology drugs, pharmaceuticals, and traditional Chinese medicine; biomedical engineering; bio-agriculture; bio-manufacturing; bioenergy; bio-environmental protection; and biological services. The plan presents the annual output values each sector is expected to reach in 2015.¹⁸⁸

The Ministry of Agriculture also released, in 2011, the 12th FYP for Development of Agricultural Science and Technology (Agricultural S&T Plan), which provides more details on the development of agricultural S&T. In this plan, the MOA proposes to strengthen research involving GM organisms. Major research projects on breeding new varieties of GM organisms will continue to be carried out in the 2011–2015 period, according to the Agricultural S&T Plan. The plan also incorporates biosafety assessment and management as focus areas of biotech industry development.¹⁸⁹

The 13th FYP lays out the vision of China's development over the years 2016-2020 and continues a theme of innovation as key to China's growth. In it, goals for development of the biotechnology industry—an SEI—are provided, including the wide application of genomics; large-scale development of personalized medicine and new drugs; and the creation of gene and cell banks.¹⁹⁰ As part of the 13th FYP, the Ministry of Science and Technology released a Biotechnology Development Plan which provides several goals and milestones to achieve with respect to China's biotechnology industry by 2020:¹⁹¹

- **Enhance originality of biotechnology.** The plan directs the Chinese biotechnology industry to focus on developing new technologies and products, as opposed to the current widespread activities of biomanufacturing existing products and non-innovative add-ons, such as biosimilars. The mandate includes goals of developing 20-30 leading new technologies, 30-50 major strategic new products, and 5-80 key application-critical technologies.
- **Create a biotechnology innovation platform.** To accelerate the industrialization of biotechnology, the plan promotes construction of biotechnology innovation centers focusing on green biomanufacturing, innovative drug R&D, and biomedical engineering. It also directs the construction of a national bioinformatics center, a human genetic resource bank, and other infrastructure to support biological and medical big data.
- **Strengthen the industrialization of biotechnology.** The plan states an intent to improve the biotechnology transfer service system through construction of biotechnology transfer and transformation centers. It instructs China to accelerate the construction of biotechnology specialized high-tech parks, including building 10-20 biopharmaceutical specialty parks and 5-10 bio-manufacturing specialty parks, each with an output value of over 10 billion yuan.

The 13th Five-Year Bioindustry Development Plan, released in 2016, sets additional goals for the biotechnology industry. Sector-specific goals for 2020 include an output of 4.5 trillion yuan (\$700 billion) for the pharmaceutical and biologics industries, an output of 1 trillion yuan (\$156 billion) for bio-agriculture (a designation that includes a variety of products, from biopesticides to veterinary drugs), and an increase in bio-based manufacturing such that bio-based products account for one quarter of chemical production.

¹⁸⁸ Bioindustry Development Plan (2012). [Chinese Language Source]

¹⁸⁹ "Restrictions on Genetically Modified Organisms: China," Library of Congress, updated June 9, 2015, <https://www.loc.gov/law/help/restrictions-on-gmos/china.php>

¹⁹⁰ "Outline of the Thirteenth Five-Year Plan for National Economic and Social Development of the People's Republic of China," People's Republic of China, updated March 17, 2016, http://www.gov.cn/xinwen/2016-03/17/content_5054992.htm [Chinese Language source]

¹⁹¹ Ministry of Science and Technology of the People's Republic of China. '13th Five-Year' Biotechnology Innovation Special Plan 2017. [Chinese Language Source].

The plan states that the scale of China's biological industry should reach 8 to 10 trillion yuan (\$1.2 to \$1.6 trillion) by 2020.¹⁹²

1.2.4. Made in China 2025

Made in China 2025 is an overarching government strategy document that outlines China's plan to become a powerhouse in high-tech and high-value industries, such as robotics, advanced IT, aviation, and new energy vehicles, plus biopharmaceuticals and other medical technologies. In the section discussing biopharmaceuticals and high-performance medical equipment, the Made in China 2025 plan identifies the types of medical products and technologies that China intends to develop. These include biologic-based therapeutics, such as antibody drugs, antibody-drug conjugates, new structural proteins, polypeptide drugs, and new vaccines; technologies to support individualized drug treatments (i.e., precision medicine); and breakthrough technologies, such as induced pluripotent stem cells. In addition, the plan calls for increasing the domestic market share of Chinese companies in several industries, including biotechnology. The market share goal for biopharmaceutical core components—which may encompass biopharmaceuticals as well as traditional pharmaceuticals—is 70 percent by 2020; for advanced medical devices (again, only some of which will be biotechnology), the goal is 50 percent, then 70 percent by 2025, and 90 percent by 2030.¹⁹³ Additional goals for China's biopharmaceutical and advanced medical devices industries have since been announced in the Made in China 2025 Key Area Technology and Innovation Greenbook – Technology Roadmap (2017). The roadmap includes specific goals for licensing of 3-5 new biotech drugs and their companion diagnostic reagents in advanced economies by 2020 plus commercialization of 30-35 innovative drugs (of all types) by 2025 as well as a broader goal of achieving world-class innovation capacity, production volume, and international competitiveness in pharmaceuticals by 2025.¹⁹⁴

Made in China 2025 emphasizes a strategy of using international resources to further the advancement of China's own industries. The concepts of "opening-up," "going-out," and "bringing-in" are highlighted as ways to utilize international expertise for the benefit of Chinese institutions. Opening-up refers to the economic reform of China that was introduced by Deng Xiaoping, former Vice Chairman of the Chinese Communist Party, and opened the country to foreign investment. Going-out and bringing-in are complementary strategies that encourage both outward and inward foreign investment. Made in China 2025 specifically targets foreign capital as a mechanism to increase investment in Chinese technology companies, including biotechnology, and then broaden their international footprint. Strategies presented in the document include encouraging foreign capital to invest in high-end manufacturing, such as next generation IT, high-end equipment, new materials and bio-pharmaceuticals; encouraging foreign enterprises and research institutions to establish global research institutions in China; and supporting legible enterprises to issue stock and bonds overseas and to carry out technology cooperation with foreign enterprises.

1.2.5. Talent Programs

In addition to directly funding targeted research programs and initiatives, the Chinese government funds a variety of so-called talent programs, which provide large financial incentives, including relocation costs, salaries, and startup funding for Chinese researchers who went abroad for training to return to China. In addition, several of these government programs also recruit leading foreign researchers from the US and other research-focused countries. The major national level government talent programs include the Thousand Talents Program, Hundred Talents Program, and the National Science Fund for Distinguished Young Scholars, which have recruited or repatriated tens of thousands of individuals to China. Hundreds

¹⁹² National Development and Reform Commission of the People's Republic of China, '13th Five-Year' Bioindustry Development Plan. [Chinese Language Source]

¹⁹³ Chinese Academy of Engineering, Expert Commission for the Construction of a Manufacturing Superpower, "Made in China 2025 Key Area Technology Roadmap," 2015, <http://www.cae.cn/cae/html/files/2015-10/29/20151029105822561730637.pdf> [Chinese Language Source]

¹⁹⁴ National Strategic Advisory Committee on Building a Strong Manufacturing Nation, *Made in China 2025 Key Area Technology and Innovation Greenbook – Technology Roadmap (2017)*, 2018. [Chinese Language Source]

more programs exist at the local government level as well. A more thorough discussion of China's talent programs can be found in Section 4.2.1).

As a top research location, the US does not experience a significant loss of research talent, and hence does not invest as heavily in retainment programs as China does. Additionally, no programs provide competing incentives to retain foreign-born researchers that may be wooed to China by their talent programs. The US does sponsor various work and training programs, though. The primary policy to retain foreign-born undergraduate and graduate students training in the US is the Optional Practical Training, which allows graduates on student visas to remain in the US for an additional period of time (12 months plus the possibility of extensions for those completing Science, Technology, Engineering, and Math [STEM] degrees).¹⁹⁵

1.2.6. Biotechnology Parks

A major strategy utilized by China to advance its biotechnology industry is building biotechnology parks. These large campuses are designed to collocate high-tech companies and are built around a common theme, such as biopharmaceuticals or nanotechnology. In addition to nationally created parks, nearly every province has a number of local bioindustry parks.¹⁹⁶ Over 100 national level high-tech and economic industrial parks involving biotechnology and more than 400 provincial level biotech industrial parks exist across China so far.¹⁹⁷ Individual parks have also expanded to form greater biotechnology networks. By 2010, three major clusters of comprehensive biological industry parks were established in the Yangtze River Delta, Pearl River Delta and Beijing-Tianjin-Hebei region.¹⁹⁸ These parks provide infrastructure, talent pools, and business support for multiple collocated companies. For example, Suzhou Biobay in the Yangtze River Delta, provides nanotechnology service platforms for 51 companies, as well as offering support with regulatory filings and financing.¹⁹⁹

The Chinese government at both the national and provincial levels has invested building biotechnology parks with the aim of developing major innovation hubs. Funds are provided by the national government, which are used to fund national biotechnology parks as well as transferred to provincial governments and used to create provincial parks. In our investigation however, these parks often fail to accomplish their goal of sparking innovation hubs in part due to the sheer number of them in simultaneous operation. Typically, governments allocate funding and construct the parks with the hope of later filling them with high-quality tenants. However, because the high-level of funding has generated a large number of parks and because these parks are geographically dispersed, companies and talented researchers also become dispersed and fail to attain the critical mass necessary to ignite and sustain innovation.

In contrast, the US tendency to let hub regions emerge organically provides several advantages over the Chinese state-managed approach. First, with limited state support and subsidies, companies have no national financial incentive to locate in a specific region and instead are likely to follow their own interests by locating where existing talent is already high, naturally assembling a small number of innovation centers. Once nucleated, by having only a few hubs each containing many companies, the higher concentration of talent at these hubs both drive innovation and naturally attracts additional participants to these hubs. Often, because of the organic nature of their development and the federal government support for technology transfer from academia into industry (through programs like SBIR²⁰⁰), these hubs

¹⁹⁵ "Optional Practical Training Extension for STEM Students (STEM OPT)," U.S. Citizenship and Immigration Services, updated 08-17/2018, <https://www.uscis.gov/working-united-states/students-and-exchange-visitors/students-and-employment/stem-opt>

¹⁹⁶ China Industry Research. *China Biomedical Industrial Park Industry Status Analysis and Market Forecast Report* Beijing: China Industry Research Network, 2017. [Chinese Language Source]

¹⁹⁷ Shenzhen Huada Gene Research Institute. *Shenzhen International Life Sciences. Bio-industrial park: Strategic Research* Shenzhen: Shenzhen Huada Gene Research Institute, 2013. [Chinese Language Source]

¹⁹⁸ H. Hu and C. C. Chung, "Biopharmaceutical Innovation System in China: System Evolution and Policy Transitions (Pre-1990s-2010s)," *Int J Health Policy Manag* 4, no. 12 (2015): 823-9.

¹⁹⁹ Aishwarya Venkatesh, "Asia's prominent biotech parks," *BioSpectrum*(2015), <https://www.biospectrumasia.com/analysis/26/7280/asias-prominent-biotech-parks.html>

²⁰⁰ The SBIR, or Small Business Innovation Research Program (<http://www.sbir.gov>) is a competitive award program that issues grants to small businesses to engage in R&D that has the potential for commercialization. SBIR grants, which are multi-part

are often collocated and intertwined tightly with top research universities leading their respective fields. For example, Silicon Valley was sparked by nearby University of California (UC) Berkeley and Stanford, two early players in computer engineering and science, and the recent trend toward biotechnology in the same region was driven by the combination of UC Berkeley, UC San Francisco, and Stanford, all early leaders in molecular biology and recombinant DNA and currently national leaders in synthetic biology. The simultaneous combination of competition and collaboration combined with a high density of high-level talent, and ingenuity has proven a successful recipe to drive innovation.

1.2.7. Local level Policies

Numerous Chinese provincial and municipal governments have published responsive guidelines and policies consistent with the 13th FYP, including Shanghai,²⁰¹ Beijing,²⁰² Tianjin,²⁰³ Shandong,²⁰⁴ Shaanxi,²⁰⁵ Yunnan,²⁰⁶ Gansu,²⁰⁷ and Wuhan.²⁰⁸ We highlight the plans of Tianjin and Shanghai—two major biotechnology areas in China—below.

In the Tianjin Industrial and Economic Development 13th FYP, the biotechnology and healthcare industry is one of eight industries prioritized for development. The goal is to achieve an industry value of 200 billion yuan (\$31.1 billion) by 2020 and to have more than 120 products with sales of more than 100 million yuan (\$15.6 million).²⁰⁹ Achieving these targets would make Tianjin one of the largest national biomedical innovative hubs. The Tianjin plan specifically lists goals for biopharmaceuticals, biomanufacturing, and agricultural biotechnology. It stressed the importance of R&D for three segments of medical technology (biologics, drug development, and medical devices) and for product development and industrialization in biomanufacturing and agricultural biotechnology. In terms of supporting policies, the plan listed seven major ways to help achieve the goals, including attracting overseas talents, improving access to financial services, and setting up special funds.²¹⁰

In response to the State Council's Guidance on Pharmaceutical Industry Development,²¹¹ the Shanghai Municipal Government issued a policy in April 2017 advocating to "maintain the lead" in biomedical

awards granted in phases, represent a key source of non-dilutive funding for new startups (i.e., SBIR awardees need not grant ownership shares to the funder [in this case, the Federal government] as a condition of funding, as is typical of venture capital). The Small Business Administration oversees the SBIR program, but individual departments and agencies offer their own SBIR programs, tailored toward the commercialization of technology within each entity's mission area.

²⁰¹ Shanghai Municipal Government, "Shanghai Technology Innovation 13th Five-year Plan," August 5, 2016, <http://www.shanghai.gov.cn/nw2/nw2314/nw2319/nw12344/u26aw48459.html> [Chinese Language Source]

²⁰² Beijing Municipal Government, "Beijing Comprehensive Plan to Enhance Building of National Technology Innovation Center," (2016), <http://zhengwu.beijing.gov.cn/gh/dt/t1453823.htm> [Chinese Language Source]

²⁰³ Tianjin Municipal Government, "Tianjin Industrial and Economic Development 13th Five-Year Plan," June 12, 2017, http://fzgg.tj.gov.cn/zwgk/fzgh/zxgh/201706/t20170612_65830.shtml [Chinese Language Source]

²⁰⁴ Shandong Provincial Government, "Shandong Economy and Social Development 13th Five-year Plan," 2016, <http://www.sdaep.cn/uploadfile/2017/0606/20170606012830770.pdf> [Chinese Language Source]

²⁰⁵ Shaanxi Provincial Government, "Shaanxi Strategic Emerging Industrial Development 13th Five-year Plan," September 2016, <http://www.fortsteuben.com/uploadfiles/files/2016091917055613.pdf> [Chinese Language Source]

²⁰⁶ Yunnan Provincial Government, "Yunnan Technology Innovation 13th Five-year Plan," January 23, 2017, <http://www.ynstc.gov.cn/sswzfzgh/201701230002.htm> [Chinese Language Source]

²⁰⁷ Gansu Provincial Government, "Gansu Technology Innovation 13th Five-year Plan," (2016), http://www.gansu.gov.cn/art/2016/11/1/art_4747_289849.html [Chinese Language Source]

²⁰⁸ Wuhan Municipal Government, "Wuhan Technology Innovation 13th Five-year Plan," December 22, 2016, http://www.wh.gov.cn/hbgovinfo_47/szfggxml/gzghjh/gmijhshfzgh_2954/201701/t20170105_97589.html [Chinese Language Source]

²⁰⁹ Tianjin Municipal Government, "Tianjin Industrial and Economic Development 13th Five-Year Plan," http://fzgg.tj.gov.cn/zwgk/fzgh/zxgh/201706/t20170612_65830.shtml [Chinese Language Source]

²¹⁰ There are seven supporting policies in the 13th FYP for all of the strategic industries, not only biotechnology: (1) attracting more central and local financial support to build the industrial investment fund for Tianjin's advanced manufacturing; (2) government investment to form an industrial cluster; (3) securing natural resources, upgrading industrial structure, improving consumption efficiency, and replacing coal use with clean energy; (4) supporting talents development through vocational training and overseas talents; (5) improving production safety standards; (6) reducing governmental intervention in business operation; and (7) bettering government's organizational role in overall economic development and implementing central policies. *Ibid.*

²¹¹ "The Pharmaceutical Industry Development Planning Guide was officially released," Ministry of Industry and Information Technology of the People's Republic of China, updated November 7, 2016, <http://www.miit.gov.cn/n1146290/n4388791/c5343514/content.html> [Chinese Language Source]

innovation nationally; to achieve 380 million yuan (\$59.1 million) of primary business; to form a center for advanced R&D, manufacturing, outsourcing and services in the Asia Pacific region; and to form a modern supply chain of global biomedical products.²¹² Earlier, in August 2016, the Shanghai Municipal Government published the Shanghai Technology Innovation 13th FYP, which identifies major focused subjects, including brain science and artificial intelligence, gene, stem cells, nanotechnology, biochemical science, biological sensors, urban agriculture, and new drugs R&D. The plan also provides goals to strengthen and improve international technological cooperation, presence, and influence as well as to support Shanghai companies to carry out outbound investments and set up research centers.²¹³ In the follow-up implementation guidance published in 2017, Shanghai specified five key areas as developmental priorities: drug development and innovation, bioproducts manufacturing, contract research activities, global supply chain building, and biotech industrialization. The corresponding supporting policies included improving financial support, setting up biopharmaceutical industry special funds, encouraging R&D financing, and improving intellectual rights protection.²¹⁴

1.3. Comparison of Chinese and US Biotechnology Programs

1.3.1. Comparison of Industrial Policies

The US does not produce overarching industrial policies like Made in China 2025 or the FYPs, but it does have some strategy documents that identify specific goals for S&T, including biotechnology. The Strategy for American Innovation, released originally in 2009 with revisions in 2011 and 2015, is a primary example of these policies. The strategy presents an overview of recommendations and initiatives to improve innovation in the United States, focusing on federal investment in R&D and highlighting areas of priority.²¹⁵ The strategy points to nine areas in need of development in order for the US to remain at the forefront of innovation, including advanced manufacturing, precision medicine, clean energy, and high-performance computing.

In 2012, the US also released the National Bioeconomy Blueprint, which highlighted the importance of biotechnology to the US economy and offered strategies for strengthening R&D, advancing research into commercial products, reducing regulatory barriers, creating a skilled workforce, and fostering public-private partnerships.²¹⁶ Since its release, however, we have seen little to no implementation of the ideals promoted therein. Both the National Bioeconomy Blueprint and the Strategy for American Innovation are intended to highlight the importance of science and technology to US economic prosperity, but do not provide funding or offer specific directives to US government agencies. Such policies, therefore, do not have the authority of Made in China 2025 and the 13th FYP; truthfully, no strategy or policy of the US or any market economy can direct an industry as comprehensively and directly as China and its state-controlled economy.

1.3.2. Comparison of Biotechnology Spending

Though detailed data on actual levels of Chinese government spending on biotech are lacking, examples from policies show the amount of support China plans to put into biomedical research. The Chinese government invested in stem cell research under both the 12th FYP (2 billion yuan, or \$311 million) and the 13th FYP (2.7 billion yuan, or \$420 million).²¹⁷ China also launched its own precision medicine initiative

²¹² "Interpretation of the 'Guiding Opinions on Promoting the Healthy Development of Biomedical Industry' in Shanghai," Shanghai Municipal People's Government, updated August 30, 2017, <http://www.shanghai.gov.cn/nw2/nw2314/nw2319/nw41893/nw42228/u21aw1253320.html> [Chinese Language Source]

²¹³ Ibid. [Chinese Language Source]

²¹⁴ Ibid. [Chinese Language Source]

²¹⁵ National Economic Council and Office of Science and Technology Policy. *A Strategy for American Innovation: Securing Our Economic Growth and Prosperity* Washington, D.C.: Executive Office of the President 2015.

²¹⁶ The White House. *National Bioeconomy Blueprint* Washington, D.C. 2012.

²¹⁷ Asian Technology Information Program. *Genome Editing Technology in China* Albuquerque, NM: Asian Technology Information Program, 2016.

as part of the 13th FYP, with an expected 60 billion yuan (\$9.3 billion) in funding over 15 years.²¹⁸ One analysis estimates that the Chinese government spends over \$600 million annually on biotech R&D.²¹⁹

The US government has countless individual, topic-specific programs to spur innovation and technology development (e.g., the National Institutes of Health (NIH)-funded BRAIN initiative to improve conditions like Alzheimer's and autism with around \$300 million in annual funding). One of the largest programs is the Precision Medicine Initiative (now called All of Us), which launched in 2015 with a budget of \$215 million in its first year and almost \$1.5 billion authorized by Congress over the program's 10-year span.²²⁰ In the 2015 fiscal year (FY), the US government obligated a total of \$63.6 billion in federal funding across all science and engineering fields; this level of funding has been relatively consistent since approximately 2010.²²¹

Though teasing out biotechnology-specific funding is exceptionally challenging due to mismatches between funding lines and various definitions of biotechnology, overall life science spending figures are available. In federal FY 2015, the US government obligated \$30.5 billion to the life sciences out of the \$63.6 billion for all science and engineering.²²² Of the total for the life sciences:

- \$1.3 billion was attributable to agricultural sciences;
- \$14.8 billion to general biological sciences;
- \$0.8 billion to environmental sciences;
- \$10.9 billion to medical sciences; and
- \$2.6 billion to other life sciences.²²³

Of those categories, agricultural sciences, general biological sciences, and medical sciences likely encompass the majority of biotechnology spending, though biotechnology may only be a fraction of that total. Of US government agencies, the largest contributors to life science spending were the Department of Health and Human Services (HHS) (\$25.1 billion), US Department of Agriculture (USDA) (\$1.8 billion), Department of Defense (\$0.8 billion), and National Science Foundation (NSF) (\$0.7 billion).²²⁴

Perhaps more notable than the single year numbers is the overall downward trend in US federal life science funding. In constant 2009-dollar terms, total life science R&D obligations peaked in 2010 at \$33.6 billion and have declined since, to \$27.7 billion in 2015 (an 18 percent drop).²²⁵ The trend in all life science subcategories, as well as across all science and engineering fields (i.e., physical sciences, engineering, social sciences, life sciences, etc.), is similar. Given that US spending is declining yet the biotech industry is expanding, US researchers may turn to China to fund their work. In addition, this slow decline in R&D funding opens a window for other nations, including China, to compete with the US; given China's continued trend in increased R&D spending and the growth of their biotech industry, China appears to be attempting to capitalize.

1.4. Outlook

Overall, predicting the future of a sector such as biotechnology that is full of rapidly evolving, emerging technologies is fraught with uncertainty. The applications of CRISPR surprised nearly everyone, both with

²¹⁸ Pearl Liu, "China initiative would pour billions into precision medicine," *BioWorld* July 17, 2018, <http://www.bioworld.com/content/china-initiative-would-pour-billions-precision-medicine-0>

²¹⁹ World Health Organization, *China policies to promote local production of pharmaceutical products and protect public health*.

²²⁰ The White House. *FACT SHEET: President Obama's Precision Medicine Initiative* Washington, D.C.2015. ; Megan Molteni, "The NIH Launches Its Ambitious Million-Person Genetic Survey," *Wired*(2018)

²²¹ National Science Board, *Science and Engineering Indicators*. [Appendix Table 4-25]

²²² *Ibid.* [Figure 4-12]

²²³ *Ibid.* [Appendix Table 4-25]

²²⁴ *Ibid.* [Appendix Table 4-24]

²²⁵ *Ibid.* [Figure 4-9; Appendix Table 4-24]

the discovery and with the explosive speed it spread through the global biotechnology community, enabling new lines of basic research and the development of new therapies barely imagined prior to its emergence. This type of basic technological surprise, like the prior discoveries of recombinant DNA and polymerase chain reaction (PCR) years prior, is likely to continue, making the development of biotech unpredictable. At the same time, policies that favor one technology or set of applications over another can significantly influence sector development. Despite these challenges that confound predictions even for the US biotechnology sector, some forecasting can be done.

Given the recent trend in development, China will likely continue to grow and expand its national capacity in medical biotechnology, especially in biologics, genomics, and molecular diagnostics. China has steadily grown capacity in these sub-sectors over the past several years and is continuing to make significant investments in related US firms (see Chapter 3). Growing this capacity would align with China's stated policies. For example, the Made in China 2025 policy mentions medical biotechnology several times, including identifying the subsector as strategic.²²⁶ Additionally, the 13th Five-Year Bioindustry Development Plan, which speaks broadly about technologies across biotech, calls for China to begin to lead instead of follow in biomedical technology by 2020.²²⁷ China's growing wealth and burgeoning middle class, combined with an aging population, may drive domestic demand for the applications of these segments. The US still holds a comparative lead in medical biotechnology, but China is becoming more competitive and showing signs of leading-edge innovations in genomics and biologics. China is also largely on-par with the US within CAR-T development, demonstrating their biotechnology sector can keep pace and develop applications in the newest technology areas.

China's agricultural biotechnology sector appears ripe for a potential rapid expansion. Currently, Chinese policies and the opinions of their population largely prevent commercialization of technology, both foreign and domestic, in this area. However, despite significant regulatory and public perception barriers to commercialization, China is undertaking significant basic research in this area. If policies change—and whether they will is uncertain—China may see an agricultural biotechnology boom as research begins to commercialize. However, the US will likely remain the leader in this area for the foreseeable future due to its massive and decades-long head start.

Industrial biotechnology is murky and poorly tracked (by everyone, including in the US), making predictions difficult. However, the limited investments made by China in this area (see Chapter 3) compared to others may indicate it is less of a focus. The major global commercial players in this sub-sector are outside China and hold significant proprietary knowledge advances that limit other firms' ability to compete. In addition, many of the most innovative ideas within this sub-sector are at the true leading-edge of biotechnology and require teams replete with world-class expertise to initiate and execute them. While China may not have this level of expertise, they do have synthetic biology research ongoing and maintain large (if not the largest globally) fermentation capacity, indicating they have some of the necessary pieces to compete in this sub-sector. China growing in this area may require developing other pieces of the innovation pipeline. Though the future of this sub-sector is particularly difficult to discern, efforts to track both American and Chinese activity will likely reveal a change in the state of play long before US leadership is lost.

Several factors may help continue the upward trend in China's biotechnology industry, from R&D expenditures to regulatory barriers. While China's \$600 million in annual government funding of biotech R&D is small compared to the \$30 billion spent by the US, total expenditures (including those in the private sector) on science and engineering research are nearly equivalent between the two countries.²²⁸ The US maintains a superior biotechnology innovation capacity including world-class research training, but China is also attempting to benefit from that through its talent recruitment programs. As federal spending on research is declining in the US, researchers may seek funding from other sources, including China, or may be tempted to emigrate there (or repatriate) in search of better opportunities. While China's

²²⁶ State Council of the People's Republic of China. *Made in China 2025* Beijing2015. [Chinese Language Source]

²²⁷ National Development and Reform Commission of the People's Republic of China, '13th Five-Year' *Bioindustry Development Plan*. [Chinese Language Source]

²²⁸ World Health Organization, *China policies to promote local production of pharmaceutical products and protect public health.*; National Science Board, *Science and Engineering Indicators*.

biotechnology industry is still far smaller and less mature than the US industry, these conditions may enable that gap to lessen. The simplest and perhaps most effective way to prevent that from happening is for the US to significantly increase (or at the minimum maintain) federal spending on R&D in biotechnology and related fields.

In addition, regulations in China for biotechnology products may favor Chinese developers and producers. China's regulatory policy for biologics reduces the market protections new products receive if they are first submitted for approval outside of China, with further reductions if the applications rely on data not collected in China. These regulations obviously aid Chinese developers of biopharmaceuticals, but could also cause multi-national biopharmaceutical companies to prioritize China as a first market of entry, especially considering the high market potential in China due to their enormous and aging population. This could cause a delay in marketing of needed biologics in the US and elsewhere, but could also be a boon to Chinese CMOs and CROs due to the heightened value of studies conducted in China. Similarly, in the agricultural biotechnology segment, China's prohibition on foreign investment in GM crop technology may give a boost to Chinese companies, especially now that global agribusiness Syngenta is Chinese-owned. However, due to limited commercial activity in this segment outside of Syngenta, the regulations may instead serve to stifle innovation and advancement of China's agricultural biotechnology industry.

While it appears the Chinese biotechnology industry may continue its upward trajectory, the US maintains a substantial lead in both volume of activity and quality of innovation. The gap between the two countries may shrink, but continued prioritization of and investment in the domestic biotechnology industry should be sufficient for the US to maintain its global dominance in the sector. China does maintain some policies and regulatory practices that disadvantage foreign companies, but recent reforms have brought other regulations more in line with global norms. External pressure from the US and others may help China to continue that trend.

2. The Role of Foreign Firms and Technologies in China's Biotechnology Development

Key Findings

- **The development of China's biotechnology sector is closely tied to interaction with foreign entities.** Initially this interaction was limited to inward foreign direct investment (FDI) but in the past decade it has been characterized by two-way flows in all investment channels, including greenfield investments, venture capital (VC), and other portfolio investments.
- **Of all inward channels, FDI has likely contributed the most to the development of China's biotech industry, but VC is increasingly present.** The establishment of operations on the ground in China through FDI provides foreign operators opportunities for transfer of IPR, integration into global supply chains, and overall sharing of expertise and practices. The most common type of FDI in China, acquisitions and greenfield investments, peaked in the mid-to-late 2000s. 84 percent of the 236 foreign M&A transactions in the Chinese pharmaceuticals and biotechnology industries since 2000 occurred in 2003-2011, and 78 percent of greenfield investment occurred after 2008. Inbound VC saw modest activity starting in 2007, averaging 5.6 funding rounds and \$140 million per year until a sharp increase to over 15 rounds and \$590 million per year from 2015-2017.
- **Only in the past decade have outbound Chinese acquisitions, greenfield FDI and venture capital become important channels of interaction.** Chinese outbound investment in the pharmaceuticals and biotech sector took off quickly starting in 2014, reaching over \$1.5 billion in 2015 and over \$3.5 billion in 2017, driven by Chinese companies positioning themselves for growth in the global and Chinese markets. Chinese VC in the global biotech industry has been steadily increasing since 2013, reaching a record of 53 funding rounds with a total value of \$3.8 billion in 2017 alone. Most Chinese cross-border activity in biotech is concentrated on North America and Europe, as well as a few countries in Asia (Singapore) and Oceania (Australia).
- **Non-investment channels have become important means to access foreign technology and know-how.** Use of foreign licensing and patents was limited in the past but has increased in the last five years, although obscure legal structures and the lack of disclosure requirements globally make a thorough assessment of these relationships complicated. Overseas training of Chinese students and researchers and their repatriation to China—through explicit government directives such as the Thousand Talents Program—is a channel that has become increasingly important in the past decade. Chinese entities have also been identified as major perpetrators of espionage and other illicit or criminal activities to obtain technology and know-how, however without access to classified or private information, it is difficult to draw conclusions about the role of government in these activities or extent these activities have contributed to the competitiveness of Chinese biotech firms.
- **Globally, there is a lack of coordination on regulating foreign investments, and no efforts to focus on biotechnology specifically.** Most nations with whom China has built extensive biotechnology ties have traditionally followed liberal economic policies that limit government intervention to a minimum, for example screening of M&A for national security risks and competition concerns and control of dual-use technology.

This chapter provides an overview of how cross-border investment and other modes of international economic and social interaction have impacted the development of China's biotechnology industry. Due to the limitations of available data, we use more aggregate data that does not only include biotechnology transactions (meeting our narrow definition) but also transactions in traditional pharmaceuticals. Thus, the data we use in this chapter are broader than our dataset in Chapter 3, which only includes narrow

biotechnology transactions and transactions in pharmaceuticals that have a confirmed biotech component.

2.1. Foreign Investment in China

Opening up to foreign investment has been one of the cornerstones of Chinese reforms since 1978 and has allowed for the transfer of both technology and knowledge to China.²²⁹ The three major channels for the inflow of foreign capital to China are direct investment, overseas listings of Chinese companies, and portfolio investment (most importantly VC). All three channels have played a role in the development of China's biotech industry, which is detailed in the following sections.

2.1.1. Direct Investment

Foreign direct investment is a type of cross-border investment that establishes a lasting interest in an overseas business. A direct investment creates a strategic long-term relationship that usually gives the investor a significant degree of influence in the management of the direct investment enterprise. In internationally recognized standards, the "lasting interest" is usually defined by a minimum threshold of at least 10 percent of equity or equivalent voting power of the direct investment enterprise.²³⁰ Of all inward channels, FDI has likely contributed the most to the development of China's biotech industry. The establishment of permanent, foreign-owned operations on the ground in China provides opportunities for transfer of IPR, integration into the global supply chains, and overall sharing of expertise and practices. Chinese government policies are supportive of inbound FDI and the biotech industry is on the encouraged list of the Chinese government's Catalog of Industries for Guiding Foreign Investment.²³¹

The future of FDI in China's biotech sector will depend on several factors. First, foreign firms will consider investments based on market potential in China, thus the actual and anticipated growth will be a critical determinant. Ample opportunity for growth remains but so do uncertainties about China's economic outlook.²³² Second, as firms face the choice between greenfield and M&A, company valuations in China will be important. Currently, Chinese biotech firms have very rich valuations compared to other markets, which makes acquisitions less attractive and would speak for further expansions of greenfield facilities instead. Finally, the Chinese policy environment for inbound FDI—both in terms of formal restrictions on foreign M&A as well as informal discrimination and policies related to the business environment in general—will shape foreign investor appetite for FDI in China's biotech sector.

2.1.1.1. Mergers & Acquisitions

The first major mode of direct investment we discuss is M&A, which are transactions in which a foreign entity or individual purchases a stake in or merges with an existing Chinese entity. Data coverage for global M&A transactions is generally comprehensive since there are several professional data providers. We identified 236 foreign M&A transactions with stakes of 10 percent or more in the Chinese pharmaceutical and biotech industries since 2000, with a combined value of \$6.2 billion (Figure 2-1). Instead of narrowly considering biotechnology deals, we defined a broader sample of "pharmaceuticals and biotechnology" transactions because most transactions in the pharmaceutical industry may involve a biotechnology component, and it can be difficult to separate the two. A preliminary analysis suggests wholly biotech deals account for about 30 percent of the 236 transactions in this sample.

More than half (53 percent) of transactions in this broader sample occurred in the period of 2003-2011. This activity was driven by bullishness of foreign firms about the Chinese market, reasonable valuations,

²²⁹ Barry J. Naughton, "Foreign Investment," in *The Chinese Economy: Transitions and Growth* (Cambridge, MA: MIT Press, 2006).

²³⁰ IMF Multimedia Services Division, *Balance of Payments and International Investment Position Manual*, Sixth ed. (Washington, D.C.: International Monetary Fund, Publication Services, 2009).

²³¹ The 2017 version of the Catalog is available at <http://www.ndrc.gov.cn/zcfb/zcfbl/201706/W020170628553266458339.pdf>

²³² Rhodium Group, China Dashboard: Tracking China's Economic Reform Program. <https://rhg.com/impact/china-dashboard/>

and a relatively open political environment for foreign acquisitions.²³³ The prospects of a fast-growing Chinese market have impelled many foreign companies to acquire local operations in China to get a head start and to circumvent formal and informal restrictions on foreign enterprises. Mid-sized deals below \$1 billion such as Cardinal Health's 2010 acquisition of Zuellig Pharma China for \$470 million, Nycomed's acquisition of a majority stake in Guangdong Techpool Bio-Pharma for \$210 million, and PerkinElmer's acquisition of SYM-BIO Lifescience for \$63 million largely accounted for this trend.

From 2010-2016, the number of deals declined as valuations increased and foreign firms became more cautious about formal and informal operational barriers in the Chinese market.²³⁴ This trajectory is similar to foreign M&A patterns in other industries.²³⁵ In 2017, foreign M&A investment in the Chinese biotech and pharma industry rebounded to 10 transactions worth \$1.5 billion, which is the biggest annual value of the past two decades. This largely reflects several large transactions including German life science company Bayer AG's \$587 million acquisition of Dihon Pharmaceutical Group and Australia's biotherapy company CSL's \$350 million acquisition of an 80 percent stake in Wuhan Zhongyuan Ruide Biological Products.

For the entire period of 2000-2017, foreign investors mainly targeted mature and established Chinese biopharmaceutical players, such as Luye Pharma Group and Harbin Pharmaceutical Group. There was a mix of market-seeking and strategic asset-seeking investments. For example, Cardinal Health's \$470 million takeover of Zuellig Pharma was primarily a market-seeking investment. This investment enabled Cardinal Health to distribute pharmaceuticals in the Chinese market.²³⁶ Another example of brand-seeking investment is Bayer's \$587 million takeover of traditional Chinese medicine-manufacturer Dihon Pharmaceutical Group, which moved Bayer to the leading position in the Chinese over-the-counter industry due to a number of well-known brands brought by Dihon.²³⁷

The key source countries for foreign M&A activity in China's pharmaceutical and biotech sectors were the US, Germany, Australia, Denmark and France. Top investors by investment value were mostly real economy firms such as Australia's biotherapy company CSL, US eye health products company Bausch + Lomb, and German life science company Bayer.

²³³ Yang Bai, Corey Ng, and Jonathan F Garner, "Asia Insight: Why New China will Resume Outperformance – Healthcare & Environment Protection Our Top Picks," *Morgan Stanley Asia Insight*(2014)

²³⁴ Jamil Anderlini, "Foreign Investment into China Slumps," *Financial Times*(2014), <https://www.ft.com/content/86808f42-3d7c-11e4-b782-00144feabdc0>

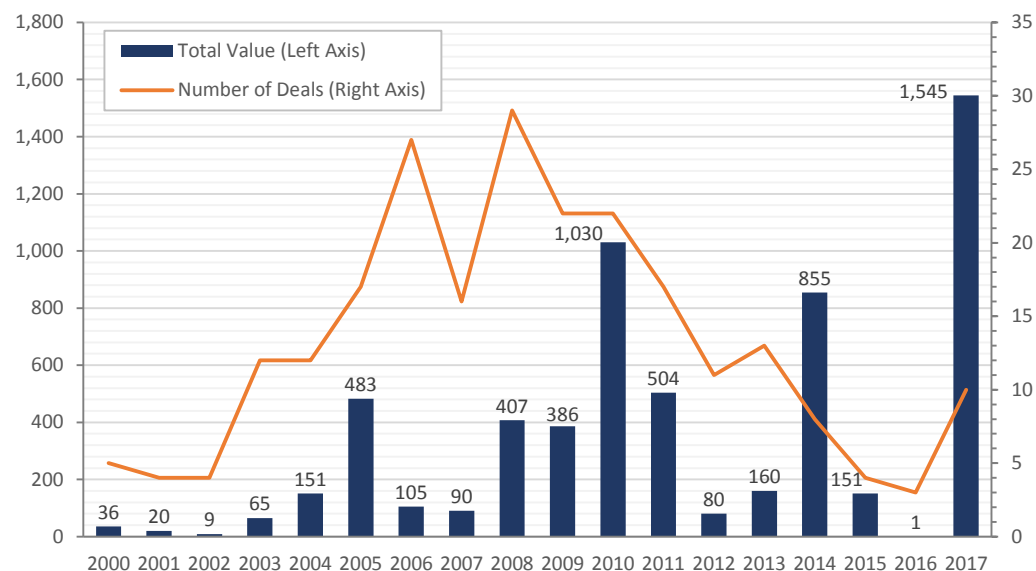
²³⁵ Thilo Hanemann, Daniel H. Rosen, and Cassie Gao. *Two-Way Street: 2018 Update US-China Direct Investment Trends* New York, NY: Rhodium Group, 2018.

²³⁶ "Cardinal Health Acquires Leading Pharmaceutical Distributor in China," Cardinal Health, updated November 29, 2010, <https://ir.cardinalhealth.com/news/press-release-details/2010/Cardinal-Health-Acquires-Leading-Pharmaceutical-Distributor-in-China/default.aspx>

²³⁷ Wang Hongyi and Li Yingqing, "Bayer acquires OTC drug firm Dihon for \$586 million," https://web.archive.org/web/20180724213133/http://www.chinadaily.com.cn/business/2014-11/18/content_18932622.htm, *China Daily*(2014), http://www.chinadaily.com.cn/business/2014-11/18/content_18932622.htm

Figure 2-1. Annual Foreign M&A in Chinese Pharmaceutical and Biotechnology Industries, 2000-2017

USD million, number of deals



Source: Rhodium Group, Bloomberg.

2.1.1.2. Greenfield FDI

The second major mode of FDI is greenfield investment, which creates new operations from scratch, either alone or in partnership with other businesses (i.e., joint ventures). Typical greenfield investments include offices, warehouses, manufacturing operations, and R&D facilities.²³⁸

Data on greenfield FDI into China are harder to find than data on M&A transactions. Official FDI data from China's Ministry of Commerce (MOFCOM) suffers from several shortcomings, including a significant time lag and substantial distortions due to the use of offshore entities. Additionally, MOFCOM statistics do not offer a breakdown detailed enough to isolate specific data on the biotech industry (the most relevant category is "manufacturing of medical and pharmaceutical products"). Data from other source countries suffer from similar shortcomings. As an alternative, we rely on combining two data sets compiled by Rhodium Group that allow us to tease out Chinese greenfield FDI transactions by US and EU companies in China's pharmaceutical and biotech industries. This is not a comprehensive global picture but—as explained above—represents the majority of global biotech investment into China and thus should be a reasonable proxy for overall activity and trends.

In total, we count over \$8 billion of greenfield investments from the EU and US in the Chinese pharmaceutical and biotech industries from 2000-2017 (Figure 2-2).²³⁹ Capital flows were small in the early 2000s but began to pick up in the mid-2000s and reached a peak of \$1.2 billion in 2012. During this time, foreign companies established operations in China to take advantage of lower production costs and expand local market share in China.²⁴⁰ Most of the operations involved manufacturing of drugs and intermediate materials for the local Chinese market. At the same time, the pharmaceutical and biotechnology sectors have generally been on the encouraged list of the Chinese Catalogue of Industries for Guiding Foreign Investment for foreign greenfield investment, receiving a variety of favorable policy

²³⁸ Organisation For Economic Co-operation and Development, *OECD Benchmark Definition of Foreign Direct Investment*, Fourth ed. (Paris: OECD Publishing, 2008).

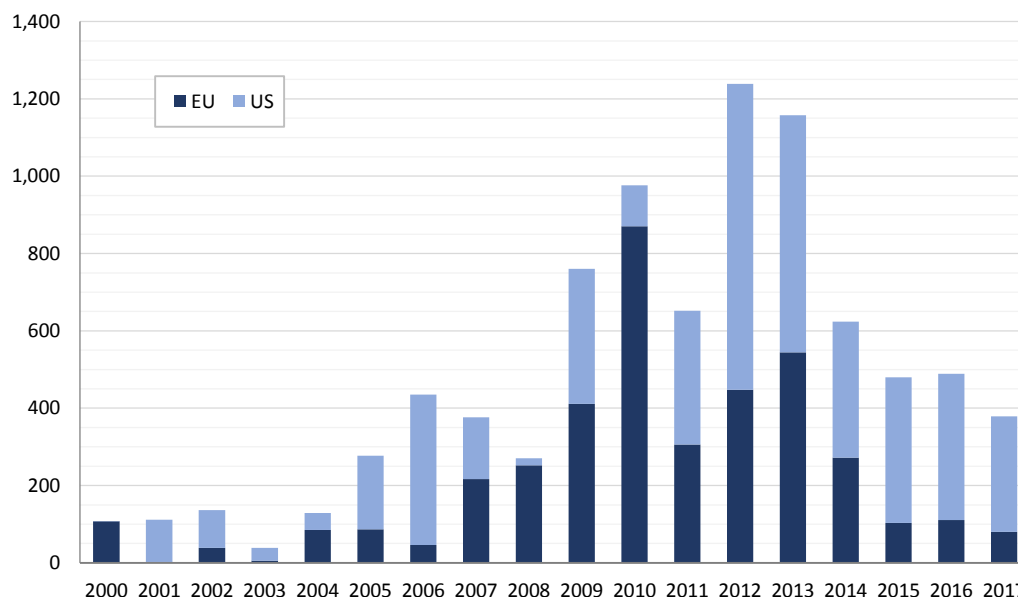
²³⁹ Data sources provide a combined "Pharmaceuticals and Biotechnology" category which we did not separate further.

²⁴⁰ Nick Marro, "Foreign Company R&D: In China, For China," *China Business Review* June 1, 2015, <https://www.chinabusinessreview.com/foreign-company-rd-in-china-for-china/>

treatments such as tax breaks. In recent years, annual investment declined as product cost advantages for large greenfield operations diminished. From 2014-2017, annual investment from the EU and US plateaued to around \$500 million per year. It is difficult to separate between traditional pharmaceuticals and biotechnology, but a preliminary review of transactions shows that the majority of EU and US greenfield projects in this period were traditional pharmaceutical investments.

Figure 2-2. Annual Greenfield FDI by US and EU Companies in Chinese Pharmaceutical and Biotech Industries, 2000-2017

Value of transactions, USD million



Source: Rhodium Group.

Biotech FDI by foreign companies into China has only been very lightly scrutinized by overseas regulators. Traditionally, most advanced economies do not control or limit their companies' overseas investments. The only exceptions are limitations on the export of controlled technology (i.e., export controls) and regulations that aim at controlling illicit activities through overseas subsidiaries, such as bribery of foreign officials, money laundering, or tax evasion. Recently, policymakers in the US and other nations have considered changing that traditional approach and imposing greater regulatory oversight on outbound investors (proposals have mostly related to "leakage" of technology and other intellectual property [IP]), but those efforts have not yielded any concrete changes. For example, the US Congress recently passed the "Foreign Investment Risk Review Modernization Act" (FIRRMA), which will broaden the scope of inbound investment screenings through the Committee on Foreign Investment in the United States (CFIUS), but the final version of the bill does not include earlier provisions that would have expanded CFIUS jurisdiction to outbound investment.²⁴¹

2.1.2. Venture Capital and Other Portfolio Investment

A second major category of cross-border capital flows under the System of National Accounts is portfolio investment.²⁴² In contrast to FDI, portfolio investments represent financial interests that generally do not include significant control over the target business, which is defined as equity stakes typically below the

²⁴¹ For more details, see: Covington & Burling LLP. *CFIUS Reform Legislation Introduced in Congress*: Covington & Burling LLP, 2017.

²⁴² The System of National Accounts (SNA) is the internationally agreed standard set of recommendations on how to compile measures of economic activity. The SNA describes a coherent, consistent and integrated set of macroeconomic accounts in the context of a set of internationally agreed concepts, definitions, classifications and accounting rules.

10 percent FDI threshold.²⁴³ In contrast to the long-term nature of FDI, portfolio investments are also typically of shorter-term nature and can be liquidated through selling in public or private markets. Since the ownership by definition does not exceed the 10 percent FDI threshold, portfolio investors generally have low levels of influence or control over their invested companies. There are certain exceptions, for example when portfolio investors work with other investors, or in the case of venture capital involving mentorship relations or board seats. The main contributions of foreign portfolio investment to the development of the Chinese biotech industry were provisioning of capital for Chinese companies as well as improving efficiency of these portfolio companies.²⁴⁴

Traditionally, portfolio investment involves the acquisition of below 10 percent stakes in publicly listed equity securities and the purchase of debt securities. Historically, China has tightly controlled the inflow (and repatriation) of these types of short-term foreign capital as it was worried about financial volatility triggered by foreign investors. Over the past decade, China has gradually opened up using pilot schemes such as the Qualified Foreign Institutional Investor (QFII) and Renminbi-QFII to invite foreign investors to participate in Chinese equity and debt markets (Figure 2-3).²⁴⁵ Private equity investors are also active in the Chinese market. However, the scale of Chinese opening remains limited to just a few specialized programs (with a list of approved investors and a quota for each) because of similar concerns about short-term capital flows causing volatility in China's fragile financial system.²⁴⁶ Despite the growth in recent years, the stock of foreign portfolio investment in China remains relatively small compared to advanced economies.²⁴⁷ In the past three years China has accelerated efforts to open up to foreign portfolio investment flows, including stock market connect schemes (such as the Shanghai-Hong Kong Stock Connect), as well as a significant opening of its bond market to foreign investors. In June 2017, index-provider MSCI announced that it would gradually add Chinese stocks to its emerging market index, a vote of confidence in China's stock market and its reform efforts.

²⁴³ For a full definition, see IMF Multimedia Services Division, *Balance of Payments and International Investment Position Manual*.

²⁴⁴ Zhou Weiming, "The Complementarity Between Foreign Direct Investment and Indirect Investment," *ChinaAcc.com* January 29, 2010, http://www.chinaacc.com/new/287_290_/2010_1_29_xu631319151419210102817.shtml [Chinese Language Source]

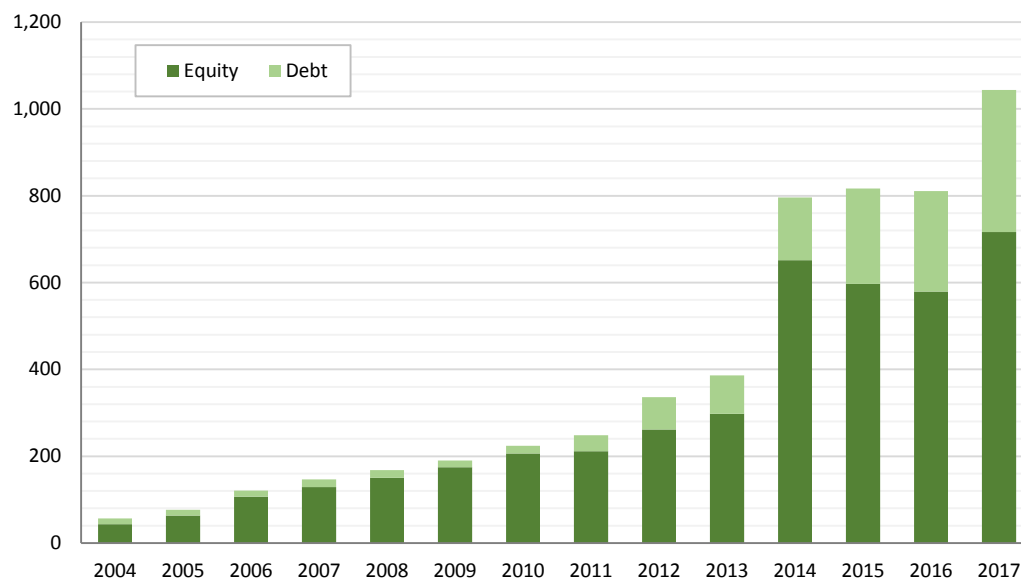
²⁴⁵ "Announcement of the State Administration of Foreign Exchange, Decree [2009] No. 1," State Administration of Foreign Exchange, updated November 13, 2009, <https://bit.ly/2MeudIs> [Chinese Language Source]

²⁴⁶ For more details on the risks of having large amounts of short-term foreign capital, see Masahiro Kawai, Richard Newfarmer, and Sergio L Schmukler, "Financial Crises: Nine Lessons from East Asia," *Eastern Economic Journal* 31, no. 2 (2005): 185-207.

²⁴⁷ As of 2017, China's stock of foreign portfolio investment assets is only 9% of the GDP, compared to 69% for Japan and 100% for the US.

Figure 2-3. Annual Stock of Foreign Portfolio Investment Assets in China, All Industries, 2004-2017

USD billion



Source: PRC State Administration of Foreign Exchange, Rhodium Group.

Since there are no comprehensive disclosure requirements, it is difficult to describe the exact scope and scale of these types of foreign portfolio transactions in China's biotech sector. Though a comprehensive picture is not available, publicly available transactions data show that most investors are either private equity firms or big institutional investors that are accredited through the QFII or R-QFII scheme to invest in Chinese equities.²⁴⁸

These investors largely provided capital (albeit the relative size remained small compared to the scale of domestic capital in the industry) used to develop China's biotech industry. As openness to overall foreign portfolio investment increases, foreign investors may in the future also be able to take on more of the typical role they play in free markets, including imposing capital discipline, creating transparency, improving corporate governance, or forcing managerial changes. All of those would, in the long run, improve the global competitiveness and efficiency of Chinese biotech firms.

Another type of portfolio investment that is particularly relevant for analyzing technology and innovation flows is VC, which is early-stage equity investment in growth enterprises. VC investments typically occur in funding rounds involving multiple investors. A typical venture-backed firm progresses through the following stages of financing: pre-revenue financing ("seed"); product and business model optimization ("Series A"); expanding initial market reach ("Series B"); rapid scaling ("Series C"); and maturation ("Series D+"). After those stages, VC investors usually exit the firm through an initial public offering, a strategic sale, or other strategy. Data on VC investments are readily available from commercial data providers, but there are certain limitations as to its quality and accuracy.²⁴⁹ There are no systematic disclosure requirements for VC investments in the United States, so commercial databases may be missing transactions where parties do not wish to make disclosures. In many cases, commercial VC investment databases do not have accurate or complete information on the ownership structure of the

²⁴⁸ For a full list of approved foreign investors see "Qualified Foreign Institutional Investor (QFII) Investment Amount Approval Form (as of October 30, 2018)," State Administration of Foreign Exchange, updated 10/31/2018, <http://www.safe.gov.cn/safe/2018/0425/8881.html>

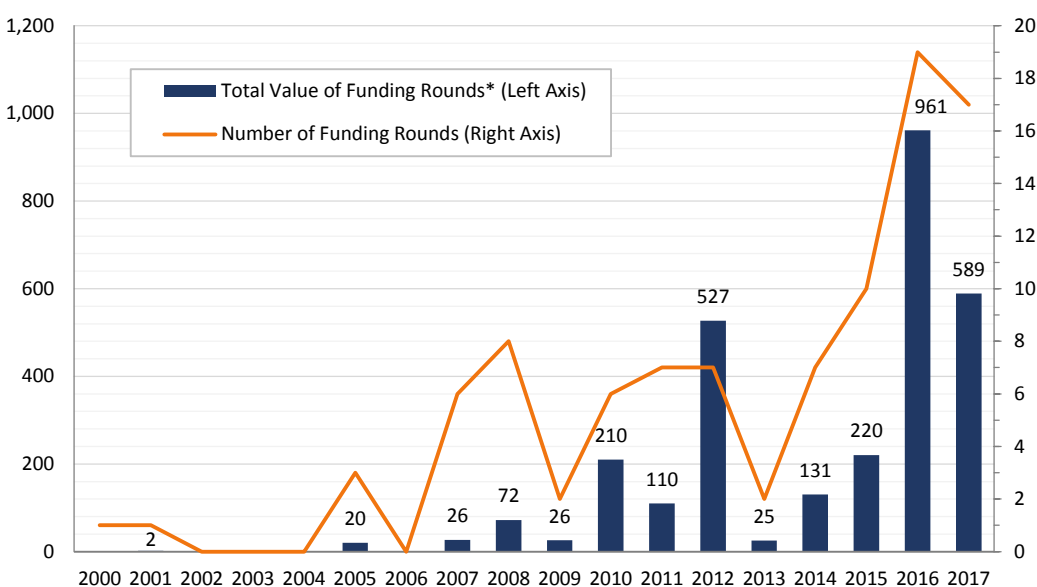
²⁴⁹ The most common VC data providers are Crunchbase, CB Insights and Pitchbook.

venture investors, making it difficult to comprehensively identify those that are ultimately Chinese owned.²⁵⁰

Foreign VC investments have played a role in nurturing Chinese biotech companies, and there are good data sets available to quantify these flows and separate “core” biotech deals from the broader pharmaceuticals category. In 2000-2017, we counted 106 funding rounds of Chinese biotech companies with foreign participation that generated a total of \$3.9 billion in funding (counting the entire amount and not only foreign capital contributions).²⁵¹ Foreign VC investments in China's biotech sector started to take off in the mid-2000s but stayed at relatively low levels between 2005 and 2015, with an average of six funding rounds raising \$137 million per year (**Error! Reference source not found.**). Major companies that have received foreign VC funding during this time include Innovent Biologics, Hua Medicine, and Zai Lab.

Figure 2-4. Annual Foreign Venture Capital Investment in Chinese Biotech Sector, 2000-2017

USD million, number of funding rounds



Source: Rhodium Group. *Includes full value of funding round not just the portion of foreign investors.

After 2014, foreign VC investment in Chinese biotech firms increased to an average of 15 funding rounds per year (raising an average of \$590 million per year). Companies that have received foreign VC financing during this time include Bii Biosciences, CStone Pharmaceuticals, and I-Mab Biopharma. This growth correlates with a rapid increase of global VC funding for biotech companies in the same period as well as strong growth in China's biotech startups. However, the role of foreign investors overall in China's biotech startup universe has declined over the past years as a strong domestic VC community has emerged.

The majority of investors were large American or European corporate VC firms, such as Lilly Asia Ventures, as well as professional VC firms, such as London-based private equity company Actis Capital. The interest of these firms is largely financial returns, and their “contribution” was capital. However, Chinese biotech firms may have also benefited from the operational and managerial know-how that

²⁵⁰ Foreign venture investors in China face restrictions like in the direct investment space. For this reason, many opt to use complicated offshore constructs (including variable interest entities, or VIEs) when they invest in Chinese firms to avoid the hurdles they must clear to participate on-shore.

²⁵¹ Includes the value of invested capital from all funding round participants regardless of domicile and ownership, not just Chinese-owned participants.

these companies brought with them. Some VC firms have nominated board members to their Chinese portfolio companies or made other contributions in terms of mentorship and informal support. For example, OrbiMed Asia, which has invested in Shanghai-based company Laekna Therapeutics, has helped Laekna identify drugs to target for licensing even before the investment, and continues to support the company with its global resources and network.²⁵²

With regard to the regulatory environment, there has traditionally not been any regulatory supervision of outbound portfolio investment flows in advanced open economies, with the exception of temporary capital controls in times of financial crises.²⁵³ There is no indication that this approach will change anytime soon.

2.1.3. Overseas Listings

Historically, a third important conduit for foreign capital flowing to China was overseas listings of Chinese companies. Technically, such activity would be captured under portfolio investment in a traditional Balance of Payments / National Accounts approach, but we treat it as a separate category because it is a specific type of fundraising with different commercial and regulatory ramifications than isolated portfolio stakes. The contributions of overseas listings to China's biotech development were similar to other portfolio flows: raising capital for Chinese biotech firms to grow larger and modernizing governance structures due to exposure to overseas regulators and investors.

Chinese companies started listings overseas in the 1990s, a process that was encouraged by the Chinese government to modernize corporate structures and state-owned enterprises in particular. Private companies also sought overseas listings as those steps allowed them to get access to international investors, more efficient regulatory processes, and lower thresholds for public listing than in the domestic market.²⁵⁴ Hong Kong was the primary target for Chinese companies to be listed before 2000, because the cost of listing was relatively low and mid and small-sized companies have better recognition in Hong Kong than in Singapore or the US.²⁵⁵ By the end of 2016, 1,002 companies from mainland China were listed in Hong Kong.²⁵⁶ Chinese companies with an ambition to gain international recognition started listings in the US in the early 2000s, due to the high level of market maturity, market size, and easier market exit.²⁵⁷ By August 2017, 168 Chinese companies were listed in the US, with 52 companies in the ICT sector²⁵⁸, and 14 companies in the energy sector.²⁵⁹

For the biotech industry, overseas listings have played a relatively minor role thus far. In 1990-2017, we count a total of 18 Chinese biotech companies listed abroad (Table 2-1). Overseas listings began in Hong Kong in the early 1990s but stayed at low levels compared to the overall number of firms making that step. By the end of 2017, 11 biotech firms were listed in Hong Kong. It took until the late 2000s for the first Chinese biotech company to go public in the US; the number has remained low at only seven by the end of 2017, reflecting commercial (low number of mature enough firms) and regulatory (listing requirements, skepticism after accounting scandals) realities. The most prominent examples are Beijing-based Sinovac (which focuses on R&D, manufacturing and commercialization of vaccines on infectious diseases); BeiGene (a global biopharmaceutical company that focuses on the R&D and

²⁵² Richard Daverman, "Exclusive Interview with Jonathan Wang of OrbiMed Asia: China's Market is a "Once-in-a-Lifetime Opportunity", *ChinaBio Today*(2018), <http://www.chinabiotoday.com/articles/Jonathan-Wang-OrbiMed-Interview>

²⁵³ Lefteris Papadimas and George Georgiopoulos, "Greece imposes capital controls as crisis deepens," *Reuters* June 27, 2015, <https://www.reuters.com/article/us-eurozone-greece/greece-imposes-capital-controls-as-crisis-deepens-idUSKBN0P40EO20150628>

²⁵⁴ China Securities Regulatory Commission. *Analysis of overseas exchanges competing for potential listing resources in China* Beijing: State Council, 2007. [Chinese Language Source]

²⁵⁵ "Where is the IPO going? The most complete comparison," PEdaily, updated December 20, 2016, <http://pe.pedaily.cn/201612/20161220406953.shtml> [Chinese Language Source]

²⁵⁶ Enoch Yiu, "Hong Kong remains in pole position for IPOs," *South China Morning Post* June 24, 2017,

<https://www.scmp.com/business/companies/article/2099755/hong-kong-remains-pole-position-ipos>

²⁵⁷ PEdaily, "Where is the IPO going? The most complete comparison," <http://pe.pedaily.cn/201612/20161220406953.shtml>

²⁵⁸ Jane Li, "Why Chinese companies are flocking to the US for a listing," *South China Morning Post* October 19, 2017,

<https://www.scmp.com/business/china-business/article/2115971/ant-financial-backed-online-lender-qudian-surges-nyse-debut>

²⁵⁹ Shenzhen Stock Exchange Comprehensive Research Institute. *Analysis of the Listing of New Energy Companies at Home and Abroad* Shenzhen: Shenzhen Stock Exchange Comprehensive Research Institute, 2010. [Chinese Language Source]

commercialization of drugs for the treatment of cancer); and BeyondSpring (which is a clinical-stage biopharmaceutical company focusing on the R&D of cancer treatment therapies). Since 2014, Chinese biotech companies became more active in listing overseas with at least one new IPO every year. 2018 is poised to be a big year with at least five Chinese biotech companies in the process of getting listed in Hong Kong.

In terms of impact, overseas listings provided opportunities for Chinese biotech firms to receive foreign financing. This was particularly important during periods of regulatory tightening or back-log for domestic listings. However, overall, biotech accounts for a small fraction of total overseas listings (less than two percent in number terms and even lower if one considers market capitalization or funds raised). This comparably low share is mostly related to commercial factors; IPOs as a fundraising strategy mostly work for more mature companies that have revenue and fulfill other requirements. In the past, there was a fairly limited number of Chinese firms in the biotech space meeting those criteria.

Table 2-1. Selected Chinese Biotech and Pharmaceutical Companies Listed Abroad

Year	Chinese Company	Listing Location	Ownership*
1994	Shijiazhuang Pharma Group	Hong Kong	Private
2000	Sino Biopharm	Hong Kong	Private
2000	Tong Ren Tang	Hong Kong	State-owned
2007	Wuxi AppTec	US	Private
2009	Sinovac	US	Private
2009	Global Cord Blood	US	Private
2009	China Biologic Products	US	Private
2014	Luye Pharma	Hong Kong	Private
2015	3SBio	Hong Kong	Private
2016	BeiGene	US	Private
2016	Hutchison China MediTech	US	Private
2016	China Resources Pharmaceutical	Hong Kong	Private
2017	BeyondSpring	US	Private
2018	Shanghai Tasly Pharmaceutical	Hong Kong	Private
2018	Shanghai Henlius Biotec	Hong Kong	Private
2018	GRAIL	Hong Kong	Private
2018	Ascentage Pharma	Hong Kong	Private
2018	Innovent Biologics	Hong Kong	Private

Source: Rhodium Group. *State-owned refers to companies with over 20 percent ownership by the government, the State Asset Supervision and Administration Commission, and other state-owned enterprises; Private refers to companies with less than 20 percent ownership by the government, the State Asset Supervision and Administration Commission, and other state-owned enterprises.

Going forward, the number of listings is poised to change as more Chinese biotech firms reach the level of maturity required to list abroad. Moreover, the recent change of overseas listing rules to allow pre-revenue biotech firms (those still in the development phase not yet receiving revenue from their products) to go public in Hong Kong could further incentivize earlier stage biotech firms to list there.²⁶⁰

²⁶⁰ "Listing Rules for Pre-Revenue Biotech Companies in Hong Kong – Consultation Conclusions and the Final Chapter 18A," O'Melveny & Myers LLP, updated April 28, 2018, <https://www.omm.com/resources/alerts-and-publications/alerts/listing-rules-for-pre-revenue-biotech-companies-in-hk-consultation-conclusions/>

Overseas regulators have scrutinized overseas listings by Chinese companies, but their priorities have been to protect investors, create transparency, and supervise behavior. In the US, Chinese company listings have caused particular concerns in that respect after a number of cases of fraudulent listing scandals, which caused heavy losses for US retail and institutional investors in the period of 2010-2012.²⁶¹ These scandals led the Nasdaq Stock Market to tighten rules and close several loopholes, such as reverse mergers.²⁶² Overseas regulators generally do not scrutinize overseas listings for criteria beyond compliance with federal regulations, such as national security or economic risk.

2.2. Chinese Outbound Investment

Outbound capital flows were very limited for the first two decades of Chinese reform, as Beijing was heavily restricting outflows (to not lose valuable foreign exchange and open venues for illicit transfer of state capital) and Chinese companies did not have the motive or capacity to invest overseas.²⁶³ This has changed over the past decade as Beijing has relaxed restrictions on outbound capital flows and firms have developed a greater appetite to invest overseas through a range of different channels.

2.2.1. Direct Investment

The first and still most important channel for Chinese outbound investment in biotech is FDI, through both acquisitions and greenfield projects, which refer to the establishment of new operations from scratch, such as offices, warehouses, manufacturing operations, and R&D facilities. Acquisitions generally yield a high degree of control over investment targets compared to other modes. The degree of control that an acquirer has over the target (and thus its technology and broader IP) depends on the size of the equity stake. Control is high if the investor acquires a controlling or a majority stake. Even a minority stake can still yield significant control, particularly if the investor is given a board seat or similar rights. Greenfield FDI projects are typically 100 percent owned (and thus controlled) by the foreign investor, unless it is a greenfield joint venture with a local partner (in which case the extent of control depends on the equity stake as well as the operating agreement and other factors).

2.2.1.1. Mergers & Acquisitions

The total value of Chinese outbound M&A in pharmaceutical and biotech industries is relatively small but has grown substantially in the past three years. Before 2014, annual M&A investment values were below \$100 million. Chinese biotech M&A abroad began to take off in 2014, with Shenzhen Hepalink's \$338 million takeover of US Scientific Protein Laboratories. Investments grew rapidly in the past few years: in 2016, annual M&A investment jumped up to over \$1.5 billion. After a slight drop in 2016, Chinese global M&A investment in pharmaceuticals and biotech more than doubled in 2017, reaching \$3.5 billion. This is particularly remarkable since total Chinese outbound FDI declined substantially in 2017. Chinese global outbound FDI was down 35 percent in 2017; the value of newly announced global acquisitions dropped by 90 percent. The combined pharmaceutical and biotech sector is one of just a few sectors in which investment levels held up or increased.²⁶⁴

Compared to China inbound M&A activity (which was mostly driven by market access motives), global outbound M&A by Chinese firms in the pharmaceutical and biotech sectors was mostly driven by strategic asset-seeking motivations. Chinese outbound investment in the pharmaceutical and biotech sectors took off quickly starting in 2014, reaching over \$1.5 billion in 2015 and over \$3.5 billion in 2017 (Figure 2-5). The rapid recent growth was mostly driven by Chinese companies upgrading technology and acquiring supply chains and other assets to position themselves for growth in the global and Chinese markets. The

²⁶¹ Hanemann and Rosen, *Chinese Investments in the United States: Recent Trends and the Policy Agenda*.

²⁶² Francine McKenna, "After China fraud boom, Nasdaq steps up scrutiny of shady listings," *MarketWatch* June 20, 2016, <https://www.marketwatch.com/story/after-china-fraud-boom-nasdaq-steps-up-scrutiny-of-shady-listings-2016-06-20>

²⁶³ Duncan Freeman, "China's Outward Investment: Institutions, Constraints and Challenges," *Brussels Institute of Contemporary China Studies, Asia Paper 7*, no. 4 (2013).

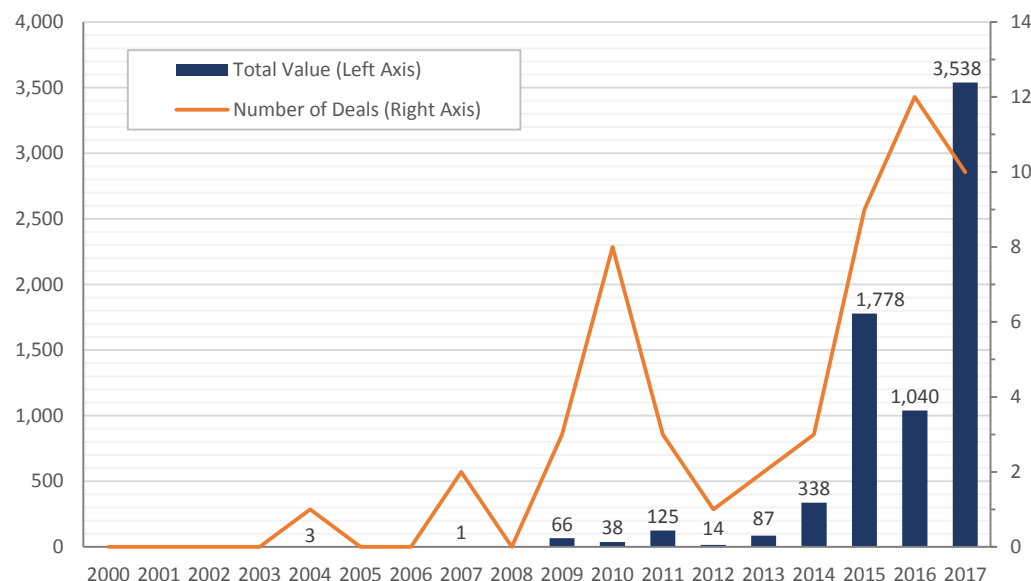
²⁶⁴ Thilo Hanemann and Daniel H. Rosen, "Chinese FDI in the US in 2017: A Double Policy Punch," *Rhodium Group* January 17, 2018, <https://rhg.com/research/chinese-fdi-us-2017-double-policy-punch/>

acquisition of established foreign companies with existing technology and customer bases allows for quicker market entry. The key investors include Creat Group, Shenzhen Hepalink Pharmaceutical, Valiant, and BGI. Financially motivated investors including private equity firms (e.g., Bank of China Group Investment and CDH) or conglomerates (e.g., Sanpower Group) also played a role.

Overall, despite the recent rapid increase, the total value of outbound M&A in the pharmaceutical and biotech sectors remains relatively small at just \$7 billion in 2000-2017, which is a small fraction (two percent) of total Chinese outbound M&A in that period. The average deal size was just around \$100 million with most deals being concentrated in the US, Germany, and Switzerland. In 1H 2018, Chinese outbound M&A in the pharmaceuticals and biotech amounted to \$1 billion.

Figure 2-5. Annual Chinese Outbound M&A in Global Pharmaceutical and Biotech Industries, 2000-2017

USD million, number of deals



Source: Rhodium Group, Bloomberg.

There are clear commercial rationales for a further increase of Chinese outbound M&A in the biotech industry, as Chinese firms are building out their global presence from a very low base of international assets. However, the political situation remains complex as Chinese regulators continue to control outbound flows and foreign regulators step up the regulation of inbound M&A transactions (see Table 2-2, below).

2.2.1.2. Greenfield FDI

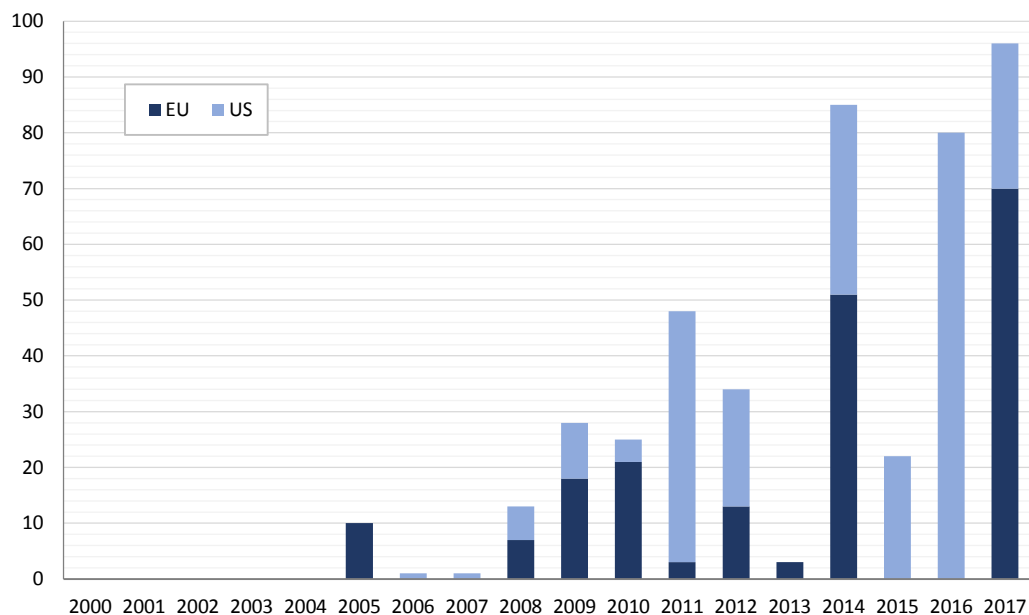
Chinese companies have steadily increased their greenfield investment abroad over the past few years. Data on greenfield FDI are harder to obtain than M&A data because official statistics from China's MOFCOM and other source countries do not offer such granularity. As an alternative, we again rely on combining two data sets compiled by Rhodium Group that allow us to tease out Chinese greenfield FDI transactions in the US and EU pharmaceutical and biotech industries. This is not a comprehensive global picture but can serve as a reasonable proxy for overall activity and trends due to the outsized role the US and EU have in the pharmaceuticals and biotechnology industry.

In total, we only count \$446 million of Chinese outbound greenfield investment in the EU and US pharmaceutical and biotech industries in 2000-2017 (\$315 million in the US and \$131 million in the EU). Even though total greenfield investment remains small compared to the value of M&A transactions,

annual flows have steadily increased over the past ten years. Starting in 2008, annual flows increased from less than \$50 million per year to \$100 million per year in 2017 (Figure 2-6). Greenfield operations were mostly established to service the local customer base and to tap into the foreign talent base for R&D activities. For example, Tasly Pharmaceutical established an R&D center in Maryland because of the location's proximity to the NIH and other major research organizations and universities in the area. In 1H 2018, we count \$454 million of newly announced Chinese outbound greenfield investments in the EU and US pharmaceutical and biotech industries. The majority of this flow is in Europe (\$394 million) due to WuXi Biologics's planned \$389 million biologics drug substance manufacturing facility in Ireland.

Figure 2-6. Annual Chinese Greenfield FDI in US and EU Pharmaceuticals and Biotech Industry, 2000-2017

Value of transactions, USD million



Source: Rhodium Group.

2.2.1.3. Host Country FDI Screening

Host countries are actively regulating inward FDI. Most of those frameworks focus entirely on acquisitions while greenfield FDI is not scrutinized. Traditionally, most countries in the Organisation for Economic Co-operation and Development (OECD) screen inbound foreign M&A for two broader sets of risk: fair competition and national security.

Competition policy reviews (or “merger control”) reviews certain types of foreign (and domestic) M&A activity to prevent over-concentration, collusion, predatory pricing, and other anti-competition behaviors. It is mainly concerned with protection welfare of the consumer, market competition, and by extension efficiency. Most countries assess the competitive impact of cross-border M&A transactions as part of their existing competition policy regime.

On the other hand, national security screenings review specifically foreign M&A for potential security risks stemming from foreign ownership of local assets. There is no universal definition for national security risk related to M&A, but US scholars generally divide concerns into three areas: (1) disruption of the provision of critical goods and services; (2) transfer of critical technology or expertise to a foreign entity or country; and (3) creation of additional conduits and opportunities for infiltration, surveillance, and sabotage.²⁶⁵ Most countries have set up a distinct process to review foreign M&A on a case-by-case basis, but there is

²⁶⁵ Edward Graham and David Marchick, *U.S. National Security and Foreign Direct Investment* (Washington, D.C.: Institute for International Economics, 2006).

a great variety of approaches among OECD economies. In many countries, those regulatory frameworks have tightened in the past five years, largely in direct response to the rise of Chinese outbound investment.

Beyond these two core considerations, some nations also screen for broader economic interests, most notably Australia, where the Foreign Investment Review Board (FIRB) reviews transactions based on a broader definition of “national interest”. Similarly, Canada applies a “net benefit” test in its review process, which takes into account security as well as a broader set of economic variables that extend beyond just fair competition. Table 2-2 offers an overview of foreign investment review practices in major OECD economies.

Table 2-2. Foreign Investment Review Practices in Major OECD Economies, June 2018

Country	Description
Australia	The FIRB is responsible for reviewing foreign investment above a threshold value and providing a recommendation to the Treasurer, who has authority to deny or place conditions on particular investments on national interest grounds. The Australian government passed the Critical Infrastructure Center bill in March 2018 to protect sectors in critical infrastructure from foreign control over these sectors.
Canada	The Canadian government screens foreign investment for both net benefit and national security. The Minister of Industry may issue a review notice if he believes a foreign investment could be “injurious to national security”. A formal national security review may then be launched. If still unresolved after the review, the case will be referred to the cabinet for final decision. While the Canadian government has not published any specific details about its decision, various public statements imply that the block of Chinese investment in Aecon is related to the fact that Aecon supplies both the military and nuclear industries and that the Canadian government may have had concerns about IP protections.
France	The French Ministry of Economy and Finance’s Treasury Department is in charge of foreign investment review. Since 2014, the scope of activities covered by national security reviews was expanded to key industries, including sensitive technology, especially for non-EU investors. Since January 2016, a commissioner of strategic information and economic security assists the Treasury with investment review.
Germany	The German government expanded its Foreign Trade and Payments Ordinance (FTAPO) in late 2017, targeting countries outside the EU, and outside Germany in the military sector. Under the FTAPO, the Ministry of Economic and Energy can review and veto the acquisition of a German company by a foreign investor when it poses a threat to public order or security. Industries such as critical infrastructure, software, cloud computing and telematics are subject to review.
Italy	The Italian Ministry of Defense, Ministry of Transport, Ministry of Communication, and other government agencies review foreign investments in key sectors. Italy has a national security screening system that applies to the national defense, energy, transport, and communications sectors “in cases where an acquisition or other form of transaction triggers a threat of severe prejudice to essential interests of the State.” Italy has also adopted the “golden powers” under which the government can veto or impose acquisitions of Italian entities in strategic sectors.

Country	Description
Japan	The Japanese government reviews foreign investment in sensitive sectors and may block foreign investment on grounds of national security, public order, public safety, or the smooth management of the economy. The Ministry of Finance and other ministries with related industry area jurisdiction are authorized to review foreign investments. In the 2017 amendments to the Foreign Exchange and Foreign Trade Act, the scope of review expanded to sensitive areas crucial to national security such as technology infrastructure.
The Netherlands	A legislative proposal was submitted in April 2018 to the Dutch Council of State to strengthen investment screening in the telecom industry. If this law passes, it will apply to both domestic and foreign investors. Other than for a few strategic sectors that are limited to foreign investment, such as transportation, energy, defense, and security, the Netherlands has no formal foreign investment screening mechanisms.
Mexico	The National Foreign Investment Commission under the Secretariat of Economy is in charge of review, enforcing the Foreign Investment Law. Certain areas are only reserved for Mexican companies, such as development banks and national land transportation. Foreign equity share is limited in a number of activities, such as weaponry, media, agriculture, port, fishing, and transportation services.
South Korea	South Korea restricts foreign investments in the following cases: where the transaction threatens the maintenance of national safety and public order; where it has harmful effects on public hygiene or the environmental preservation; or is against Korean morals and customs.
Spain	Generally, foreign investment is not subject to specific review. Exceptions apply to activities related to national defense and real estate investments for diplomatic purposes from non-EU investors. The Spanish Council of Ministers can suspend foreign investments if these activities affect public authority, security, public health, and order.
Turkey	There is no general national security review system. Areas open to Turkish private sectors are also generally open to foreign investment, except for certain sectors, such as petroleum, mining, broadcasting, maritime transportation, and aviation.
UK	The UK government expanded its powers to review M&A transactions on the grounds of national security, and changes to the Enterprise Act of 2002 were adopted in June 2018. The Competition and Markets Authority carries out the review, and reports to the Secretary of State. The turnover required for review is lowered from \$96 million to \$1.4 million ²⁶⁶ ; industries such as ICT, technology and military items are of special public interest.
United States	The Committee on Foreign Investment in the United States reviews the national security implications of foreign investments in the US. Congress in 2018 passed a new bill (FIRRMA) that tightens and expands the scope of review, especially in "critical technology" sectors.

Source: Authors' compilation from government documents.

2.2.2. Venture Capital and Other Portfolio Investment

Similar to FDI, Beijing has traditionally kept outbound portfolio investment flows heavily restricted. That has changed in recent years as China has opened up certain channels for what it deems qualified

²⁶⁶ GBP values in the report are converted to USD using the year-to-date 2018 exchange rate of 1 GBP = 1.37 USD

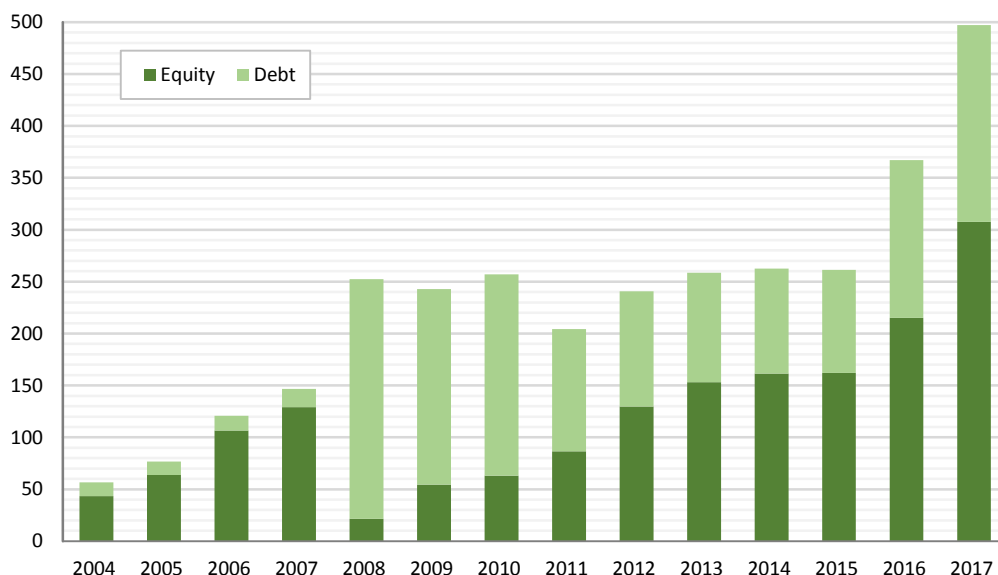
investors. The most prominent channel is the qualified domestic institutional investors (QDII) program, which allows certain financial institutions to invest in offshore markets such as securities and bonds. There are also state-owned or state-related institutional investors that are tasked with overseas portfolio investments, including large sovereign wealth funds (the China Investment Corporation [CIC] and the State Administration of Foreign Exchange) and the National Social Security Fund. In addition to “permitted” outflows, there are many channels for illicit portfolio investment outflows, including trade mis-invoicing, tourism, FDI, and others.²⁶⁷ As with inward portfolio flows, most transactions did not yield any technology or access to other IP for Chinese investors. However, there are certain exceptions, for example transactions that led to a board seat or other special access despite a formally low equity threshold.

This situation makes it difficult to quantify overall levels of portfolio investment outflows as well as flows into specific sectors such as biotech. Official Chinese statistics show total portfolio investment abroad reached \$500 billion in 2017 from an average of only \$250 billion annually between 2006 and 2015 (Figure 2-7). However, this figure likely underestimates the extent of portfolio outbound investment because it does not capture outflows through non-official channels. The major players are financial investors that aim at generating financial returns and diversifying their assets from dominantly domestic holdings to a more international portfolio. In some instances, portfolio investments have also contributed to the transfer of technology or were a first step toward a full-blown takeover.

Going forward, portfolio investment is poised to grow rapidly. Chinese households and corporations are not well-diversified and suffer from a huge “home bias” toward domestic assets. A normalization of holdings toward an optimally diversified portfolio could trigger trillions of dollars of additional outflows in coming decades. This shift will depend on whether the Chinese government is confident enough to allow such outflows and what the timetable for further opening will be.²⁶⁸ In the near term, policymakers will continue to heavily control outbound portfolio investment flows until efforts to generate greater inflows have reached a desired level.

Figure 2-7. Annual Stock of Chinese Portfolio Investment Abroad, All Industries, 2004-2017

USD billion



Source: PRC State Administration of Foreign Exchange, Rhodium Group.

²⁶⁷ For example, see Dev Kar and Sarah Freitas, “Illicit Financial Flows from China and the Role of Trade Misinvoicing,” *Global Financial Integrity* October 2012, <https://www.ciponline.org/images/uploads/commentary/gfi-china-oct2012-report-web.pdf>.

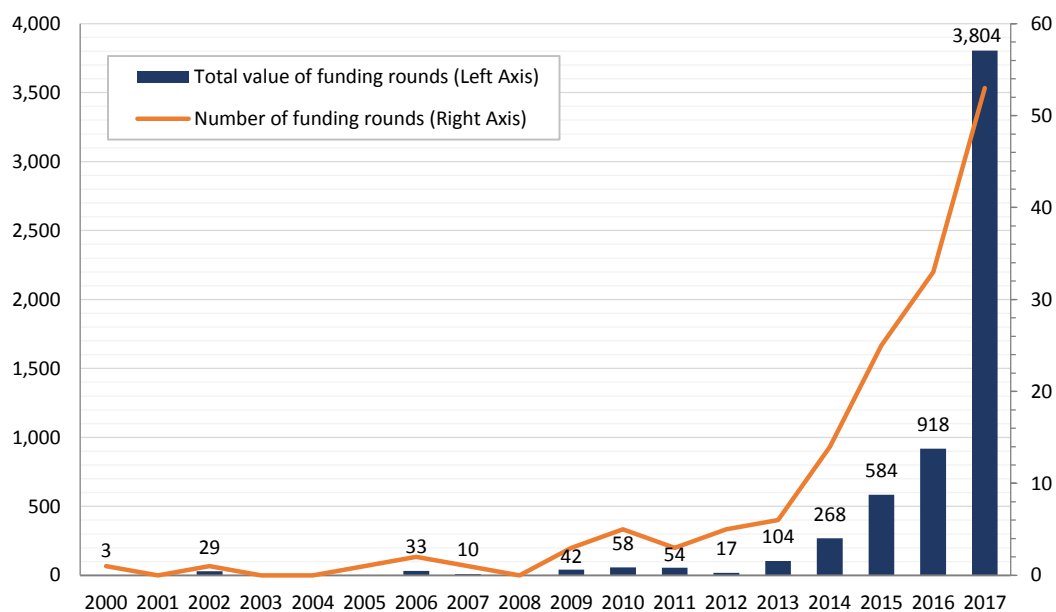
²⁶⁸ Henny Sender, “China’s cat-and-mouse game over capital outflows set to continue,” *Financial Times* 2017, <https://www.ft.com/content/5737f420-86fb-11e7-bf50-e1c239b45787>

One type of outbound portfolio investment that has risen particularly rapidly in recent years is VC, or financing of early stage technology companies (for a more detailed definition see 2.1). While VC investors generally stay way below the 10 percent threshold, they can exert strong influence over portfolio companies in some instances, through appointed directors, mentorship, and other means.

Chinese outbound VC investments in the global biotech industry were almost nonexistent until 2013, mirroring the situation in other industries. After 2013, VC investment increased every year, and the number of rounds with Chinese participation increased six-fold from 2013-2017 (Figure 2-8). In 2017, VC investments reached a record of 53 funding rounds with a total value of \$3.5 billion. In 2000-2017, Chinese VC investors participated in 153 global biotech funding rounds worth a combined \$5.9 billion (including the value of contributions from non-Chinese co-investors). Major recipients were mostly startup firms with proprietary technology or innovation, including GRAIL, Intarcia Therapeutics, and Viela Bio. The majority of target companies are located in the US (131 out of 153 deals), followed by Asia (11 out of 153 deals) and Europe (7 out of 153 deals). Most of the target companies are engaged primarily in biotechnology (77 deals), followed by the drug discovery (34 deals) and drug delivery (8 deals) markets of traditional pharmaceuticals (although which may have a biotechnology component). Overall, the combined category of pharmaceuticals and biotech is a top industry in Chinese outbound VC investment, second only to ICT.

Figure 2-8. Annual Chinese Biotech Venture Capital Investment Abroad*

USD million, number of rounds



Source: Rhodium Group. *Includes full value of funding round not just the portion of Chinese investors.

Host country regulators have traditionally not scrutinized Chinese portfolio investment for purposes other than compliance with financial regulations such as insider trading, money laundering, and similar provisions. However, recently politicians in the US and other advanced economies have started to discuss potential implications from portfolio investment, in particular VC. Most of these investments target cutting-edge technologies, which raises potential national security risks (leakage of dual use technologies) as well as potential economic risks (loss of long-term innovative capabilities in the case of malicious or industrial policy-driven investment behavior). Because the United States is the major recipient of Chinese outbound VC investments, US lawmakers and politicians are spearheading this debate.²⁶⁹

²⁶⁹ Cory Bennett and Bryan Bender, "How China acquires 'the crown jewels' of U.S. technology," *Politico*(2018), <https://www.politico.com/story/2018/05/22/china-us-tech-companies-cfius-572413>

2.3. Other Channels

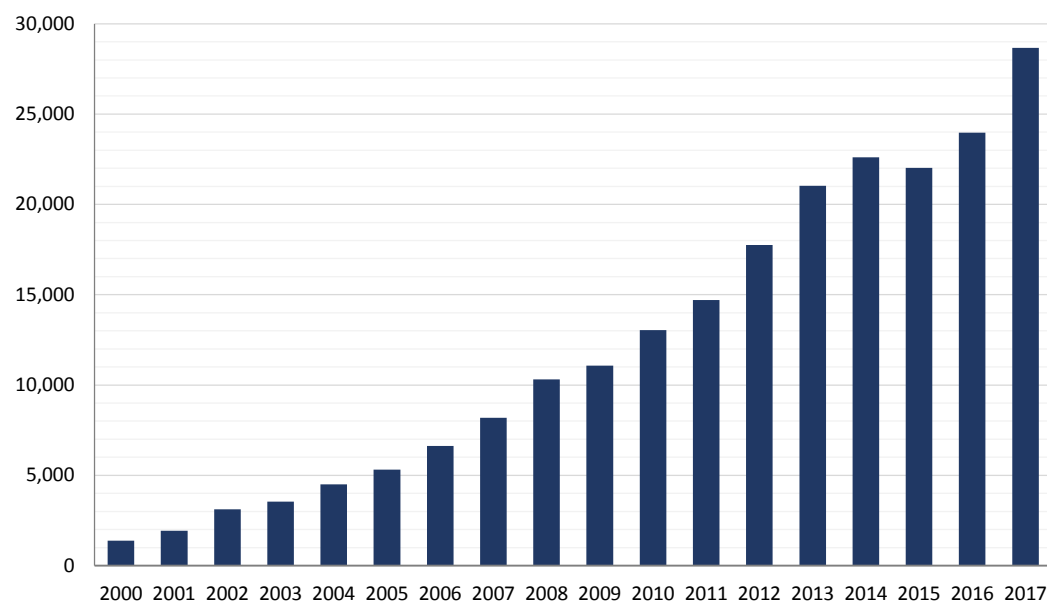
In addition to investment flows, other types of international economic interactions have also influenced the development of China's biotech industry. The three most important conduits are patent acquisitions and licensing; research partnerships and other collaborations; and overseas education and training for Chinese students and scientists.

2.3.1. Patent Acquisitions and Licensing

Chinese companies have in recent years started to purchase and license technology from overseas. According to China's Balance of Payments statistics, the annual value of Chinese payments for the use of foreign IP has steadily increased from less than \$1 billion per year in the early 2000s to over \$30 billion in 2017 (Figure 2-9).

Figure 2-9. Annual Chinese Purchase of IPR Services under the Current Account, All Industries, 2000-2017

USD million



Source: State Administration of Foreign Exchange.

While this high-level view illustrates the pace of growth, official statistics do not provide any comprehensive data that break down these payments by country, sector, or type of IP. The only way to paint a comprehensive picture of the IP dynamics between China and the world would be to collect, review and aggregate information on individual transactions. However, global IP transactions are heavily distorted by tax efficiency considerations, so building a novel database on biotechnology IP transactions between China and the world is beyond the scope of this report. However, we provide some context and illustrative examples that provide a starting point for assessing IP patterns.

The first important element of global interaction for Chinese companies is the outright purchase of IP from foreign firms. Patents and trademarks give their owners the right to exclusively use and profit from a technology, brand or trademark in a specified jurisdiction. Patent applications are generally made public after 18 months of filing, and granted patents are in force for a period of 20 years from invention. The purchase of IP from foreign firms is an important component of the catch-up process of Chinese pharmaceutical and biotechnology companies as they have relatively little self-developed IP in certain areas, which makes patent acquisitions a prerequisite for expanding into global markets. Most of the

patent purchases we found, however, involved medical devices such as prosthetics or traditional (small molecule) pharmaceutical drugs and therefore do not fall under our definition of biotechnology.

A more important channel for technology acquisition is licensing of technology. Licensing has been a major channel for Chinese companies to legally access foreign technology and other IP. A licensing agreement is a contractual arrangement between an intellectual property rights owner (licensor) and another entity authorized to use the IP (licensee) in exchange for monetary compensation (fee or royalty). Licenses are typically use- and jurisdiction-specific. They generally include the right to sell, produce or use something in certain territories for a certain amount of time and stipulate a royalty mechanism to compensate the licensor. Within the bounds of the license agreement, the licensee has full freedom to exploit the IP. Compared to IP purchases, licensing agreements can often be more effective for knowledge transfer since they often include provisions requiring the licensor to provide training and support to the licensee in the use of a licensed technology, making them a potent conduit for transferring technical capabilities and expertise. Table 2-3 provides several examples that illustrate the range of Chinese IP purchases in the biotech industry. Technologies covered by these licenses include diagnostic assays, anti-inflammatory molecules and antimicrobial molecules, cells with applications in cancer immunotherapy, and methods for cellular biology research.

Table 2-3. Examples of Licensing Agreements in the Biotechnology Sector Allowing Chinese Companies to Utilize Patents Held by US Firms in the Chinese Market

Date	Licensor	Licensee	License Description
11/17/2017	Ortho-Clinical Diagnostics, Inc.	Ortho-Clinical Diagnostics, Inc. (Overseas Subsidiary)	Methods and compositions for diagnosing and prognosing renal injury and renal failure
9/20/2017	Duke University	Beijing C&N International Sci-Tech Co., Ltd.	Peptides for inhibiting inflammation
12/18/2015	Argos Therapeutics	Chongqing Lummy Pharmaceutical Co., Ltd.	Mature dendritic cell compositions and methods for culturing them
6/13/2012	BioMarin Pharmaceutical	Zhengda Tianqing Pharma. Group Co., Ltd.	Novel semi-synthetic glycopeptides as antimicrobial agents
5/21/2012	University of Illinois	Tianhe Stem Cell Biotechnologie	Stem cell immunoregulatory application method and apparatus

Source: Rhodium Group.

2.3.2. Research Partnerships and other Collaborations

Chinese biotech firms have benefitted from relationships with US institutions that were not based on a formal joint venture or other equity investment. There are no legal requirements to disclose research collaborations or other partnerships, making comprehensive coverage through public filings difficult. Similarly, unlike acquisitions, there is currently no mechanism for government review of these transactions. We also do not have any existing databases or academic research that would allow a comprehensive review of the state of such relationships. For this reason, we have attempted to develop a typology of the most common types of partnerships in the biotech industry, explain what they entail, and provide examples.

Historically, many firms have sought Chinese partners to facilitate sales/distribution in the Chinese market or to access low-cost production capabilities. As one of many examples, Celsion Corporation paid

Zhejiang Hisun Pharmaceutical \$5 million for the manufacturer of Celsion's ThermoDox® drugs.²⁷⁰ Similarly, Intuitive Surgical and Fosun Pharma formed a joint venture in 2016 to manufacture and distribute catheter-based medical devices in China.²⁷¹ This section provides evidence that, beyond these tactical and limited engagements, Chinese entities are entering deeper, longer-term and more speculative partnerships.

(1) Industry-to-industry collaborations: Chinese biotech companies have entered partnerships with foreign biotech firms for the purposes of joint R&D; co-development of drugs; supply of products and services; and joint sales and marketing of products. Most early collaborations were driven by foreign firms entering the Chinese market but in recent years such partnerships are increasingly driven by the growing global presence of Chinese companies. There has been a marked increase in activity in the past three years, but the exact scope of global activity is difficult to capture due to a lack of data. Examples include:

- A partnership between Eli Lilly and Shanghai-based Innovent Biologics in early 2015 to co-develop cancer drugs, through which Eli Lilly gained access to two of Innovent's cancer drugs and the Chinese market, while Innovent gained one of Eli Lilly's drugs;²⁷²
- A partnership between UK genomics software company Congenica and BGI Genomics in 2017 to bring advanced drugs to China, through which Congenica received funding from BGI and access to genomic data from the Chinese population, and BGI gained access to Congenica's DNA analysis software Sapientia;²⁷³
- The aforementioned technology transfer and commercial supply partnership between Celsion Corporation and Zhejiang Hisun Pharmaceutical in 2016;²⁷⁴ and
- A partnership between BGI and five Canadian biotech companies in late 2016 to apply sequencing technology to patient therapy, wherein BGI provides low-cost, high-throughput sequencing capabilities while gaining access to Canadian genomic data.²⁷⁵

(2) Corporate partnerships with universities, think tanks, and other research institutions:

Partnerships between industry and academia have become common. As part of this trend, Chinese firms have partnered with foreign universities, for example, WuXi AppTec's 2015 development and manufacturing partnership with the University of Pennsylvania's gene therapy program to develop viral vectors to deliver gene therapies.²⁷⁶ This partnership provided Penn researchers with new cell and gene therapy manufacturing capabilities while WuXi could leverage the viral vector production expertise of the researchers. Chinese universities are also participating in partnerships with foreign firms, for example, Shanghai Tech University's iHuman Institute and Shanghai Institute of Materia Medica's participation in the GPCR Consortium, an open-source research collaboration with drug makers such as Amgen, Sanofi and ONO.²⁷⁷ In this instance, consortium members get access to protein structural coordinates, reagents and supporting data, while researchers gain access to compounds and data from industry partners.

²⁷⁰ "Celsion Corporation and Zhejiang Hisun Pharmaceutical Company Enter Into Technology Development Agreement for ThermoDox® for the Greater China Territory," Celsion Corporation, updated January 22, 2013, <http://investor.celsion.com/news-releases/news-release-details/celsion-corporation-and-zhejiang-hisun-pharmaceutical-company>

²⁷¹ "Intuitive Surgical and Fosun Pharma Establish Joint Venture to Research, Develop, Manufacture and Sell Lung Cancer Diagnostic and Therapeutic Tools in China," Intuitive Surgical, updated September 29, 2016, <http://investor.intuitivesurgical.com/mobile.view?c=122359&v=203&d=1&id=2206833>

²⁷² Peter Loftus, "Lilly Joins With Chinese Biotech to Develop, Market Cancer Drugs," *The Wall Street Journal* March 19, 2015, <https://www.wsj.com/articles/lilly-joins-with-chinese-biotech-to-develop-market-cancer-drugs-1426820402>

²⁷³ Angus Mcneice, "Top DNA sequencing provider partners UK genomics group," *China Daily* May 10, 2017, http://europe.chinadaily.com.cn/business/2017-05/10/content_29280036.htm

²⁷⁴ Celsion Corporation, "Celsion Corporation and Zhejiang Hisun Pharmaceutical Company Enter Into Technology Development Agreement for ThermoDox® for the Greater China Territory," <http://investor.celsion.com/news-releases/news-release-details/celsion-corporation-and-zhejiang-hisun-pharmaceutical-company>

²⁷⁵ Chuck Chiang, "Chinese genomics giant enters B.C. health research partnership," *Vancouver Sun* (2016), <https://vancouver.sun.com/news/local-news/chinese-genomics-giant-enters-b-c-health-research-partnership>

²⁷⁶ John George, "Penn in partnership to produce gene therapies at Navy Yard," *Philadelphia Business Journal* (2015), https://www.bizjournals.com/philadelphia/morning_roundup/2015/06/phil-penn-gene-therapy-wuxi-apptech-navy-yard.html

²⁷⁷ "GPCR Consortium," GPCR Consortium, <http://gpcrconsortium.org/>

(3) Government-promoted networks and initiatives: Chinese firms and research institutions are also increasingly involved in government-related biotechnology R&D programs. Examples are the China-Germany Bioscience Innovation Platform, which was launched by China's Ministry of Science and Technology and Germany's Federal Ministry of Education and Research (BMBF) in 2002 with the goal to facilitate academic research, cooperation, and innovation projects on biomedicine, biopharmaceuticals, and new biological materials.²⁷⁸ In 2013, China and the UK set up the UK-China Research and Innovation Partnership Fund, and both sides promised to provide \$273 million within five years to support research and cooperation in areas including stem cells, health, food security and other topics.²⁷⁹

(4) Research partnerships and collaborations between universities: Partnerships between Chinese and foreign universities provide avenues for exchange of knowledge and capabilities. For example, Peking University and Yale University launched Peking-Yale Joint Center for Plant Molecular Genetics and Agro-biotechnology in 2000 to facilitate research exchange on plant biology and genomics research, and has received funding from Monsanto, the Rockefeller Foundation, and the Chinese Ministry of Education (MOE).²⁸⁰ In early 2018, Shenzhen University and the State University of New York at Buffalo set up the first translational medicine research platform in China, together with Hong Kong Polytechnic University and Roswell Park Comprehensive Cancer Center.²⁸¹ This partnership involves utilizing joint expertise to push forward R&D in cancer, genomics, translational medicine, and other topics in biotechnology. In another example, Washington State University has a broad research and exchange partnership with China's Northwest Agriculture and Forestry University on agriculture, biofuels and bio-products production.²⁸²

While our sample of transactions is by no means comprehensive, several trends stand out. First, collaborations between Chinese and foreign firms have evolved from a mostly domestic focus on the Chinese market to a global scope. Second, the most integral countries for these engagements seem to be the United States, Canada, Japan, Singapore, Australia, and Western European nations, which correlates with the abundance of advanced biotech companies and talents working in the industry. Third, these collaborations offer an important complement to investments and other forms of interaction, and they contribute to the commercial success and profitability of the companies. Lastly, looking forward, it seems that Chinese companies have strong interests to further increase these kinds of partnerships to address gaps and make up for missing capabilities.

Foreign regulators have traditionally not scrutinized research partnerships between domestic firms and overseas entities. As described in Section 2.5, while debates about the national security risks surrounding these relationships always existed, Western liberal democracies have traditionally taken the approach to limit government intervention to a minimum to encourage global commerce and let corporations make decisions based on profit interests. This hands-off approach may be changing, though; recently, the US Congress passed rules to expand protection to include "foundational technologies," through reform of export control rules and the CFIUS review process.²⁸³ There have also been discussions to restrict research partnerships with Chinese entities in certain areas through other means, but no concrete steps

²⁷⁸ Lin Xingxiu. *Science and technology cooperation between major developed countries and China: How do countries in Europe and the United States understand China's science and technology, How to cooperate with China*: Center for Research and Development Strategy: Japan Science and Technology Agency, 2016. [Chinese Language Source]

²⁷⁹ "About Partnering Countries: China," Newton Fund, <http://www.newtonfund.ac.uk/about/about-partnering-countries/China/>

²⁸⁰ YaleNews, "Peking-Yale Center Receives Gift from Monsanto for Plant Biology Research Fellowships," (2002), <https://news.yale.edu/2002/11/14/peking-yale-center-receives-gift-monsanto-plant-biology-research-fellowships>

²⁸¹ "The First Greater Bay Area Biotechnology and Translational Medicine International Collaboration in the United States · China · Guangdong - Hong Kong - Macau Greater Bay Area," The Hong Kong Polytechnic University, updated February 2, 2018, https://www.polyu.edu.hk/web/en/media/media_releases/index_id_6507.html

²⁸² "Collaboration with Northwest Agriculture & Forestry University in China," Washington State University, Biological Systems Engineering, updated November 13, 2017, <https://bsyse.wsu.edu/2017/11/13/collaboration-with-northwest-agriculture-forestry-university-in-china/>

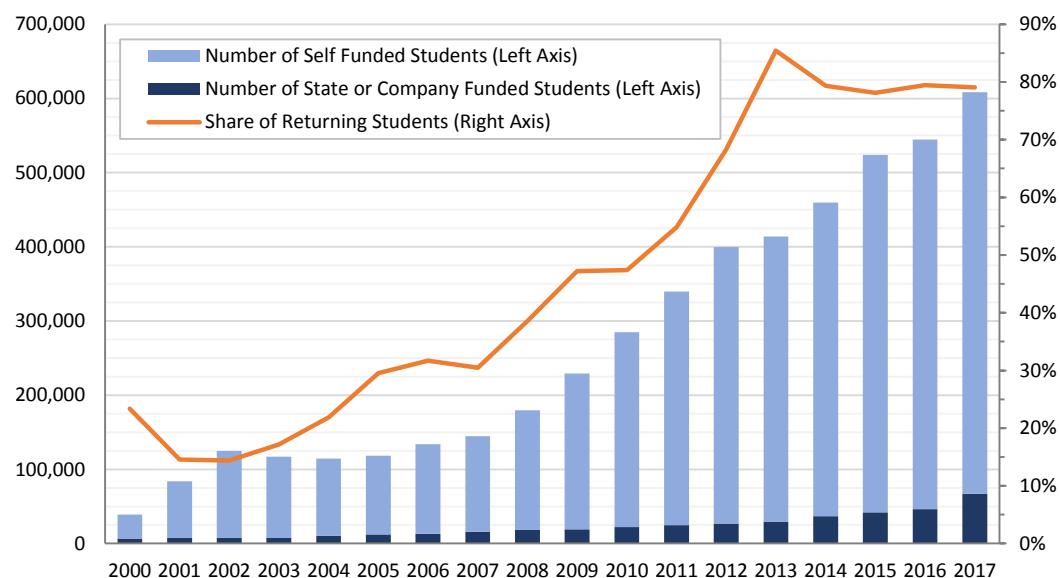
²⁸³ National Law Review Staff, "Export Control Reform Act Introduced in Congress," *National Law Review* March 8, 2018, <https://www.natlawreview.com/article/export-control-reform-act-introduced-congress>; IEEE-USA Staff, "Congress Looks to Update Export Controls to Include 'Emerging and Foundational Technologies'," *IEEE-USA InSight* June 16, 2018, <https://insight.ieeeusa.org/articles/congress-looks-update-export-controls-include-emerging-foundational-technologies/>

have been taken.²⁸⁴ Of critical importance in these reforms is how one defines foundational technologies and what technologies will be included; the legislation only determines a process by which a definition is to be developed. As the responsible agencies proceed, caution must be exercised so that excessive restriction does not inhibit the growth of technologies and innovation within the US. A more thorough discussion of US protective measures on technology is presented in Chapter 3.

2.3.3. Overseas Scientists

The development of China's S&T capabilities benefits from students and researchers at institutions around the world, both from Chinese students at foreign universities returning to China and from recruitment of top scientists and academicians abroad to work at Chinese institutions. According to Chinese sources, the number of overseas Chinese students in all fields has grown from an average of 100,000 before 2008 to 300,000 in 2011 and to more than 600,000 in 2017 (Figure 2-10).²⁸⁵

Figure 2-10. Annual Number of Overseas Chinese Students



Source: Chinese Ministry of Education; Institute of International Education.

While the numbers provided by MOE do not provide a breakdown of Chinese overseas students in biotech-related fields, we know that a significant share of overseas students are studying STEM subjects. Using available figures from the US (which hosts around half of total Chinese overseas students) as a proxy for global distribution, we estimate more than 40 percent of total students are studying STEM subjects (Figure 2-11).²⁸⁶

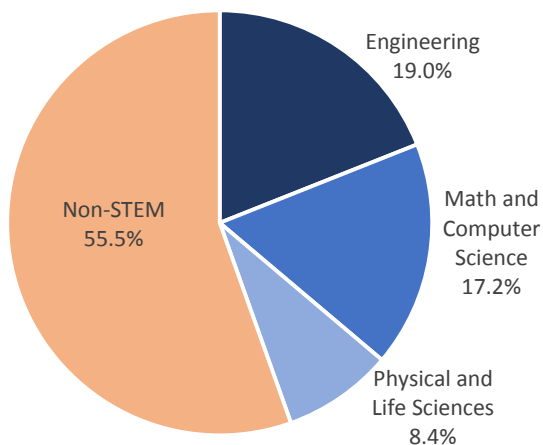
²⁸⁴ Koh Gui Qing, "Exclusive: U.S. considers tightening grip on China ties to corporate America," *Reuters* April 27, 2018, <https://www.reuters.com/article/us-usa-trade-china-regulations-exclusive/exclusive-u-s-considers-tightening-grip-on-china-ties-to-corporate-america-idUSKBN1HY0FJ>

²⁸⁵ "In 2017, the Number of Students Studying Abroad and Returning to China Doubled," Ministry of Education of the People's Republic of China, updated March 30, 2018, http://www.moe.gov.cn/jyb_xwfb/gzdt_gzdt/s5987/201803/t20180329_331771.html [Chinese Language Source]

²⁸⁶ Institute of International Education, "International Students by Field of Study, 2015/2016 - 2016/2017," *Open Doors Report on International Educational Exchange 2017*, <https://www.iie.org/Research-and-Insights/Open-Doors/Data/International-Students/Fields-of-Study>

Figure 2-11. Chinese Students in the US by Field of Study, 2015-2016 Academic Year

Percent of Students



Source: Institute of International Education.

In earlier years the majority of Chinese overseas students stayed in their host countries, with fewer than 25 percent of students returning to China at the beginning of this century (Figure 2-10). However, this trend has reversed: since 2013, over 80 percent of Chinese students abroad have returned. Reasons for the changing trends include improved career opportunities back home but also policies preventing graduates from staying in their host countries.²⁸⁷

As a result, hundreds of thousands of high-skilled young scholars and entrepreneurs are returning to China every year, providing a significant boost to the development of the Chinese biotech industry. Many of China's biotech startups have founders that were educated abroad. Biomics Biotechnologies was founded in 2006 by Yuanyuan Zhu, who holds an MD degree from Japan's Nagoya University and has served as lead scientist and research directors at several biopharmaceutical companies in Silicon Valley. Another example is Singlera Genomics, which was first founded in San Diego in 2014 by Yuan Gao, an associate professor at Johns Hopkins University. One of the founders of WuXi AppTec, Ge Li received his PhD in Chemistry from Columbia University. He was also one of the founding scientists of New Jersey-based Pharmacopeia.²⁸⁸ Samantha Du received her PhD in Biochemistry from the University of Cincinnati, and was in charge of Pfizer's global metabolic licensing program; she is also the cofounder of Hutchison Medi-Pharma, a Nasdaq-listed biopharmaceutical company.²⁸⁹ Xiaodong Wang, founder of BeiGene, received his PhD in Biochemistry from the University of Texas and founded US-based oncology company Joyant Pharmaceuticals.²⁹⁰ Steve Yang, former vice president of AstraZeneca, received his PhD in Chemistry from the University of California, San Francisco, and his Bachelor of Science degree from Michigan Technological University. He is now the Executive Vice President of WuXi AppTec.²⁹¹

In addition to market factors and overseas policy, the Chinese government has also put in place programs that aim to facilitate recruitment of top scientists abroad, including the return of achieved scholars in S&T fields. The Hundred Talents Program, established in 1994 by CAS, was the first of many programs designed to recruit scholars from abroad with an initial goal to recruit 100 "outstanding scholars" by the end of the 20th century.²⁹² By 2002, 839 participants had joined the academy through the

²⁸⁷ Wang Huiyao et al. *Annual Report on the Development of Chinese Studying Abroad 2017* Beijing: Center for China & Globalization, 2017. [Chinese Language Source]

²⁸⁸ "Dr. Ge Li," WI Harper Group, https://wiharper.com/team_member/dr-ge-li/

²⁸⁹ "Management Team," Zai Lab, <http://www.zailaboratory.com/about/management-team.php>

²⁹⁰ "Xiaodong Wang, Ph.D.," BeiGene, <http://www.beigene.com/team/xiaodong-wang-ph-d-3/>

²⁹¹ "Dr. Steve Yang," WuXi AppTec, <http://idsu.wuxiapptec.com/steve-yang/>

²⁹² "Hundred Talents Program," University of Science and Technology of China School of Engineering Science, <http://en.ses.ustc.edu.cn/7386/list.htm>

program.²⁹³ The Thousand Talents Program was established in 2008 and aimed at bringing back global experts from abroad with scientific backgrounds (PhD degrees) to support innovation and entrepreneurship in China. Originally designed to entice repatriation of Chinese citizens but now accepting foreign nationals as well, the program awards monetary support ranging from \$150,000-\$450,000 to set up their projects once they are back in China.²⁹⁴ The National Science Fund for Distinguished Young Scholars is funded by the National Natural Science Foundation of China and supports Chinese scholars under the age of 45 with 1-2 million yuan (\$155-310 thousand) to do four years of research in China.²⁹⁵ The expertise sought by these programs is not solely focused on biotechnology or the physical and life sciences, but S&T research is a significant component of each of them.

Participants in talent programs include professors and scholars in foreign universities and research institutes, advanced technical talents and managers in top companies or financial institutes, professionals with entrepreneurial experience and patents, and talents in other national strategic industries. In practice, the majority of these global experts are Chinese citizens with overseas experience or former Chinese citizens living abroad. According to Chinese government information, the Thousand Talents Plan has facilitated the return of 114 overseas scholars in the biomedicine and biotechnology areas to China (out of 7,018 total through August 2017).²⁹⁶ For example, Lizhong Dai, who holds a PhD degree from Princeton University and completed his postdoc study at the Massachusetts Institute of Technology (MIT), founded Sansure Biotech in 2008 and was selected by the Thousand Talent Program in 2010. A more detailed look at the talent programs and Chinese researchers in the US is presented in Section 4.2.

In recent years, law enforcement in the US and other countries has become increasingly wary of potential theft of trade secrets and other illicit transfer of technology through the overseas Chinese student and research community (see Section 2.4). Over the past year, the US government has also considered plans to restrict visas for Chinese students and scholars in areas relevant to national security as well as alleged IP theft.²⁹⁷ In June 2018, the first such policy was announced, shortening the duration of visas from five years to one year for students planning to study aviation, robotics, and advanced manufacturing (students who remain in the US will not be forced to leave, but those who travel abroad after one year, for instance, to present their work at international conferences, would need to reapply).²⁹⁸ While this policy does not yet impact students in the biotechnology field, discussions about student restrictions continue and similar policies for the biotechnology field could be enacted in the future.

2.4. Espionage and Other Illicit Activities

In addition to legitimate commercial and social interaction, China's biotech industry may have also benefited from illicit extraction of overseas technology through espionage or the theft of trade secrets. Only so much can be said about this topic without the release of classified materials, so the scope and patterns of criminal activities benefitting Chinese entities is impossible to describe accurately in a public document. However, court documents and other public materials illustrate that the biotech industry has been a target for such activity since at least the 1990s (Table 2-4).

The majority of these cases involve Chinese citizens who targeted genetically engineered agricultural products, seeds, IP-related information, or chemical or biological products. At least six theft attempts have occurred within the medical industry. Theft and espionage attempts have targeted a wide range of

²⁹³ Cong Cao, "China's Brain Drain at the High End," *Asian Population Studies* 4, no. 3 (2008): 331-45.

²⁹⁴ China Youth Daily, "海归青年科学家：回到生我养我的地方做点事很光荣," (2018), http://www.xinhuanet.com/science/2018-03/01/c_137007383.htm

²⁹⁵ "NSFC Launched the National Science Fund for Distinguished Young Scholars (Chinese Bearing Foreign Nationality)," National Natural Science Foundation of China, <http://www.nsf.gov.cn/publish/portal1/tab158/info39616.htm>; "National Science Fund for Distinguished Young Scholars," <http://www.nsf.gov.cn/Portals/0/fj/english/fj/pdf/2013/081.pdf>

²⁹⁶ "Terms under the category 'Biomedicine and Biotechnology'," Thousand Talents Plan Network, <http://www.1000plan.org/wiki/index.php?category-view-13> [Chinese Language Source]

²⁹⁷ Jessica Donati and Te-Ping Chen, "It Just Got Harder for Chinese People to Secure U.S. Visas," *The Wall Street Journal*(2018), <https://www.wsj.com/articles/u-s-toughens-visa-process-for-chinese-nationals-1527705281>

²⁹⁸ Jeffrey Mervis, "Stricter Chinese student visas raise alarm," *Science* 360, no. 6394 (2018): 1161.

treatments and equipment, including robotic surgical equipment, cancer treatments, treatments for organ recipients, cornea regeneration, hepatitis C diagnostics, and an anemia drug. The agricultural industry has also been targeted on multiple occasions. Two theft attempts involved stealing genetically engineered rice or corn seeds, while other thefts have targeted organic pesticides, engineered food products, and livestock feed supplements.

The majority of theft attempts were directed against a current or former employer (Table 2-4). Ventria Bioscience, GlaxoSmithKline, Dow AgroSciences LLC, Cargill Inc, Roche Diagnostics, and Amgen have all experienced theft of trade secrets or biological materials perpetrated by a current or former employee(s) with the intent to sell it to a Chinese competitor. In the academic sector, researchers have stolen information or samples from their employers at Cornell University, Harvard University, and UC Davis. Most individuals were motivated by personal financial gain. These individuals would sell the trade secrets and information to Chinese companies that planned to commercialize the stolen trade secrets or market copy-cat products in China.

In addition to these cases, biotech firms have also reportedly been a major target of state-sponsored cyber espionage. According to US-based cybersecurity firm Mandiant, there has been an increased number of hacking incidents targeting biotech companies from China since 2008, and these activities are associated with government-directed groups.²⁹⁹ Relevant reports claim that hacking efforts are correlated with Chinese industrial policy goals and aim at accessing relevant drug information, formulas, and data from leading US companies.³⁰⁰ Beijing has refuted these claims.

While hacking activity seems to have declined after high-level dialogues between the US and China, it remains a constant threat. US law enforcement and counter intelligence have doubled their efforts in recent years – which has led to harsh criticism by overseas Chinese communities against racial profiling.³⁰¹

Table 2-4. Select Cases of Chinese Espionage and Trade Secret Theft in the Biotech Industry

Date	Description	Industry Targeted
2017	Chinese scientist Weiqiang Zhang convicted of conspiracy to steal trade secrets after stealing samples of genetically engineered rice seeds from his employer, Ventria Bioscience Inc, and providing them to employees of a Chinese crop research institute. ³⁰²	Agriculture
2017	Chinese-Canadian citizen Liu Dong charged with attempting to steal trade secrets and attempting to intentionally access a computer without authorization in an effort to steal information from Medrobotics Corp, a manufacturer of robotic surgical products. ³⁰³	Medicine
2016	Two employees and three outside accomplices charged with stealing trade secrets from GlaxoSmithKline after downloading data on multiple company products, including a monoclonal antibody involved in cancer treatment, and transferring the data to Chinese associates who planned to market the stolen products in China. ³⁰⁴	Medicine

²⁹⁹ Shannon Ellis, "U.S. Biopharma Firms Hit by Cyber Attacks from China," *Bioworld*(2018), <http://www.bioworld.com/content/us-biopharma-firms-hit-cyber-attacks-china-0>

³⁰⁰ Ibid.

³⁰¹ Andrew Kim. *Prosecuting Chinese "Spies: An Empirical Analysis of the Economic Espionage Act* Washington, DC2017.

³⁰² Reuters, "China scientist convicted in U.S. of theft of engineered rice," (2017), <https://www.reuters.com/article/us-usa-justice-rice-idUSKBN15V2W0>

³⁰³ "U.S. charges Chinese-Canadian citizen with trade secret theft," (2017), <https://ca.reuters.com/article/topNews/idCAKCN1BB2K8-OCATP>

³⁰⁴ Katie Thomas, "5 Accused of Stealing Drug Secrets From GlaxoSmithKline," *The New York Times*(2016), <https://www.nytimes.com/2016/01/21/business/5-accused-of-stealing-drug-secrets-from-glaxosmithkline.html>

Date	Description	Industry Targeted
2015	Chinese hackers allegedly tied to massive data breach at the US healthcare insurance agency Anthem by using malicious software. Report published by a security firm tied the hackers to Chinese military and intelligence agency. ³⁰⁵	Healthcare
2015	US provider of healthcare services Premera Blue Cross says an intrusion into its network may have resulted in the breach of financial and medical records of 11 million customers. Arlington, Va. based security firm ThreatConnect, Inc. published a blog saying the attack may have been linked to a Chinese state-sponsored hacking group known as "Deep Panda." ³⁰⁶	Healthcare
2013	Chinese employee of Dabeinong Technology Group Company Mo Hailong convicted for participating in a long-term conspiracy to steal proprietary inbred corn seeds from DuPont Pioneer and Monsanto. ³⁰⁷	Agriculture
2011	Chinese national Huang Kexue convicted on charges of economic espionage for stealing trade secrets related to organic pesticides and engineered food products from his employers, Dow AgroSciences LLC and Cargill Inc, and transferring the information to individuals in China and Germany. ³⁰⁸	Agriculture
2006	Chinese researcher Zhu Jiangyu and his Japanese wife Kayoko Kimbara accused of stealing antibodies involved in treatments for organ recipients from Harvard University and mailing samples to a Japanese biotech company for commercialization. ³⁰⁹	Medicine
2002	Chinese researcher Qingqiang Yin at Cornell University convicted of stealing biological materials related to a livestock feed supplement and attempting to transport the materials to China. ³¹⁰	Agriculture
2002	Han Bing, a naturalized US citizen of Chinese descent and researcher at UC Davis, charged with stealing an experimental protein involved in cornea regrowth and wound healing with intent to transport materials to China. ³¹¹	Medicine
2001	US citizen from China Pei Huang Dao charged with attempting to steal proprietary information about a hepatitis C diagnostic kit from his former employer Roche Diagnostics with intent to develop and sell a similar kit in China. ³¹²	Medicine

³⁰⁵ ThreatConnect Research Team, "The Anthem Hack: All Roads Lead to China," *ThreatConnect*(2015), <https://threatconnect.com/the-anthem-hack-all-roads-lead-to-china/>

³⁰⁶ Brian Krebs, "Premera Blue Cross Breach Exposes Financial, Medical Records," *KrebsSecurity*(2015), <https://krebsonsecurity.com/2015/03/premera-blue-cross-breach-exposes-financial-medical-records/>

³⁰⁷ United States Department of Justice. "Chinese National Sentenced to Prison for Conspiracy to Steal Trade Secrets." 2016. <https://www.justice.gov/opa/pr/chinese-national-sentenced-prison-conspiracy-steal-trade-secrets>

³⁰⁸ "Chinese National Sentenced to 87 Months in Prison for Economic Espionage and Theft of Trade Secrets First Prosecution in Indiana for Foreign Economic Espionage." 2011. <https://archives.fbi.gov/archives/indianapolis/press-releases/2011/chinese-national-sentenced-to-87-months-in-prison-for-economic-espionage-and-theft-of-trade-secrets-first-prosecution-in-indiana-for-foreign-economic-espionage>

³⁰⁹ Doug Most, "Stealing Science," *Boston*(2006), <https://www.bostonmagazine.com/2006/05/15/stealing-science/>

³¹⁰ Charles Choi, "Lab theft conviction," *The Scientist*(2002), <https://www.the-scientist.com/news-analysis/lab-theft-conviction-52348>

³¹¹ Tom Abate, "Trade secrets case troubles UC Davis / Missing protein, ticket to China found in home of research worker," *SFGate*(2002), <https://www.sfgate.com/business/article/Trade-secrets-case-troubles-UC-Davis-Missing-2830842.php>

³¹² Peter J. Toren, "Federal Prosecution of Thefts of Trade Secrets Under the Economic Espionage Act of 1996 " 2001, <http://www.fcoverup.com/docs/library/2001-03-28-Trade-Secrets-and-Enforcement-of-Intellectual-Property-Rights-Conference-NIPLI-Prof-James-P-Chandler-Mar-28-2001.pdf>

Date	Description	Industry Targeted
1993	Amgen fired one employee after discovering a plot to steal a vial of cell cultures for Epogen, a billion-dollar anemia drug, and sell it to a Chinese buyer. ³¹³	Medicine

2.5. Regulatory Supervision of Foreign Interaction with Chinese Biotech Firms and Individuals

While our global coverage is imperfect, we show that most Chinese cross-border activity in biotech is concentrated on North America and Europe, as well as a few countries in Asia (Singapore) and Oceania (Australia). These countries have major biotechnology industry concentrations with the highest number of companies and talents.

Most of these nations have traditionally followed liberal economic policies that limit government intervention to a minimum, which means screening of M&A for national security risks and competition concerns and control of dual-use technology through export control regimes (Table 2-5). There are efforts to increase supervision of other flows (including the screening of venture capital or restrictions on students and researchers), but this is mostly limited to the United States. In addition, there is no meaningful coordination among OECD governments on investment screening and no initiatives on biotech specifically.

Table 2-5. Regulatory Tools in OECD Countries to Review Conduits of Economic Interaction with China

Overseas Regulatory Measures	
Foreign Investment in China	
Direct Investment: Greenfield FDI and Acquisitions	Restrictions on the export of sensitive dual-use technologies
Overseas Listings	Transparency and financial disclosure requirements by securities regulators
VC and other portfolio investment	No restrictions
Chinese Outbound Investment	
Direct Investment: Greenfield FDI and Acquisitions	National security screening for inbound foreign acquisitions in most countries
VC and other portfolio investment	Transparency and disclosure requirements if stakes exceed certain threshold
Other Channels	
Technology acquisitions and licensing	Restrictions on the export of sensitive dual-use technologies
Research partnerships	Restrictions on the export of sensitive dual-use technologies
Overseas university education	Restrictions on the export of sensitive dual-use technologies

³¹³ Ann Harrington, "China's Spies Target Corporate America In the great game of economic espionage, China is emerging as a bold new player. Its primary mission: to get its hands on the world's most advanced technology.," *Fortune*(1998), http://archive.fortune.com/magazines/fortune/fortune_archive/1998/03/30/240104/index.htm

Overseas Regulatory Measures	
Espionage and Other Illicit Activities	
Espionage and Other Illicit Activities	Law enforcement; counter espionage

Source: Authors' compilation.

Given the extensive linkages between the Chinese and overseas biotech industries as well as the growing uncertainty about China's economic and political outlook, it is legitimate and important for policymakers to re-assess traditional approaches to regulating these cross-border interactions to ensure that potential security risks and economic concerns are addressed.

However, the deep interconnectedness and the nature of the biotech industry also means that potential downsides from policy disruption are substantial. Any policy changes need to be considered carefully for their costs to consumers, patients and businesses. Furthermore, international coordination of "like-minded" countries could be a very promising avenue for accomplishing effective policy changes. Compared to other sectors, the biotech industry is relatively concentrated and China's interaction with OECD nations is focused on a handful of countries. That means that international coordination to address potential security and economic concerns would require fewer nations to participate, increasing the prospect for success.

3. Chinese Investment in the US Biotechnology Industry

Key Findings

- Chinese investment in the US biotechnology sector was small but has grown rapidly in the past five years, reaching over \$500 million per year since 2014.** The sector accounts for only two percent (\$3.8 billion) of cumulative Chinese investment in the US in 2000-2017, but investment has picked up since 2014 and remained resilient despite a sharp overall drop in Chinese investment in North America in 2017 and 2018. In 2018, the health and biotechnology industry became the top recipient of Chinese capital in the US, surpassing real estate and entertainment.
- Chinese investment in US biotech predominantly (96 percent) came in the form of acquisitions and startup financing:** 67 percent of Chinese capital can be attributed to acquisitions of US companies, while VC and other portfolio investment contributed 29 percent. Greenfield FDI in R&D centers and manufacturing remained small (4 percent).
- Almost all Chinese investment occurred in medically-related biotechnology segments.** Seventy percent of total Chinese investment has been in biologics and contract research and manufacturing (which support the biologics industry), reflecting China's stated policy interest in biopharmaceuticals and demand on the healthcare market and mirroring the high level of biologics development activity occurring domestically in China. Another 22 percent was in genomics, molecular diagnostics, and precision medicine. Correlation between Chinese investment and the level of existing domestic activity in the target biotech segments indicates that Chinese investment is focused on reinforcing existing capacities back home rather than expanding into newer fields.
- Chinese investment in the US biotech sector is overwhelmingly private—only 3 percent of the total Chinese investment in biotech since 2000 came from formally state-owned actors.** The role of state-owned investors is much smaller in biotech than in overall Chinese investment in the United States (24 percent). However, the Chinese government can influence investment decisions of Chinese firms through various channels including investment approvals, industrial policy and coercion.
- US regulatory reform is providing new abilities to address security concerns raised by Chinese investments into biotechnology.** A long-standing investment screening regime, CFIUS, has allowed the US government to review inbound M&A from China but not VC transactions that stayed below a certain equity threshold. Recent reform of US investment screening and export control rules will allow the US government to expand its review to include foreign VC transactions meeting certain criteria and impose restrictions on the licensing and transfer of critical emerging technologies.
- The growth potential for Chinese outbound investment remains large, but policy uncertainty in both China and the United States clouds the outlook.** Economic fundamentals indicate significant growth opportunities but the policy environment in China and the United States is complicated. China continues to impose restrictions on certain types of outbound investment, and the US has passed a reform of the CFIUS process while considering additional restrictions on foreign investment. The direction of these developments could overshadow the expansion of Chinese capital flows to the US biotech market.

This chapter provides an overview of Chinese investments in the US biotechnology industry by type, volume, and value. We also analyze how these investments have contributed to the development of China's biotech industry with segment-specific analyses. Finally, we review the existing US regulatory framework for reviewing inbound investment from China.

3.1. Annual Flows and Stock

This section provides an overview of the landscape of Chinese investment in the US biotechnology sector from 2000-2017. The data are based on Rhodium Group's proprietary database, which aggregates nearly 200 individual investment transactions in the biotech industry, including Chinese acquisitions of US biotech companies, greenfield establishments in the US, and participation in VC and other portfolio investment rounds. Compared to those used in Chapter 2, this dataset is narrower and more substantiated and includes all Chinese investments with a biotechnology component in the US. Another key difference is that for this more detailed perspective, we estimate and include only the Chinese portion of each venture capital fundraising round, as opposed to the full value in the overview in Chapter 2. For the full methodology of datasets that we utilize for Chapter 3, please refer to the Methodology Appendix.

Our data cover investments in target companies that wholly engage in biotechnology activities as well as those that only partially engage in biotechnology activities. The latter category adds up to \$539 million in Chinese investment from 2000-2017, and the two most prominent transactions are WuXi PharmaTech's 2008 acquisition of AppTec (\$163 million) and Legend Capital and CITIC's investment in Pharmaron (\$280 million).

In total, we record \$3.8 billion in Chinese investment in the US biotechnology sector in 2000-2017. Investments were barely visible before 2009 with the exception of WuXi PharmaTech's acquisition of AppTec in 2008. Annual flows began to pick up in 2010 with several sizable deals that year (Decheng Capital's investment in Ion Torrent, IDG Capital's investment in Origene, 3SBio's investment in EnzymeRx, and CIC's investment in Globelmmune). From 2014 to 2016, annual investment climbed to over \$500 million per year. The biggest deals during this time include Shenzhen Hepalink's investment in Scientific Protein Laboratories, Valiant's investment in MP Biomedicals, and WuXi PharmaTech's investment in NextCODE Health. In 2017, annual investment jumped up dramatically to over \$1.5 billion, tripling the amount in the previous three years (Figure 3-1). This was mostly due to one big deal: Sanpower's acquisition of Dendreon Pharmaceuticals for \$820 million.

Table 3-1. Top 10 Chinese Biotech Investments in the US (by value)

Value (millions)	Year	Type	US Target	Chinese Investor (Ownership)*	Category
\$820	2017	Acquisition	Dendreon Pharmaceuticals	Sanpower Group (private)	Biologics: Gene and cellular therapy
\$338	2014	Acquisition	Scientific Protein Laboratories	Shenzhen Hepalink Pharmaceutical (private)	Contract research or manufacturing
\$280	2015	Acquisition	Pharmaron Holding	Legend Capital, Citic M&A Fund Management (state-owned)	Contract research or manufacturing
\$206	2015	Acquisition	Cytovance Biologics	Hepalink USA (private)	Contract research or manufacturing
\$163	2008	Acquisition	AppTec Laboratory Services	WuXi PharmaTech (private)	Contract research or manufacturing
\$163	2017	Acquisition	SomaLogic	iCarbonX (private)	Genomics and related technologies
\$162	2017	Venture Capital	GRAIL	Decheng Capital, Tencent Holdings (private)	Molecular diagnostics and precision medicine

Value (millions)	Year	Type	US Target	Chinese Investor (Ownership)*	Category
\$143	2016	Acquisition	MP Biomedicals	Valiant (state-owned)	Research/discovery platforms, tools, and support products
\$118	2013	Acquisition	Complete Genomics	Beijing Genomics Institute (private)	Genomics and related technologies
\$65	2015	Acquisition	NextCODE Health	WuXi PharmaTech (private)	Genomics and related technologies

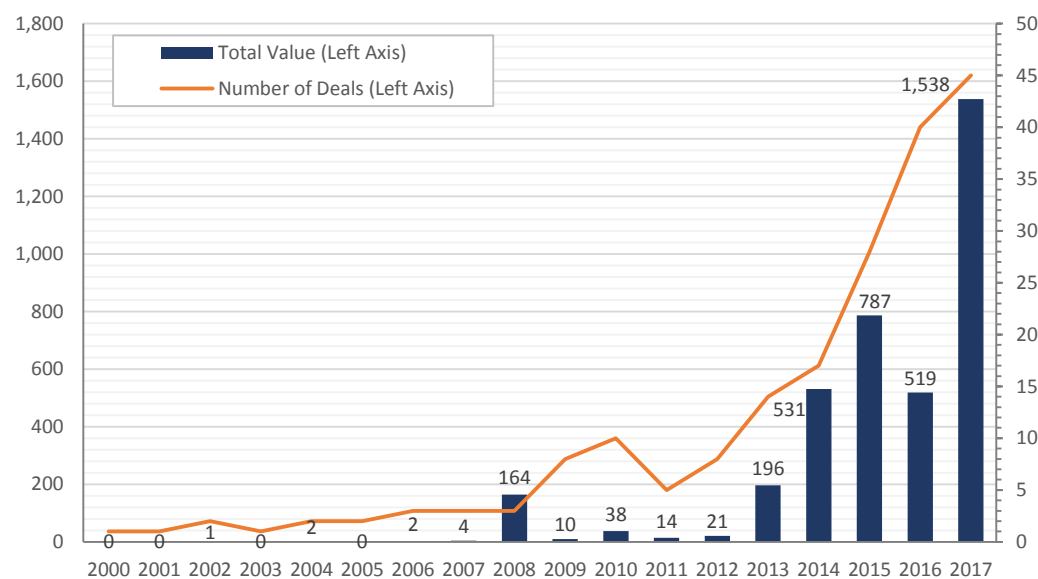
Note (*): State-owned refers to investments that have at least one investor with over 20 percent ownership by the government, the State Asset Supervision and Administration Commission, and other state-owned enterprises.

Source: Rhodium Group.

The numbers of transactions show a smooth and quick take-off in the past few years: doubling from less than ten transactions per year before 2013 to 28 transactions in 2015 and then doubling again to 45 transactions in 2017. While the headline investment figures are more volatile due to one-time, large deals, the smooth increase in the number of transactions per year shows that Chinese investment in the US biotech industry is indeed growing at an exponential speed.

Figure 3-1. Annual Chinese Investment in the US Biotechnology Sector, 2000-2017

USD million, number of transactions



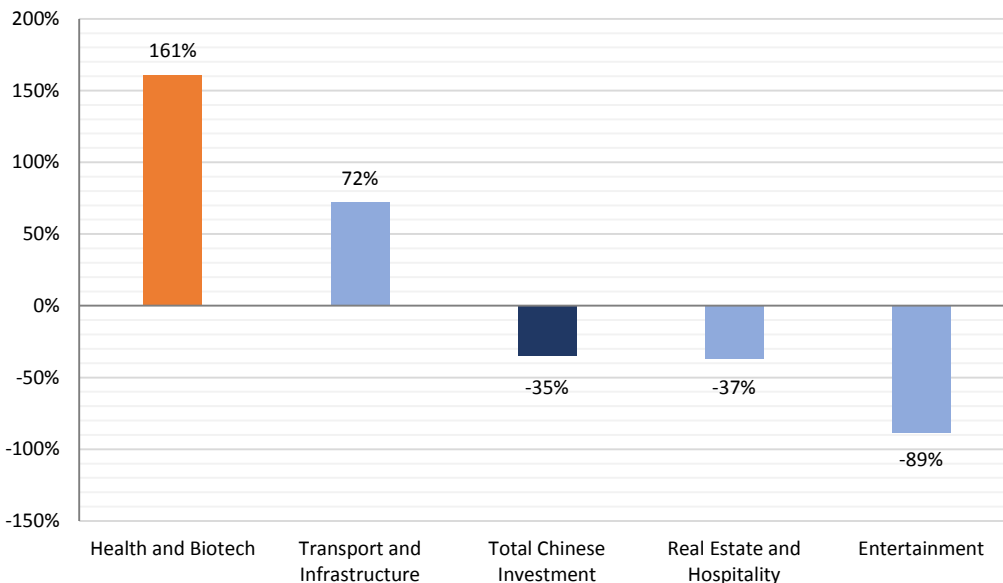
Source: Rhodium Group. Includes direct investment (acquisitions of 10% and more and greenfield projects), venture capital and other equity portfolio investments. For venture capital, only the estimated share of Chinese investors is counted.

Chinese investment in the US biotech sector makes up a small share of the overall Chinese investment in the US in 2000-2017 (\$3.8 billion out of a total \$175 billion, or 2 percent). However, it stands out as one of the fastest growing sectors in Chinese FDI in the US in recent years. In 2017, Chinese investment in the US biotechnology industry grew 187 percent, and investments in the broader industry group healthcare and biotechnology grew 161 percent (Figure 3-2).

The upward trend in the biotech sector between 2016 and 2017 is in stark contrast to overall Chinese FDI in the US: Chinese investment in the biotech sector more than doubled from \$405 million to \$1.5 billion in 2017, while overall Chinese FDI in the US dropped nearly 30 percent from \$52 billion to just \$38 billion. In terms of new activities, the drop in overall investment was even sharper; the value of newly announced Chinese FDI in the US dropped by 90 percent in 2017 compared to the previous year. The big increase in Chinese biotech investment in the US is driven by a few big deals in the biologics segment: Sanpower Group's \$820 million takeover of Dendreon Pharmaceuticals, iCarbonX's \$163 million acquisition of SomaLogic, and Decheng and Tencent's \$162 million investment in GRAIL.

Figure 3-2. Growth Rate of Chinese Investment in the US, Select Industry Groups

Percent growth rate 2017 vs. 2016



Source: Rhodium Group.

3.2. Entry Mode

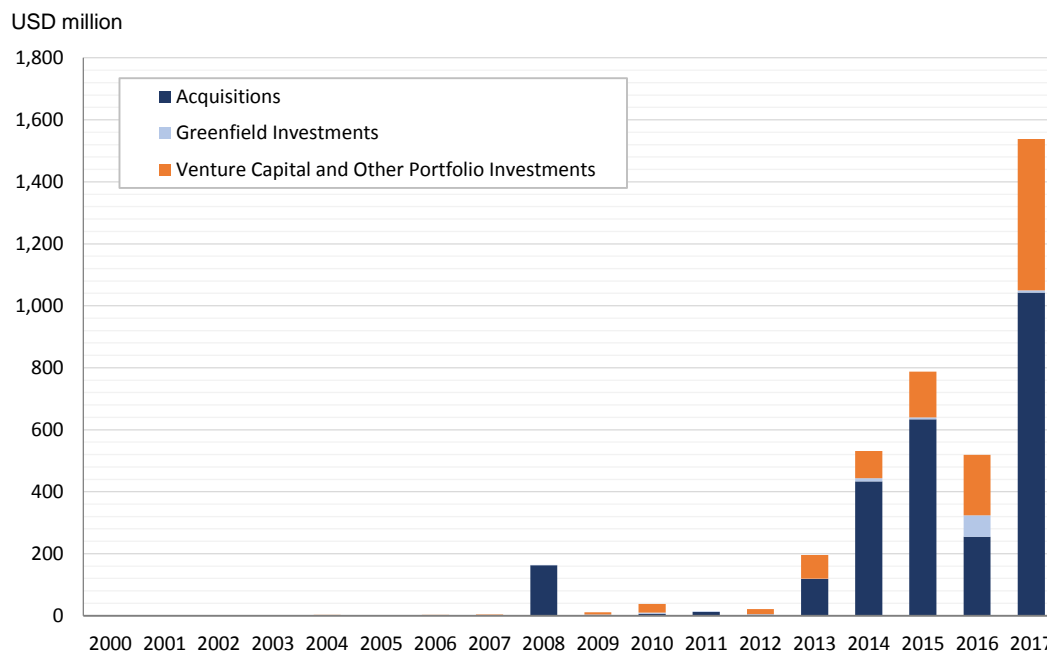
The majority of Chinese investments in the US biotech sector were M&A transactions (acquisition of more than a 10 percent stake in existing US companies). In total, acquisitions constitute 67 percent of cumulative Chinese biotech investment from 2000 to 2017 (Figure 3-3). In 2017, the value of biotech acquisitions surged due to a few big deals, contributing to the overall uptick. However, the relative share of acquisitions in total investment declined slightly in 2017 due to the increasing share of VC activity. In comparison, M&A made up 74 percent of total Chinese investment in the US in 2017.

Greenfield investment was traditionally a key channel for investing prior to 2009, making up on average 40 percent of annual values between 2000 and 2009. Since 2010, however, the share of greenfield investments in the total dropped dramatically as acquisitions and VC investments grew. As of 2017, greenfield biotech investments only made up 4 percent of the total cumulative Chinese investment. However, there was an uptick in 2016 due to a few sizable projects (WuXi AppTec's expansion in Philadelphia, Origin Agritech's office in Iowa, and BGI's office in Iowa). For overall Chinese investments in the US, greenfield investments also made up less than 10 percent between 2000 and 2017.

Chinese VC and other portfolio investments in the US biotech sector were very low before 2010, but have grown quickly in the past few years, making up 29 percent of the total as of 2017. Interestingly, VC investments were the earliest type of Chinese investment in the US biotech sector, emerging as early as 2002, while greenfield investments and acquisitions only followed later. This is in contrast with Chinese

investments in the rest of the US economy, where VC followed greenfield and M&A transactions at a later stage. This mostly reflects a greater propensity of the biotech industry to rely on VC as a financing source as well as existing linkages between early investors and the United States biotech industry.

Figure 3-3. Annual Chinese Investment in the US Biotechnology Industry by Entry Mode, 2000-2017



Source: Rhodium Group. Includes direct investment (acquisitions of 10% and more and greenfield projects), venture capital and other equity portfolio investments. For venture capital, only the estimated share of Chinese investors is counted.

In terms of the numbers of investments, greenfield investment has been steady at around four new projects per year since 2008. Acquisitions have grown slightly from less than three transactions per year before 2014 to six transactions per year in 2015-2017. VC and other portfolio investment rounds drive the recent growth in the number of investments: from virtually none to 10 rounds in 2014 and nearly 30 rounds in 2017.

3.3. Investor Mix

The investor mix of Chinese investment in the US biotech sector is overwhelmingly private (Figure 3-4), mirroring the sector overall (China's domestic biotechnology sector is one of the most open and private sector-dominated industries in China.).³¹⁴ In 2000-2017, only three percent of the total investment came from state-owned actors (Chinese companies that are at least 20 percent owned by the government, the State Asset Supervision and Administration Commission, and central state-owned enterprises). This is much lower than in overall Chinese investment in the US where more than 24 percent of total investment in the same period came from state-owned companies. In addition to formal state ownership, we count an additional \$56 million of "state-affiliated" investment (less than 20 percent state-ownership, or ownership by local state-owned enterprises), but together composes less than five percent of the total Chinese investment in the US biotech industry. Beyond nominal ownership, the Chinese government can influence investment decisions of Chinese firms through various channels including investment approvals, industrial policy and coercion (see Box 2).

³¹⁴ State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; private entities refer to companies with less than 20% ownership by the government, State-owned Assets Supervision and Administration Commission, and other SOEs.

Figure 3-4. Annual Chinese Investment in the Biotech Sector by Ownership*, 2000-2017

Note (*): State-owned refers to investments that have at least one investor with over 20 percent ownership by the government, the State Asset Supervision and Administration Commission, and other state-owned enterprises.

Source: Rhodium Group.

Box 2: State Influence on Chinese Outbound Investment Beyond Nominal Ownership

Nominal government ownership only plays a minor role in Chinese biotech investment in the US. However, there are a few other channels through which Beijing can still exert influence on private Chinese firms' overseas investments: First, Beijing can use capital controls to steer outbound investment. In 2016, China imposed capital controls on outbound investment, which brought down the overall levels of investment, particularly targeting investments in entertainment or real estate. Second, China's central and local governments often set up special funds to promote development in strategic sectors. For example, the Chinese central government established the \$22 billion National Integrated Circuit Fund for the semiconductors industry in 2014. In biotech, direct government investment funds come mainly in the form of large biotech industrial parks, which help develop small and medium-sized business as well as attract foreign companies. In addition to direct investment funds, there is ample financing support from state industry foundations and research funds, which are administered by national agencies such as the Ministry of Science and Technology (MOST). While most of these funds only invest in China, some also have a mandate to support outbound investment or international expansion of relevant companies. For example, the Wuhan Donghu District established in 2017 a special 1 billion yuan (\$155 million) fund for international development, supporting high-tech Chinese companies to innovate, industrialize, and expand their global footprint.³¹⁵ Lastly, most capital for private enterprises comes from government-owned banks, and those are bound by rules imposed by Chinese regulators. Though it is difficult to gauge its extent, direct government interference in individual transactions is always possible as Chinese companies have no legal recourse against government interference.

While VC and other financial investors comprised a quarter of the total, Chinese investment in the US biotech sector is still mostly for strategic purposes (72 percent) (Figure 3-5). This composition is very similar to overall Chinese investment in the US, where 77 percent of the total is made up of strategic investments, and only 23 percent is financial investments in 2000-2017. Strategic investments are those made primarily for long-term business integration and development. These include both investments made by biotech companies as well as those by funds of biotech companies (i.e., corporate VC funds).

³¹⁵ Xinhua News Agency, "Wuhan "China Optics Valley" set up 1 billion yuan to support internationalization," (2017)

Financial investments comprised only 28 percent of the total. These are investments that are made primarily for financial returns and consist of investors such as general VC funds and other pharmaceutical and biotech focused VC funds.

Figure 3-5. Annual Chinese Investment in the Biotech Sector by Motivation*



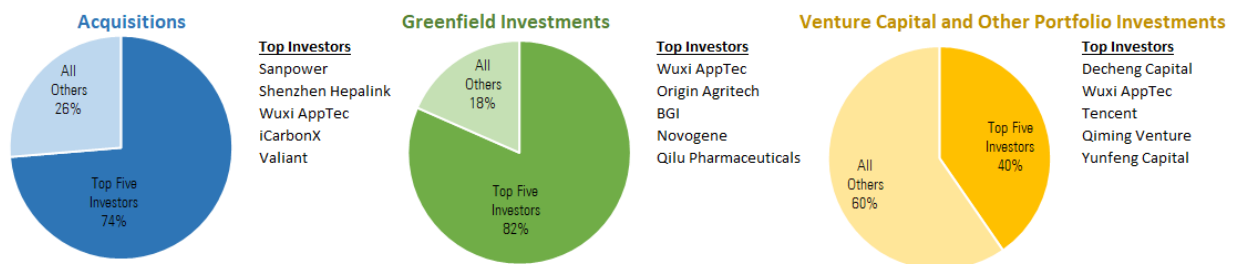
Note (*): Financial investments are those made primarily for financial returns, such as most venture capital and portfolio investments. Strategic investments are those made for long-term integration and business development, including most investments by corporate investors and biotech-focused funds.

Source: Rhodium Group.

Finally, we analyze the top Chinese investors in US biotech. Figure 3-6 shows the ranking and concentration of these companies as a share of total investment. Chinese investment in the US biotech sector has been largely driven by a few key players: three-quarters of total Chinese acquisitions are by the top five investors, and more than 80 percent of greenfield investments come from the top five Chinese companies. VC and other portfolio investments are less concentrated, but the top five actors still comprised 40 percent of total investment in 2000-2017. Combining all three channels, the top three investors are Sanpower, WuXi AppTec, and Shenzhen Hepalink. Sanpower and Shenzhen Hepalink surpassed the others through a few large deals, such as Dendreon Pharmaceuticals (Sanpower) and Scientific Protein Laboratories (Shenzhen Hepalink). WuXi AppTec, on the other hand, had numerous large and medium-sized investments that collectively pushed it to the top of the investors list.

Figure 3-6. Top Investors Concentration by Type of Investment, 2000-2017

Share of total investment value, 2000-2017



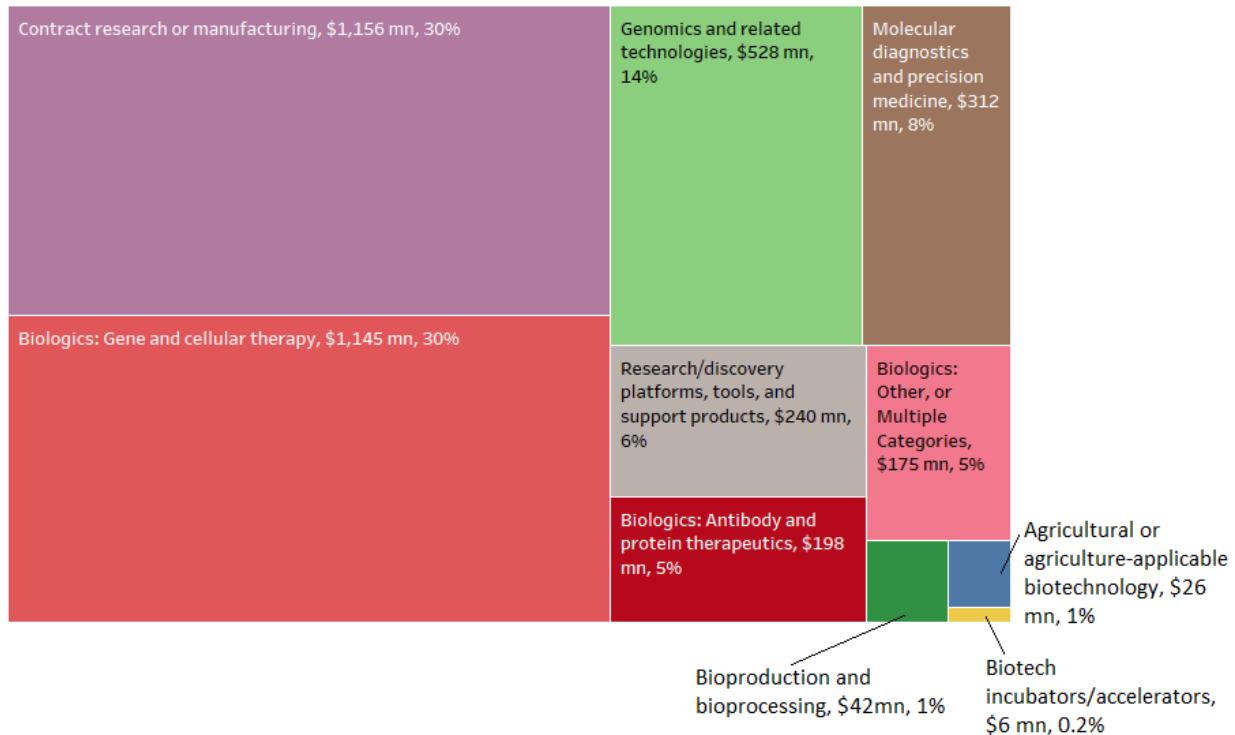
Source: Rhodium Group.

3.4. By Segments

Biologics and contract research and manufacturing are the two biggest segments for Chinese biotech investments in the US based on value. Together they made up 60 percent of total Chinese investment into biotech between 2000 and 2017. Other segments receiving significant Chinese investment are genomics and related technologies (\$528 million, 14 percent of the total) and molecular diagnostics and precision medicine (\$312 million, eight percent of the total). Agricultural or agriculture-applicable biotechnology, industrial bioproduction and bioprocessing, and biotech incubators and accelerators are new areas with very little Chinese investment thus far (less than \$50 million each in the past 17 years).

Figure 3-7. Chinese Investment in the Biotech Sector by Segments, 2000-2017

Percent of total value (\$3.8 bn)

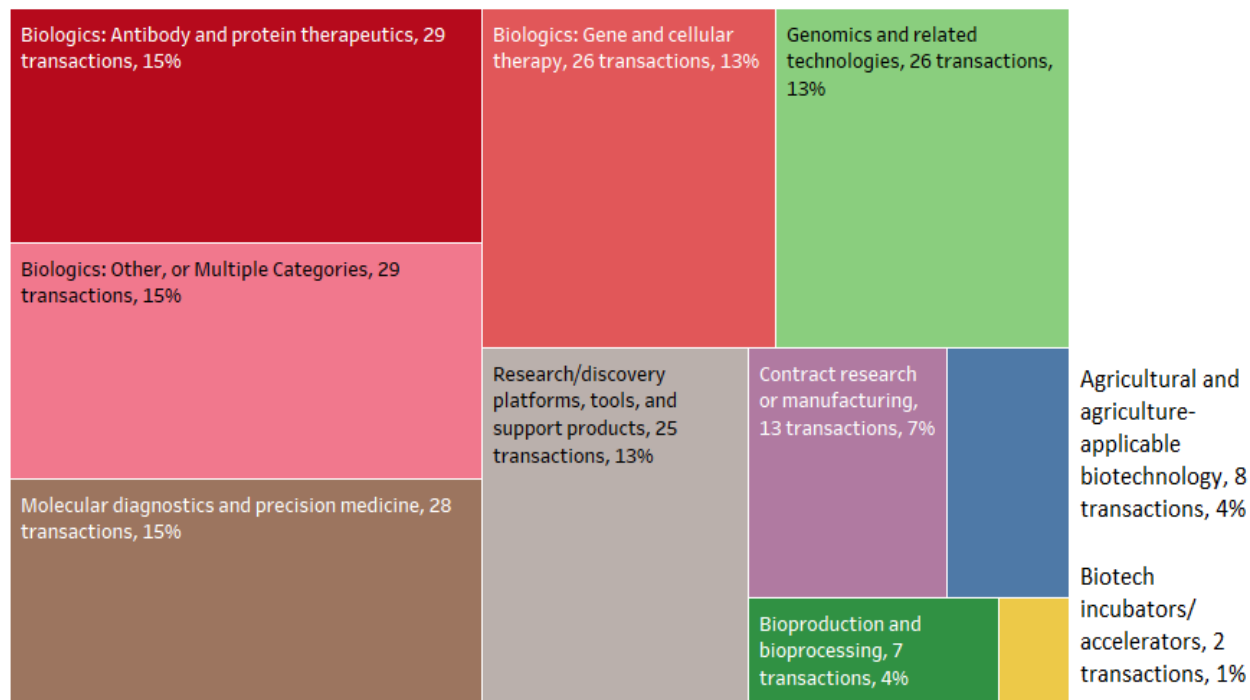


Source: Rhodium Group.

In terms of quantity of transactions (Figure 3-8), the three biologics segments (antibody and protein therapeutics, gene and cellular therapy, and all other biologics) received the greatest number of investments (making up 43 percent of the total). Other segments that received significant numbers of investments are molecular diagnostics and precision medicine; genomics and related technologies; and research/discovery platforms, tools, and support products. Together these constituted another 31 percent of the total transactions. Overall, the distribution of Chinese investment by number of transactions is more evenly spread out than by value: almost all segments have received more than five investments since 2000.

Figure 3-8. Chinese Investment in the Biotech Sector by Segments, 2000-2017

Percent of total number of transactions (193 transactions)



Source: Rhodium Group.

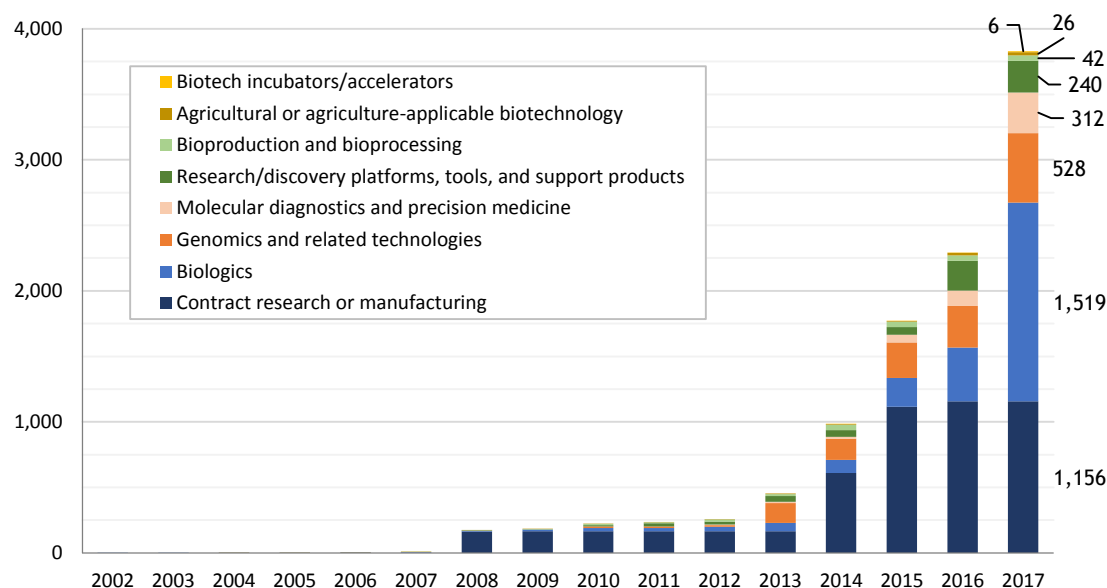
Overall, Chinese investment patterns reflect the level of industrial activity and technological development in the corresponding target industries (though this does not necessarily correspond to market size). We see significant investments—in terms of total capital and number of transactions—in health-related biotechnologies, an area with substantial R&D and market activity domestically in China. In comparison, Chinese investments in agricultural and industrial biotech, areas with limited numbers of commercialized products in China, are much fewer. Correlation between Chinese investment and the level of developmental activity in the target biotech segments indicates that Chinese investment is focused on reinforcing existing capacities back home rather than expanding into newer fields.

Many of the investments into US biotech appear to have granted the Chinese investors access to new markets outside of China, indicating access to new markets may be driving investment decision-making. This is supported by the mirrored trends between Chinese investments in the US and China's biotech industry, and explains the slant toward acquisitions versus other types of investments.

Still, Chinese VC in the US has grown rapidly in the last few years. In our conversations with the VC industry (both investors and receivers), Chinese firms are attempting to strongly compete with US-based firms and have become a ubiquitous presence in US biotech venture investing. Should this trend toward VC continue, investments may turn from reinforcing existing capacities to investing in advanced technologies to grow new capacities. However, given that new and advanced technologies are present in all segments of biotechnology, a greater tendency toward VC may or may not change which segments of the US biotech industry predominate in Chinese investments.

Figure 3-9. Cumulative Chinese Investment in the US Biotech Sector by Segment, 2002-2017

Cumulative investment by segment, USD million



Source: Rhodium Group.

The distribution of Chinese investment by segment has evolved over the years (Figure 3-9). Starting with WuXi PharmaTech's acquisition of AppTec in 2008, contract research and manufacturing was the first segment to receive significant Chinese investment. In the past few years, however, the distribution shifted to biologics investments, mostly due to large deals such as Sanpower's acquisition of Dendreon Pharmaceuticals. There is a similar uptick for genomics, molecular diagnostics, and precision medicine in the past three years as Chinese companies switch to higher value-added activities.

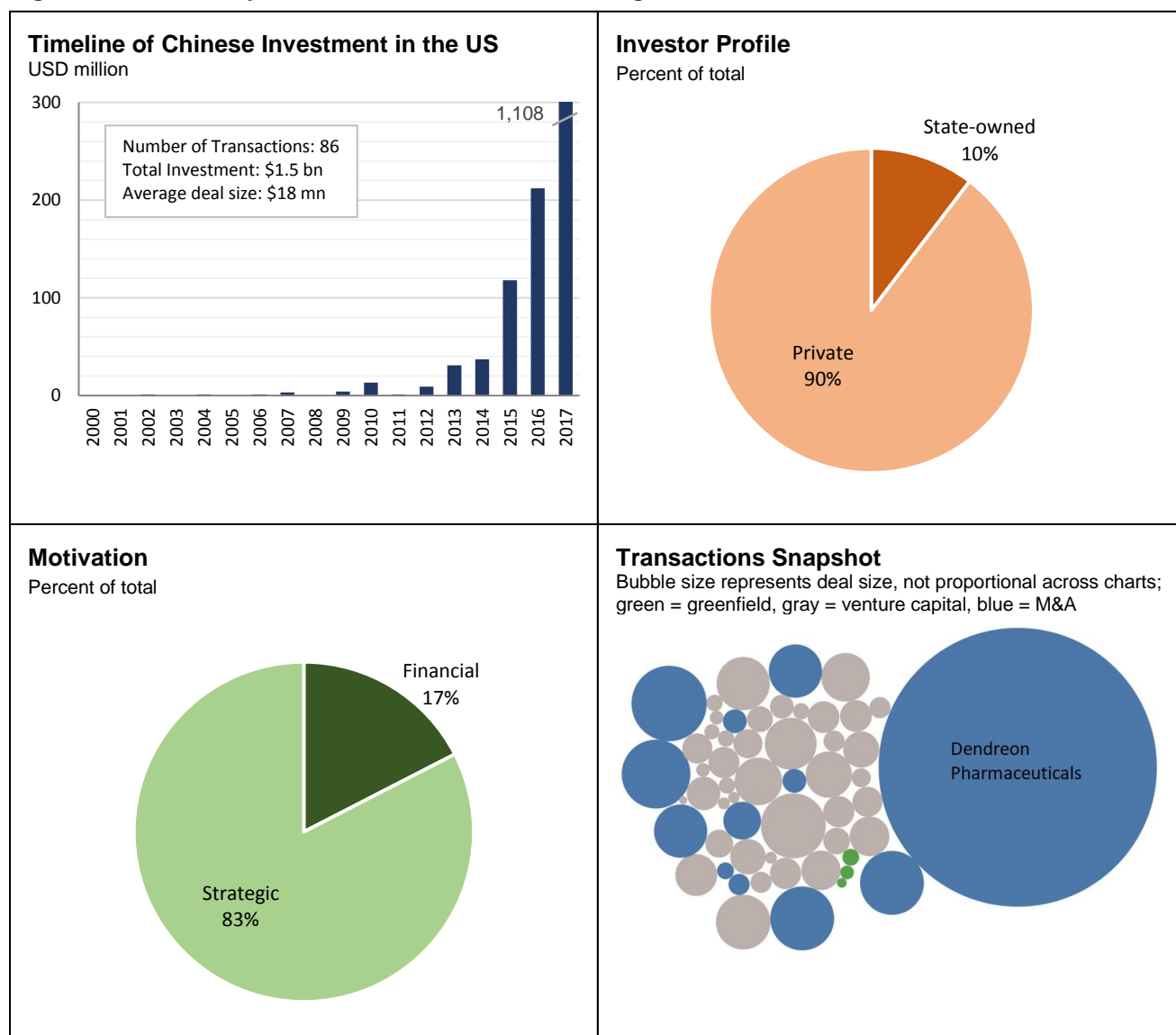
Despite some recent large transactions, Chinese investments in US biotech have yet to have a major impact on the overall industry, with a few exceptions. Acquired US biologics companies tend to be producers of niche therapies with one or a few marketed products, as opposed to the major biopharmaceutical players; similarly, acquisition of US CROs has enabled Chinese companies to expand their footprints but have not been among the top contributors in the US market. One segment where Chinese investments are having an outsized impact is genomics and related technologies. Here, Chinese companies have acquired key leading technologies and some of the largest genetic and clinical databases to further their capabilities and cement their standing as global leaders in the field.

In the following pages, we discuss the investment trends for each of the eight biotech segments in detail, based on the amount of activity, and their importance to the US market.

3.4.1. Biologics

Biologics is the largest biotech segment in terms of cumulative Chinese investment, receiving \$1.5 billion in investment in 2000-2017. At \$1.1 billion, investments in gene and cellular therapy made up 75 percent of total biologics investment, while antibody and protein therapeutics constituted another 13 percent (\$198 million). Biologics has largely driven the growth of Chinese biotech investment in the past five years, with total investment in this sector increasing ten-fold from 2016-2017. We record a total of 86 deals in biologics. The biggest deal and the reason for the jump in 2017 is Sanpower Group's acquisition of Dendreon Pharmaceuticals, a developer of targeted therapeutics for cancer treatment. Despite the intense interest in US biologics companies, Chinese investors so far have invested in more niche companies with only one or a few marketed products, as opposed to the major innovators and producers of top biopharmaceuticals.

Figure 3-10. Summary of Chinese Investments in Biologics*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

Cellular immunotherapies for cancer treatment are a major draw for Chinese investment. Sanpower Group's (Chinese) acquisition of Dendreon (US) accounted for half of the Chinese investment in US-based biologics. Dendreon is the maker of Provenge, a personalized immunotherapy in which a patient's immune cells are collected, trained to respond to prostate cancer, and reintroduced to stimulate an immune response against the cancer.³¹⁶ Provenge was approved by the FDA in 2010.³¹⁷ However, Dendreon struggled to find a market for Provenge, largely due to the high cost of the complicated

³¹⁶ "Questions and Answers - Provenge," U.S. Food & Drug Administration, updated March 16, 2018, <https://www.fda.gov/biologicsbloodvaccines/cellulargenetherapyproducts/approvedproducts/ucm210037.htm>

³¹⁷ "Sipuleucel-T (Provenge®)," National Cancer Institute Division of Cancer Treatment & Diagnosis, updated November 10, 2015, https://dtp.cancer.gov/discovery_development/scientific_Sipuleucel-T.htm

manufacturing process, and went bankrupt in 2014.³¹⁸ Valeant Pharmaceuticals (Canadian) bought bankrupt Dendreon in 2015 for \$495 million and eventually re-sold it to Sanpower Group in 2017 for \$820 million.³¹⁹ In announcing their acquisition of Dendreon, Sanpower Group cited an interest in leveraging their role as the world's largest operator of umbilical cord blood banks for personalized medical treatments; they also noted the rising incidence of prostate cancer in China as a motivation.³²⁰ A year after the acquisition, a Sanpower executive indicated that the company had taken steps toward drug approval and manufacturing in China and Hong Kong, including consultation with the CFDA.³²¹

Another major area of global interest for cancer treatment is the cellular immunotherapy CAR-T and related approaches involving engineered T cells. CAR-T therapies have shown remarkable results in the treatment of cancers, particularly blood cancers, that have not responded to traditional therapies, and clinical trial leaders have observed patients with otherwise terminal cases reach remission.³²² Belief in the promise of this technology is evidenced in large, financially-motivated Chinese VC investments in F1 Oncology, TCR2 Therapeutics, and Tmunity (all US-based).

CAR-T is a therapeutic approach of broad interest globally and an area where China has demonstrated indigenous innovation. Substantial M&A activity is also occurring between US companies, as demonstrated by the acquisition of two major players by large biotech companies in late 2017 through early 2018: Kite Pharma (US) was acquired by Gilead (US) and Juno Therapeutics (US) by Celgene (US).³²³ Two CAR-T therapies were approved by the US FDA in 2017, one by Novartis (Swiss) to treat advanced leukemia and one by Kite Pharma to treat large B-cell lymphomas.³²⁴ Meanwhile, development of CAR-T technology in China is strong, with many ongoing clinical trials, though at the time of writing no therapies have yet been approved.³²⁵ (See Chapter 1 for discussion of China's progress in CAR-T).

Other biologics, including antibody and protein therapeutics, constitute a large market, with many commercialized products. A search of the Drugs@FDA database reveals approximately 80 approved monoclonal antibody drug products in the US,³²⁶ with the first such drug reaching approval in 1986.³²⁷ Antibody drugs are used to treat a range of conditions, primarily autoimmune disease and cancer. Antibody therapeutics, particularly biosimilars, have shown to be an area of interest for Chinese companies, and the Made in China 2025 plan cited antibody drugs and antibody-drug conjugates among the types of products targeted for development in medicine.³²⁸ A substantial amount of Chinese FDI has targeted antibody and protein therapeutics, ranging from biosimilars to more innovative products or those with more complex structures like antibody-drug conjugates. For example, Livzon Mabpharm Inc. (Chinese) invested and signed a collaboration agreement with biosimilar antibody developer EPIRUS

³¹⁸ Eric Palmer, "China's Sanpower takes on expensive Provenge manufacturing with Dendreon deal," *FiercePharma* January 17, 2017, <https://www.fiercepharma.com/manufacturing/china-s-sanpower-takes-expensive-provenge-manufacturing-dendreon-deal>

³¹⁹ Jen Wiczner, "Valeant Just Made a Killing on a Series of Drug Deals," *Fortune* January 10, 2017, <http://fortune.com/2017/01/10/valeant-stock-dendreon-cerave/>

³²⁰ "Sanpower Group Agrees to Acquire Dendreon From Valeant for \$819.9 Million," Sanpower Group, updated January 25, 2015, <https://www.prnewswire.com/news-releases/sanpower-group-agrees-to-acquire-dendreon-from-valeant-for-8199-million-300388346.html>

³²¹ Angus Liu, "Dendreon chairwoman figures Provenge growth, infrastructure can pave its way into CAR-T," *FiercePharma* April 2, 2018, <https://www.fiercepharma.com/marketing/dendreon-expects-10-annual-provenge-growth-looks-for-car-t-tcr-t-buy-chairwoman>

³²² "CAR T Cells: Engineering Patients' Immune Cells to Treat Their Cancers," National Cancer Institute, updated December 14, 2017, <https://www.cancer.gov/about-cancer/treatment/research/car-t-cells>

³²³ Ned Pagliarulo, "CAR-T growing up with big pharma's big bet," *BioPharma Dive* February 20, 2018, <https://www.biopharmadive.com/news/car-t-growing-up-with-big-pharmas-big-bet/517135/>

³²⁴ National Cancer Institute Staff, "With FDA Approval for Advanced Lymphoma, Second CAR T-Cell Therapy Moves to the Clinic," *Cancer Currents: An NCI Cancer Research Blog* October 25, 2017, <https://www.cancer.gov/news-events/cancer-currents-blog/2017/yescarta-fda-lymphoma>

³²⁵ Bloomberg News, "In Race for Blood Cancer Therapy, a Chinese Biotech Firm Surges 500%," *Bloomberg* (2018), <https://www.bloomberg.com/news/articles/2018-02-13/in-race-for-blood-cancer-therapy-a-chinese-biotech-surges-500>

³²⁶ Searched <https://www.accessdata.fda.gov/scripts/cder/daf/index.cfm> on 6/21/18 for keyword mab (manually removed products where mab was not the ending)

³²⁷ S. Singh et al., "Monoclonal Antibodies: A Review," *Current Clinical Pharmacology* (2017).

³²⁸ State Council of the People's Republic of China, *Made in China 2025*.

Biopharmaceuticals (US) in 2014 (EPIRUS filed for bankruptcy two years later).³²⁹ As another example, in 2015, a Chinese consortium that included WuXi PharmaTech acquired Ambrx (US), which develops antibody-drug conjugates.³³⁰ Acquisition of US biologics companies could ease entry of their products into the Chinese market, provided Chinese approval is sought first.

3.4.2. Contract Research or Manufacturing

Contract research and manufacturing organizations provide support services to the pharmaceutical, medical device, and medical biotechnology (*i.e.*, biologics) industries and can support development at preclinical, clinical, and post-approval stages. CROs offer outsourcing support to drug development companies and play an important role in the value chain worldwide: of the addressable market (measured in USD), 25 percent of discovery, 30 percent of preclinical development, and 41 percent of clinical development are outsourced to CROs.³³¹ (For a more detailed discussion of China's role in the global CRO/CMO market, see Chapter 1). For the purpose of this study, we narrowed our scope to CROs and CMOs with an emphasis on biologics and biotech-specific capabilities, and thus excluded those that offer services that either focus on developing pharmaceuticals or medical devices, or those that focus on the clinical stages of development.

Chinese companies invested \$1.2 billion in CRO/CMO companies in the US in 2000-2017. This is the second largest segment within all Chinese biotech investments, and was just overtaken by biologics in 2017. Investment in this sector consists of organizations that conduct research for others, which is the business model for several Chinese biotech leaders such as Shenzhen Hepalink and WuXi PharmaTech. We record 13 transactions total in this segment. The biggest investments include WuXi PharmaTech's acquisition of AppTec, Legend and CITIC's investment in Pharmaron, Hepalink's investments in Scientific Protein Laboratories and Cytovance Biologics, and WuXi AppTec's greenfield operations.

Chinese investments in US-based CROs or CMOs have a large average deal size (mainly stemming from large acquisitions, as well as greenfield investments), across a small number of total deals. Two large acquisitions were by Shenzhen Hepalink Pharmaceutical (Chinese), a leading manufacturer of heparin (an anticoagulant).³³² In 2014, the company acquired Scientific Protein Laboratories (US), which manufactures active pharmaceutical ingredients including heparin sodium and pancreatic enzymes, as well as offering contract development and manufacturing services including natural product extraction and fermentation.³³³ While Scientific Protein Laboratories does have a contract manufacturing segment, their capacity as a supplier of particular biopharmaceutical products (particularly, heparin) appears to have been a major driver of this deal. The following year, Hepalink USA, a subsidiary of Shenzhen Hepalink Pharmaceutical, acquired Cytovance Biologics (US), a contract development and manufacturing organization specializing in the production of antibody and protein therapeutics from mammalian cells and microbial fermentation.³³⁴ These acquisitions expanded Hepalink's manufacturing capabilities and gave them ownership of providers of a broader range of services, namely contract development and manufacturing. WuXi AppTec (Chinese), a large CRO/CMO, also initiated investments in this category,

³²⁹ Damian Garde, "EPIRUS and Livzon Mabpharm, Inc. Enter Collaboration Agreement for China," *FierceBiotech*(2014), <https://www.fiercebiotech.com/biotech/epirus-and-livzon-mabpharm-inc-enter-collaboration-agreement-for-china>; BioPharma-Reporter, "Epirus files for bankruptcy protection and hands Remicade bioism to Reliance Life Sciences," *BioPharma-Reporter*(2016), <https://www.biopharma-reporter.com/Article/2016/07/27/Epirus-files-for-bankruptcy-protection-and-hands-Remicade-biosim-to-Reliance-Life-Sciences>

³³⁰ "Chinese Consortium Enters into Agreement to Acquire Ambrx," Ambrx, updated May 25, 2015, <http://ambrx.com/chinese-consortium-enters-into-agreement-to-acquire-ambrx/>

³³¹ Wilson, Willoughby, and Wallach, *CRO Industry Primer*.

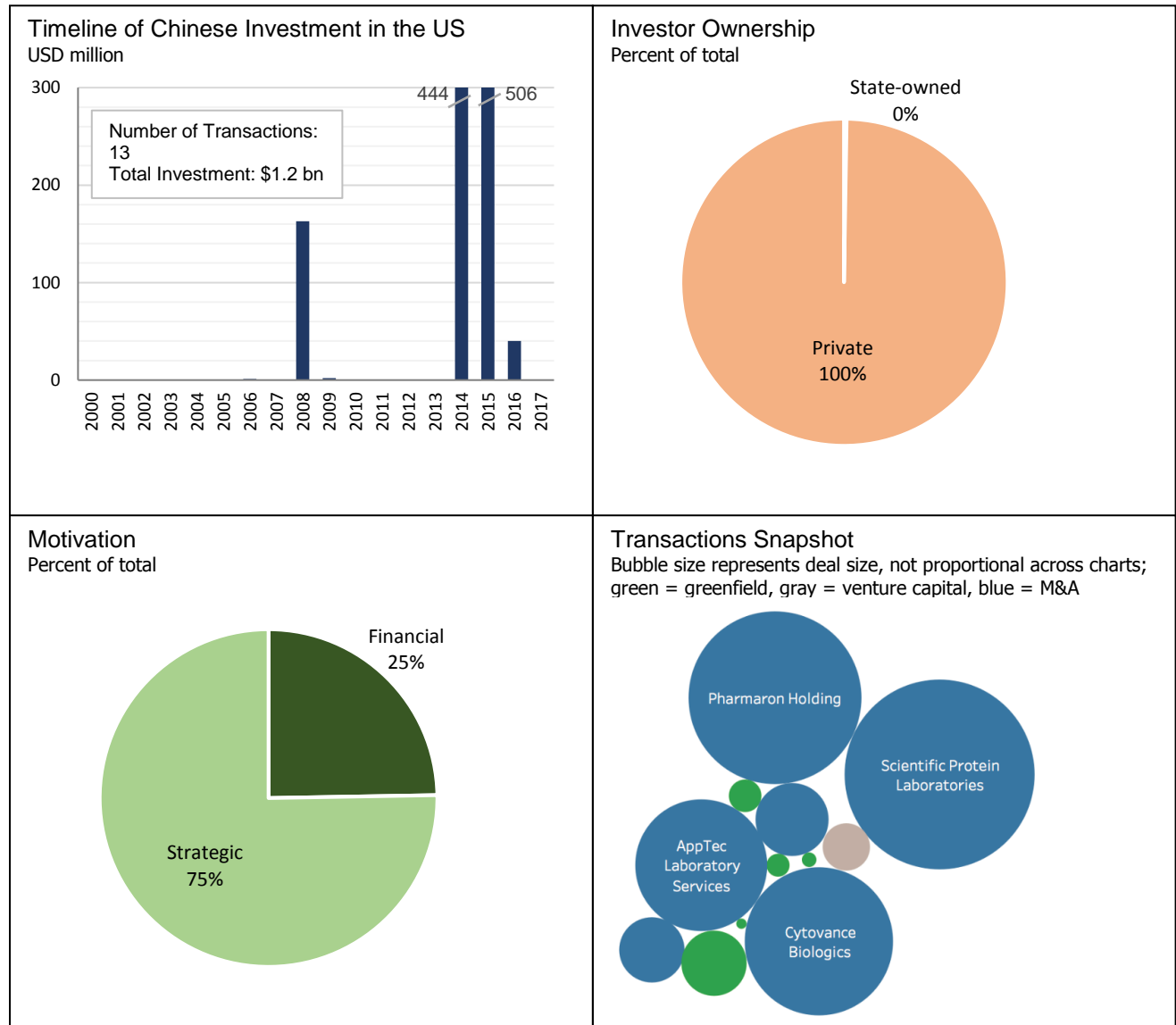
³³² "Hepalink Signs Agreement to Acquire Scientific Protein Laboratories," The Harbour Group, updated December 26, 2013, <https://www.businesswire.com/news/home/20131226005071/en/Hepalink-Signs-Agreement-Acquire-Scientific-Protein-Laboratories>

³³³ *Ibid.*

³³⁴ GEN Staff, "Hepalink USA to Buy Cytovance Biologics for \$205.68M+," *Genetic Engineering & Biotechnology News*(2015), <https://www.genengnews.com/gen-news-highlights/hepalink-usa-to-buy-cytovance-biologics-for-205-68m/81251657/>

including a 2016 greenfield investment into a biomanufacturing facility for cell therapy products.³³⁵ This facility was WuXi's third and largest facility for production of biologics in the Philadelphia Navy Yard, with a size of 150,000 square feet and the capacity to employ a staff of 200. Based on the combined capacity of its three sites in Philadelphia, including capacity to implement GMP and to produce cell therapy and gene therapy products, WuXi AppTec was chosen as a manufacturing partner by the IQVIA Stem Cell Center (US).³³⁶

Figure 3-11. Summary of Chinese Investments in Contract Research or Manufacturing*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

³³⁵ "Press Releases: WuXi AppTec Unveils Manufacturing Center for Cutting Edge Cell and Gene Therapies," WuXi AppTec, updated October 6, 2016, <http://www.wuxiapptec.com/press/detail/330/18.html>

³³⁶ "WuXi AppTec Selected by IQVIA Stem Cell Center to Serve as GMP Manufacturer of Advanced Therapies," updated November 17, 2017, <https://www.prnewswire.com/news-releases/wuxi-apptec-selected-by-iqvia-stem-cell-center-to-serve-as-gmp-manufacturer-of-advanced-therapies-300558487.html>

Chinese acquisition of US biopharmaceutical manufacturing companies raises concerns over quality of biopharmaceutical ingredients entering the supply chain, although the companies have not been among the largest in the sector. Scientific Protein Laboratories' Changzhou manufacturing plant was at the center of the 2008 heparin crisis in which adulterated heparin ingredients caused at least 81 deaths in the US, even though it was under US ownership at the time. The FDA has since opened a post in China to facilitate inspections, although in 2016 only 11 of 18 positions were filled.³³⁷ China's entry into the international standards organization ICH in 2017 provides some hope that quality of its products will improve, although the move is not a panacea.

Beyond a few large strategic investments, there are only nine outbound Chinese investments in US CROs/CMOs. A possible explanation for the small number of deals is that lower costs are an important advantage for Chinese CROs/CMOs, and thus any technological or strategic advantage gained by buying a US-based operation might be negated when higher labor costs are considered.

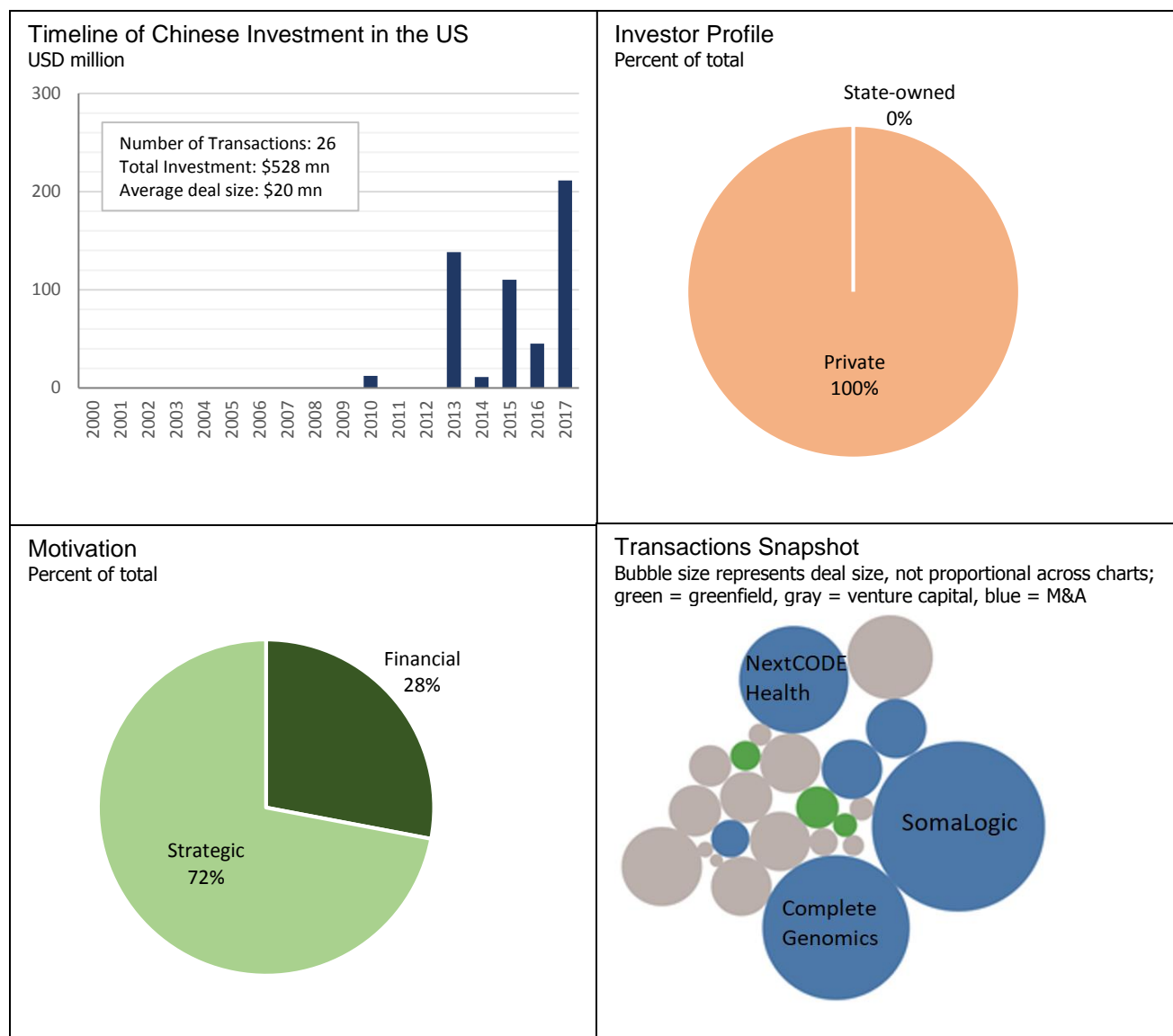
3.4.3. Genomics and Related Technologies

Chinese companies have invested \$528 million in genomics and related technologies in the US in 2000-2017. This is the third largest segment for Chinese biotech investment in the US. Investments in this segment target genetic sequencing assets. We record 26 transactions total in genomics and related technologies.

The level of Chinese investment in US companies working on genomics and related technologies has been high, at over \$500 million, and has included several large, strategic acquisitions. Notable transactions include the acquisition of Complete Genomics (US) by BGI (Chinese), investment in SomaLogic (US) by iCarbonX (Chinese) and acquisition of NextCODE Health (US) by WuXi PharmaTech (Chinese).

³³⁷ United States Government Accountability Office. *FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of Its Foreign Offices* 2016.

Figure 3-12. Summary of Chinese Investments in Genomics and Related Technologies*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

BGI's acquisition of Complete Genomics gave them ownership of proprietary sequencing technology, reducing reliance on outside vendors, and access to a base of operations in the US (see Box 3). iCarbonX's investment brought SomaLogic into their Digital Life Alliance, a collaborative effort by several companies to establish an ecosystem of biological data and artificial intelligence meant to provide personalized health information; SomaLogic contributes a proteomics platform (i.e., tools for protein measurement). WuXi PharmaTech's investment in NextCODE Health increased their access to CLIA-certified sequencing facilities and one of the world's largest clinical genetics reference databases to augment their capabilities for the development of genomic products.³³⁸ The US companies that are the

³³⁸ Genetic Engineering and Biotechnology News, "WuXi Snaps Up NextCODE Health for \$65M," (2015), <https://www.genengnews.com/topics/omics/wuxi-snaps-up-nextcode-health-for-65m/>

recipients of Chinese investment provide platforms and tools for omics data collection. These investments and their implications are all discussed in greater depth in Chapter 5.

Box 3. Acquisition of Complete Genomics by BGI.

In 2013, BGI acquired the US sequencing company Complete Genomics for \$117.6 million. Complete Genomics pioneered a novel approach by offering sequencing-as-a-service on proprietary technology rather than selling sequencing machines to laboratories. However, they struggled financially and were in the midst of layoffs when the acquisition was announced in September 2012. BGI acquired Complete Genomics through its subsidiary, Beta Acquisition Corporation, and the deal allowed Complete Genomics to continue operating as a separate wholly-owned subsidiary under BGI.³³⁹

Prior to the acquisition, BGI offered sequencing services using machines bought from Illumina, one of the largest manufacturers of sequencing technology in the world. However, Illumina began offering their own whole-genome sequencing services, putting them in direct competition with BGI and Complete Genomics. The acquisition of Complete Genomics and their intellectual property gave BGI a base of operations in the United States as well as their own proprietary sequencing technology, thus reducing their reliance on Illumina's products.³⁴⁰ After the acquisition was announced, Illumina made a competing bid to acquire Complete Genomics for \$123 million, \$5 million more than offered by BGI. However, the board rejected the bid, stating the BGI's offer was superior.³⁴¹

The acquisition required antitrust clearance from the FTC, clearance from a national security review by CFIUS, and approval from China's Ministry of Commerce and State Administration of Foreign Exchange. Some scientists, politicians, and industry experts raised concerns that the takeover was a threat to the US sequencing industry and to national security. They worried that BGI might use low prices to undercut US sequencing companies that dominated the market. Some also worried about protecting the privacy of genetic information and the potential for BGI to use genetic information for nefarious purposes. Illumina promoted these concerns by hiring lobbyists to raise opposition to the deal in Congress, citing national security.³⁴² In response, BGI and Complete Genomics accused Illumina of hypocrisy, noting that Illumina had long sold its sequencing technologies to foreign entities, including a record-setting 128 machines to BGI, without security concerns. They further suggested that Illumina was trying to derail the deal out of desire to acquire Complete Genomics for themselves rather than out of concern for national security. CFIUS cleared the deal in December 2012, the FTC concluded its investigation in January 2013, and the acquisition was completed in March 2013. In a company press release, BGI stated that after the acquisition of Complete Genomics, "BGI rapidly achieved technology transformation and re-innovation" resulting in the production of two new gene sequencer machines in 2015 and 2016.³⁴³

3.4.4. Molecular Diagnostics and Precision Medicine

Chinese companies have invested \$312 million in molecular diagnostics and precision medicine in the US in 2000-2017. This is the fourth largest segment among all Chinese biotech investments. Most of the investments in this sector are involved in diagnostic testing services. We record 28 transactions total, and the largest deals are Decheng Capital and Tencent's VC investment in GRAIL, Inc. and Hermed Capital's investment in Epic Sciences.

Chinese firms have invested in a relatively large number of molecular diagnostics companies in the US compared to companies in other biotech segments. Note that the precision medicine aspect of this category refers to applied precision medicine, such as the application of genetic tests for cancer to make

³³⁹ Andrew Pollack, "Chinese Company to Acquire DNA Sequencing Firm," *New York Times Dealbook* September 17, 2012, <https://dealbook.nytimes.com/2012/09/17/chinese-company-to-acquire-dna-sequencing-firm/>

³⁴⁰ Ibid.

³⁴¹ Bob Grant, "Feds Scrutinize Genomics Merger," *The Scientist*(2012), <https://www.the-scientist.com/?articles.view/articleNo/33567/title/Feds-Scrutinize-Genomics-Merger/>

³⁴² Andrew Pollack, "U.S. Clears DNA Firm's Acquisition by Chinese," *New York Times* December 30, 2012, <https://www.nytimes.com/2012/12/31/health/chinese-firm-is-cleared-to-buy-american-dna-sequencing-company.html>

³⁴³ Office of the United States Trade Representative, *Findings of the Investigation into China's Acts, Policies, and Practices Related to Technology Transfer, Intellectual Property, and Innovation Under Section 301 of the Trade Act of 1974*.

treatment decisions for individual patients. Work in genomics, with the general goal of developing precision medicine approaches, would be included in the genomics and related technologies category.

A large and illustrative investment in this category is the financing of GRAIL, Inc. (US) by two Chinese VC firms in 2017. GRAIL is developing approaches for early cancer detection based on circulating tumor DNA in the bloodstream (known as liquid biopsy) using sequencing technology and machine learning to identify and model which DNA fragments in the blood may be indicative of tumors—a “needle in the haystack problem” requiring large data sets to conquer. The company has initiated two large-scale clinical studies.³⁴⁴ In 2017, GRAIL merged with another Chinese company, Hong-Kong-based Cirina, which is also developing liquid biopsy technology, resulting in Cirina becoming a GRAIL subsidiary. This move will enable GRAIL to reach Asian markets and allow the two companies to combine their scientific resources.³⁴⁵ Another large transaction in this category was the investment of Hermed Capital in Epic Sciences (US), which provides a test that predicts the response of prostate cancer cases to different drug classes using circulating tumor cells from liquid biopsy.³⁴⁶

The pattern of Chinese investment in this category demonstrates a major interest in companies implementing molecular diagnostics for diagnosis and monitoring of cancer, often through liquid biopsy. This pattern seems to align with market-wide trends: molecular diagnostics is a sizeable and growing market, with substantial recent activity arising from small, niche companies focused on cancer.³⁴⁷

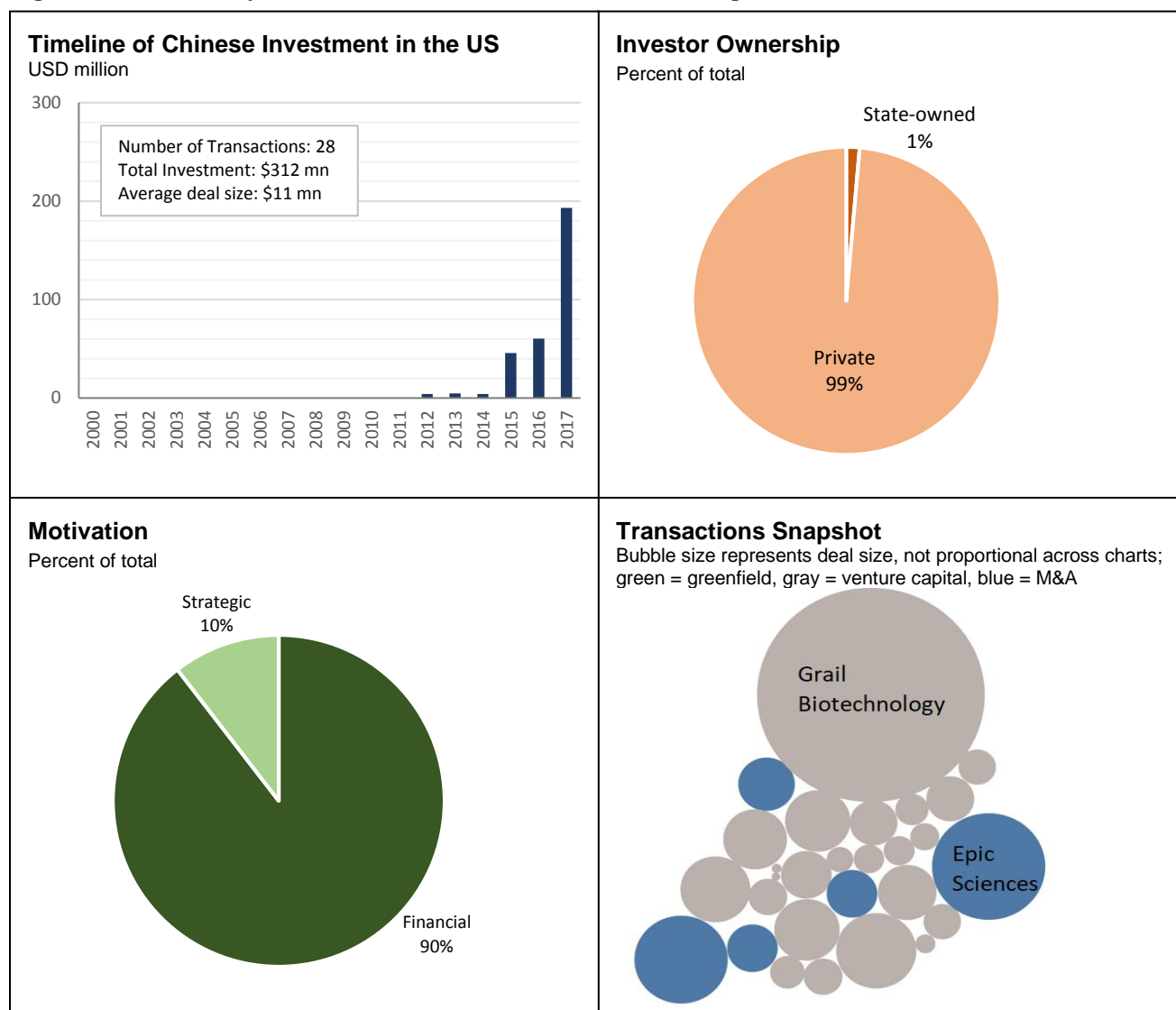
³⁴⁴ "Grail: Science," Grail, <https://grail.com/science/>; "Grail: Clinical Studies," <https://grail.com/clinical-studies/>

³⁴⁵ "Grail and Cirina Merge to Focus on Early Cancer Detection," *GenomeWeb*(2017), <https://www.genomeweb.com/cancer/grail-and-cirina-merge-focus-early-cancer-detection>

³⁴⁶ "AR-V7 Liquid Biopsy Test," Epic Sciences, <https://www.epicsciences.com/ar-v7-test>

³⁴⁷ Alex Philippidis, "20 Molecular Diagnostics Companies to Watch," *ClinicalOMICS* February 8, 2017, <https://www.clinicalomics.com/articles/20-molecular-diagnostics-companies-to-watch/947>

Figure 3-13. Summary of Chinese Investments in Molecular Diagnostics and Precision Medicine*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

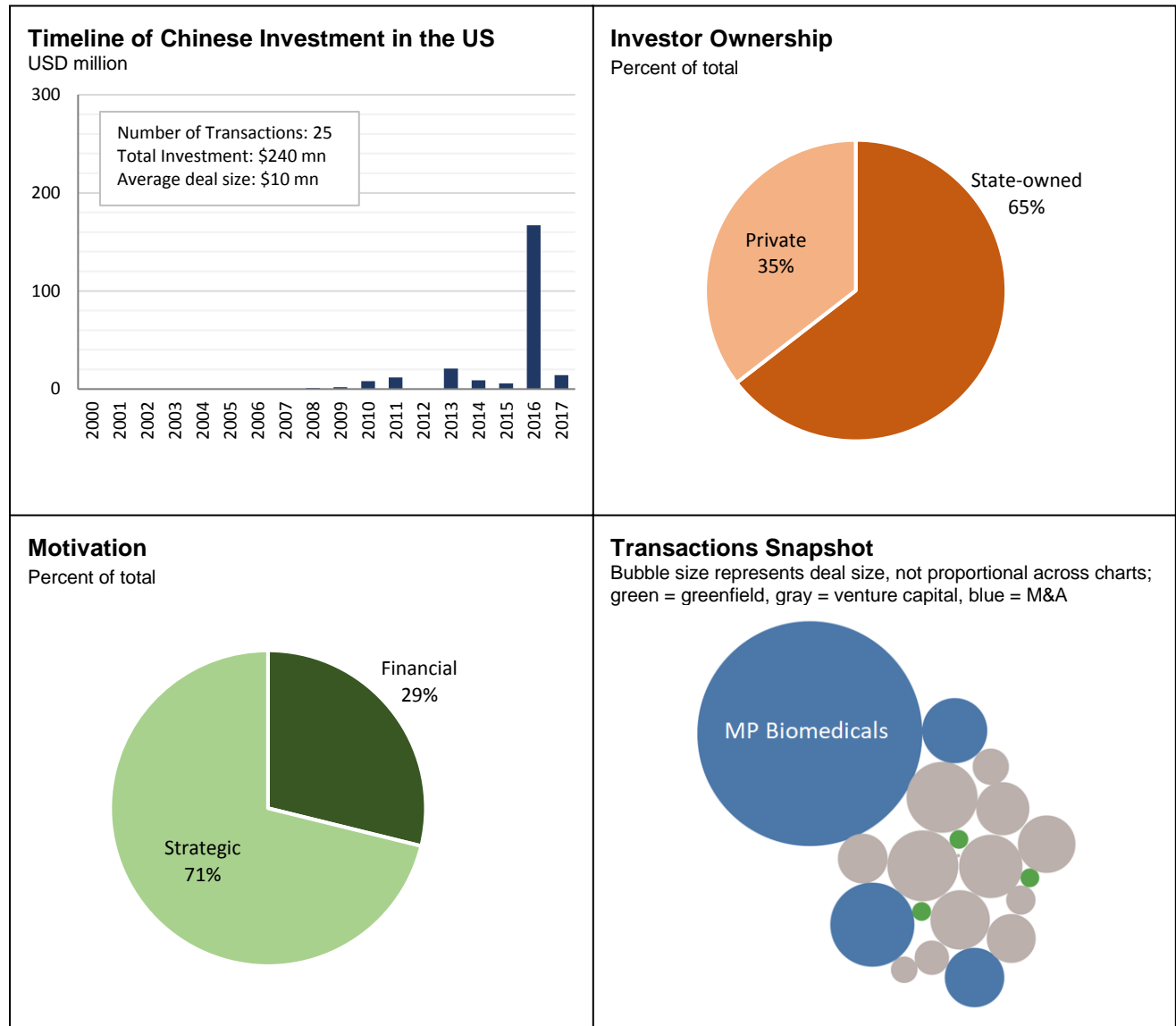
3.4.5. Research/Discovery Platforms, Tools and Support Products

Chinese companies have invested \$240 million in biotechnology research and discovery platforms, tools and support products in the US. This is the fifth largest segment among Chinese biotech investment. Investment targets in this segment range from makers of reagents, to developers of tools, to stem cell producers. We record 25 transactions total. The biggest investments were Valiant's investment in MP Biomedicals, Hermed Capital and Ping An Ventures' investment in Applied StemCell Tianjin Pharmaceutical Group's investment in Neuralstem, and IDG Capital and Qiming Venture Partners' investment in Origene.

Companies in this category support biotechnology R&D by providing products and basic services broadly useful in this type of research, as well as specialized discovery platforms based in biotechnology. This

category contains a variety of companies ranging from producers of biological reagents to developers of more technologically advanced platforms supporting research and biotechnology development.

Figure 3-14. Summary of Chinese Investments in Research/Discovery Platforms, Tools and Support Products*



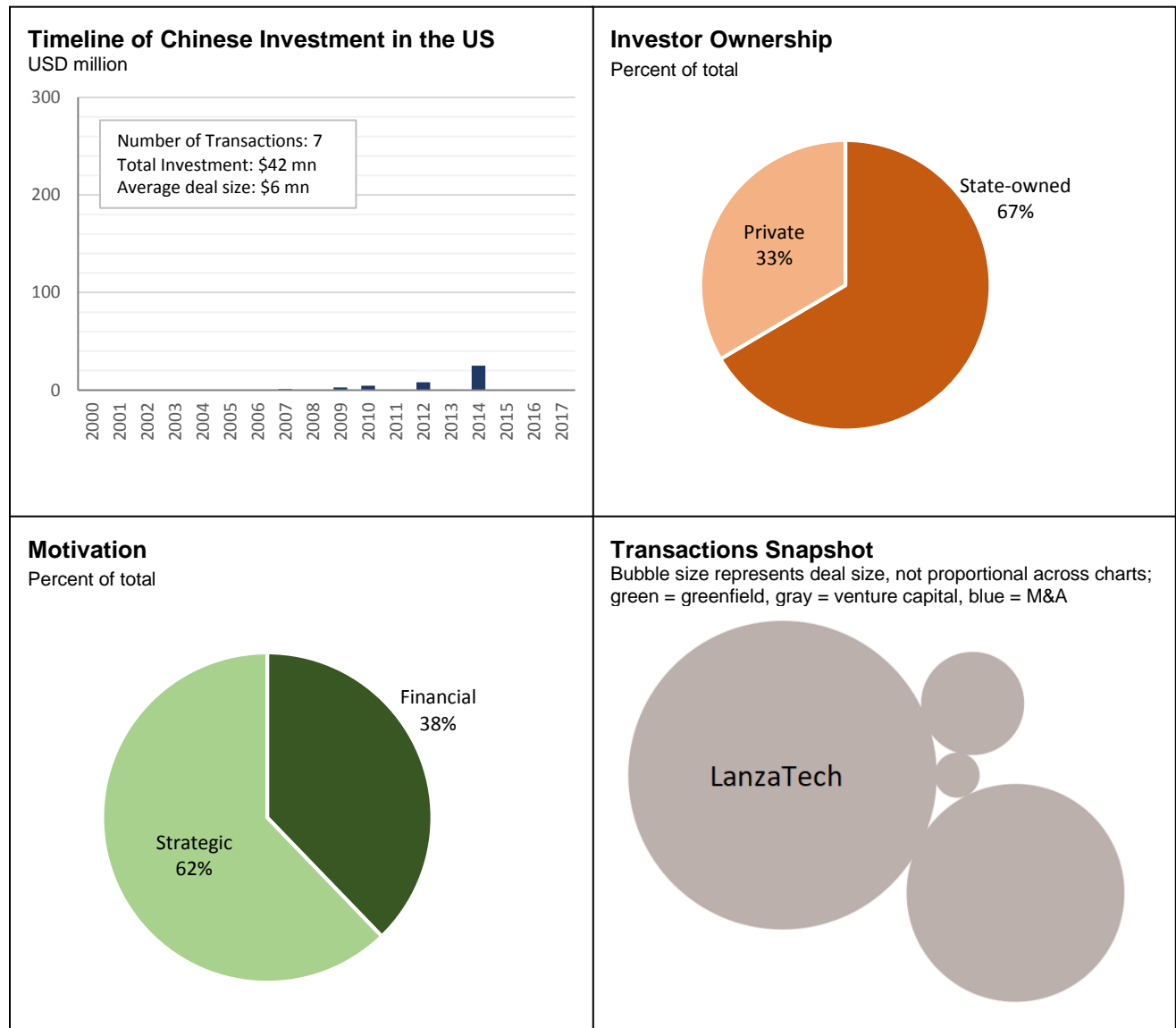
Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

3.4.6. Industrial Bioproduction and Bioprocessing

Chinese companies have only invested \$42 million in industrial bioproduction and bioprocessing in the US in 2000-2017. This is the third smallest segment within all Chinese biotech investments. Investments in this sector are all venture capital investments, and they consist of investments in biofuel or bioprocessing for waste treatment. We record seven transactions in total. The biggest investments are CLI Ventures and SV Tech Ventures in Industrial Microbes, and CICC and Qiming Venture Partners in LanzaTech.

Figure 3-15. Summary of Chinese Investments in Industrial Bioproduction and Bioprocessing*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

The level of Chinese investment in US industrial bioproduction/bioprocessing companies is limited and consists mainly of venture capital financing rather than acquisition activity. One large investment in this category is a 2014 venture capital investment by China International Capital Corporation and Qiming Venture Partners in LanzaTech (US). LanzaTech develops processes for the conversion of carbon in waste gases to useful products via fermentation, using microbes that feed on gas.³⁴⁸ LanzaTech has engaged in joint ventures with other Chinese companies both before and after the time of the 2014

³⁴⁸ "Technical Overview," LanzaTech, <http://www.lanzatech.com/innovation/technical-overview/>

funding round, establishing China-based facilities to convert steel mill waste to biofuels, especially fuel ethanol.³⁴⁹

The few investments in industrial biotechnology companies suggest that China is not bolstering its capabilities via acquisition of US companies in this segment of biotechnology. The reliance on VC in these investments reflects the exploratory, R&D-heavy nature of the invested companies.

3.4.7. Agricultural or Agriculture-Applicable Biotechnology

Chinese companies have only invested \$26 million in agriculture or agriculture-applicable biotechnology in the US in 2000-2017. This is the second smallest segment within all Chinese biotech investments. Agriculture and agriculture-application biotechnology mainly consist of investments in plant biotech in order to improve agriculture safety and efficiency. We record eight deals in total in this segment. The biggest investments are seed producer Origin Agritech's office in Iowa, Syngenta Venture's investment in GreenLight Biosciences, and Tencent's investment in Clear Labs.

Chinese investment into US agricultural biotechnology (i.e., GM crops) and agriculture-applicable biotechnology (i.e., other uses of biotechnology to aid agriculture beyond direct modification of agricultural products, including, for example, animal vaccines) has been limited. The largest investment was the 2016 opening of a US office by Origin Agritech, a Chinese GM seed company. The company hoped to launch its GM corn products on the US market, as China's policies on GM crops impede the commercialization of such products in China.³⁵⁰ While the US market may offer commercialization opportunities, the US market is strongly competitive due to major global players like Monsanto (now owned by Bayer) and DuPont Pioneer holding entrenched positions.³⁵¹ In 2017, Origin Agritech suspended operations at its US office, stating that it intended to continue activity in the US but oversee these operations from its Beijing headquarters.³⁵²

The low level of Chinese investment in US agriculture companies extends beyond biotechnology into the general agriculture sector. A report by the USDA Economic Research Service found that while Chinese companies are increasing foreign investment in general agriculture, these investments tend to target countries with less-developed markets, where there is less competition and more potential to add value with Chinese technology, and investment in US holdings is limited. Chinese direct investment in overseas agriculture holdings amounted to \$2.6 billion in 2015 and \$3.3 billion in 2016, while, in those same years, Chinese investments in US agriculture and food amounted to \$129 million and \$15 million. Other than a spike due to a large acquisition of Smithfield Foods in 2013, agricultural and food investments accounted for less than 1 percent of Chinese investment in the US in 2000-2016.³⁵³ General motivations of Chinese investment in foreign agricultural holdings, other than financial motivations, include improving China's food security and extending China's influence over agricultural supply chains.³⁵⁴

³⁴⁹ "Beijing Shougang LanzaTech New Energy Science & Technology Company Earns Roundtable on Sustainable Biomaterials (RSB) Certification," updated November 5, 2013, <http://www.lanzatech.com/beijing-shougang-lanzatech-new-energy-science-technology-company-earns-roundtable-on-sustainable-biomaterials-rsb-certification/>; "World's First Commercial Waste Gas to Ethanol Plant Starts Up," updated June 8, 2018, <http://www.lanzatech.com/worlds-first-commercial-waste-gas-ethanol-plant-starts/>

³⁵⁰ Dominique Patton, "With China's GMO sector in limbo, local seed firm targets U.S.," *Reuters* December 6, 2015, <https://www.reuters.com/article/us-china-origin-agritech-usa-idUSKBN0TPOUG20151206>

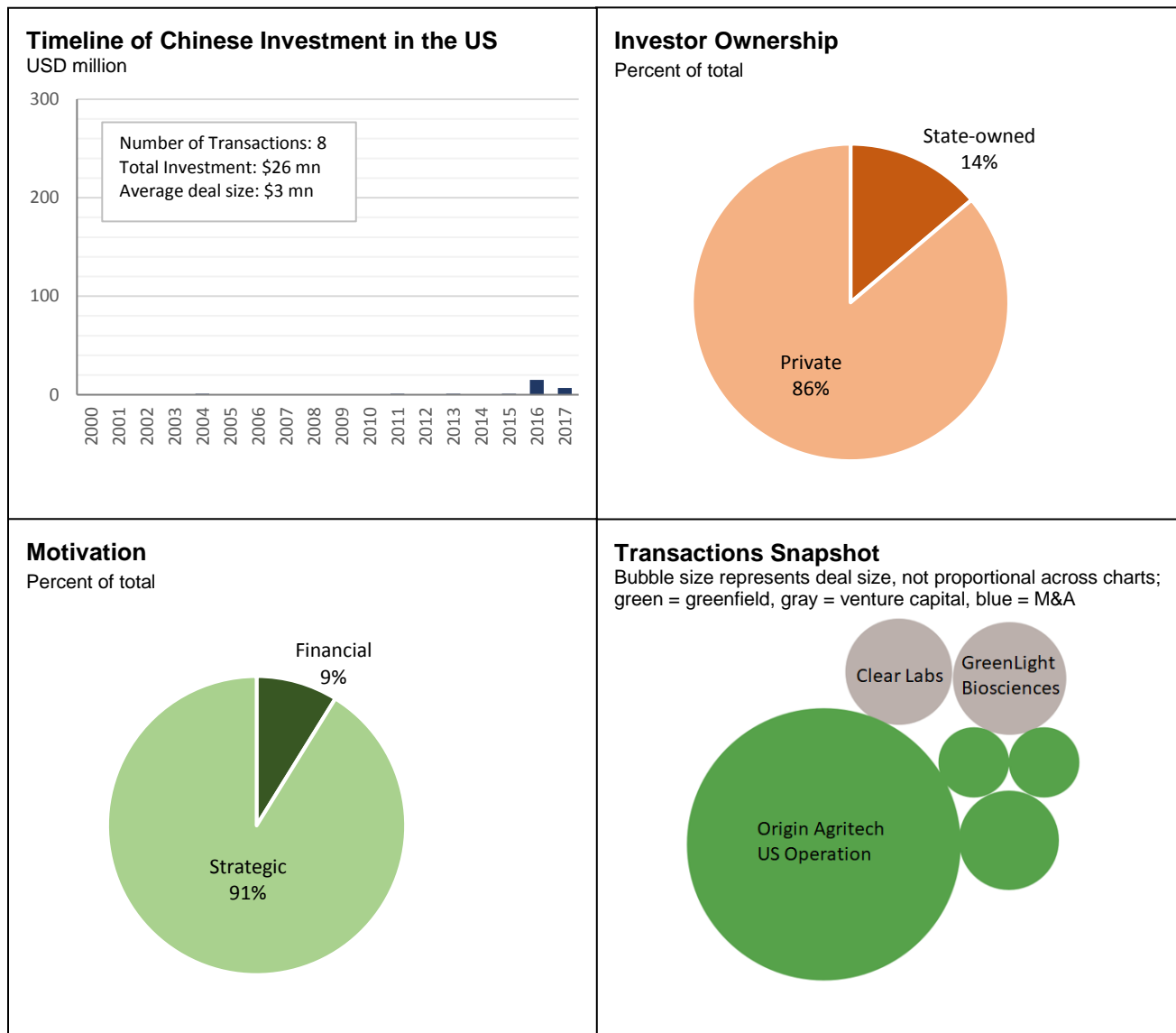
³⁵¹ Reuters, "Chinese firm begins testing GMO corn seeds in U.S. greenhouse," *ibid.* December 15, 2016, <https://www.reuters.com/article/us-origin-agritech-gmo-usa/chinese-firm-begins-testing-gmo-corn-seeds-in-u-s-greenhouse-idUSKBN1442OP>

³⁵² "Origin Agritech Announces Resignation of CEO and Suspending of North American Office," Origin Agritech Limited, updated Dec 01, 2017, <https://www.prnewswire.com/news-releases/origin-agritech-announces-resignation-of-ceo-and-suspending-of-north-american-office-300565328.html>

³⁵³ Elizabeth Gooch and Fred Gale. *China's Foreign Agriculture Investments* Washington, D.C.: United States Department of Agriculture Economic Research Service, 2018. [Note that some data in this source are from Rhodium Group, one of the authors of this report]

³⁵⁴ *Ibid.*

Figure 3-16. Summary of Chinese Investments in Agricultural or Agriculture-Applicable Biotech*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

Other investments in agriculture-applicable biotechnology in the US include a VC investment by Tencent (Chinese) in Clear Labs (US), a company applying genomics tools for food analytics such as sequencing tests for food product authenticity or GM content.³⁵⁵ Another example is a VC investment by Syngenta Ventures (China) in GreenLight Biosciences (US). Syngenta Ventures is the VC arm of agricultural biotechnology company Syngenta, which was recently acquired by ChemChina.³⁵⁶ GreenLight is developing an RNA production platform with a variety of intended applications, including agricultural pest

³⁵⁵ "Clear Labs: Food Safety Reimagined," Clear Labs, <https://www.clearlabs.com/>

³⁵⁶ "Company Overview of Syngenta Ventures," Bloomberg, <https://www.bloomberg.com/research/stocks/private/snapshot.asp?privcapId=78937909>

control.³⁵⁷ Investments in this category vary, and no clear technology focus can be gleaned from available data.

3.4.8. Biotech Incubators/Accelerators

Chinese companies have invested just \$6 million so far in US biotech incubators and accelerators. This is the smallest segment within all Chinese biotech investments. We record two transactions in this segment: Qilu Pharmaceuticals' lab in Massachusetts and Gloria Pharmaceuticals' Cumberland Emerging Technologies incubator in Tennessee.

While data in this category are limited, anecdotal evidence indicates that opportunities to license products are a motivator for Chinese investment in overseas incubators. By developing connections with early-stage companies, Chinese investors can gain access to new biotechnology products developed overseas and acquire the rights to commercialize those products on the Chinese market. The incubator ecosystem in the US is robust, with 65 incubators and related centers for biotech and pharmaceutical companies.³⁵⁸ The amount of Chinese investment in this space is small in comparison, although has the potential to grow in the future.

We identified two instances of Chinese FDI in US-based incubators with a biotechnology or life science focus. In 2017, Chinese firm Qilu Pharmaceutical opened an operation in Boston consisting of QLB Biotherapeutics, a branch company with an interest in cancer immunotherapy, and Qilu Boston Innovation Center (QBIC), a biotech incubator.³⁵⁹ QBIC is in the same building as QLB Biotherapeutics' office and laboratory space. In addition to offering space and funding to biotech startups working on drug discovery, this incubator will serve as a conduit for Qilu to build long-term relationships with US-based startups and license new therapeutics, which may then be marketed in China.³⁶⁰ In 2014, Chinese firm Gloria Pharmaceuticals invested in the Cumberland Emerging Technologies (CET) incubator and joined as a partner.³⁶¹ Nashville-based CET was established years earlier in 2000 by Cumberland Pharmaceuticals working jointly with Vanderbilt University and Launch Tennessee (all US-based).³⁶² CET partners with academics and entrepreneurs to commercialize biopharmaceutical research and provides laboratory space and resources to life science companies in its incubator facility.³⁶³ Current tenants include, for example, a company building a next generation sequencing (NGS) platform.³⁶⁴ This partnership will give Gloria Pharmaceuticals the opportunity to license new products for distribution in China.³⁶⁵

³⁵⁷ "GreenLight Biosciences: Powering the RNA Revolution," GreenLight Biosciences, <https://www.greenlightbiosciences.com/>

³⁵⁸ Alex Philippidis, "65 U.S. Biotech and Pharma Incubators," *Genetic Engineering & Biotechnology News* May 11, 2015, <https://www.genengnews.com/the-lists/65-us-biotech-and-pharma-incubators/77900440>

³⁵⁹ Hong Xiao, "Biotechnology incubator opens doors in Boston," *China Daily USA* May 22, 2017, http://usa.chinadaily.com.cn/world/2017-05/22/content_29449554.htm; "QLB Biotherapeutics," QLB Biotherapeutics, <http://qlb-bio.com/>

³⁶⁰ Robert Weisman, "China likes what it sees in Boston biotech," *The Boston Globe* May 26, 2017, <https://www.bostonglobe.com/business/2017/05/26/china-likes-what-sees-boston-biotech/ToXpTLMyatPKIX11LPLwoN/story.html>

³⁶¹ Emily Kubis, "Cumberland, Chinese company invest \$2M in incubator," *Nashville Post* May 7, 2014, <https://www.nashvillepost.com/business/health-care/article/20476467/cumberland-chinese-company-invest-2m-in-incubator>

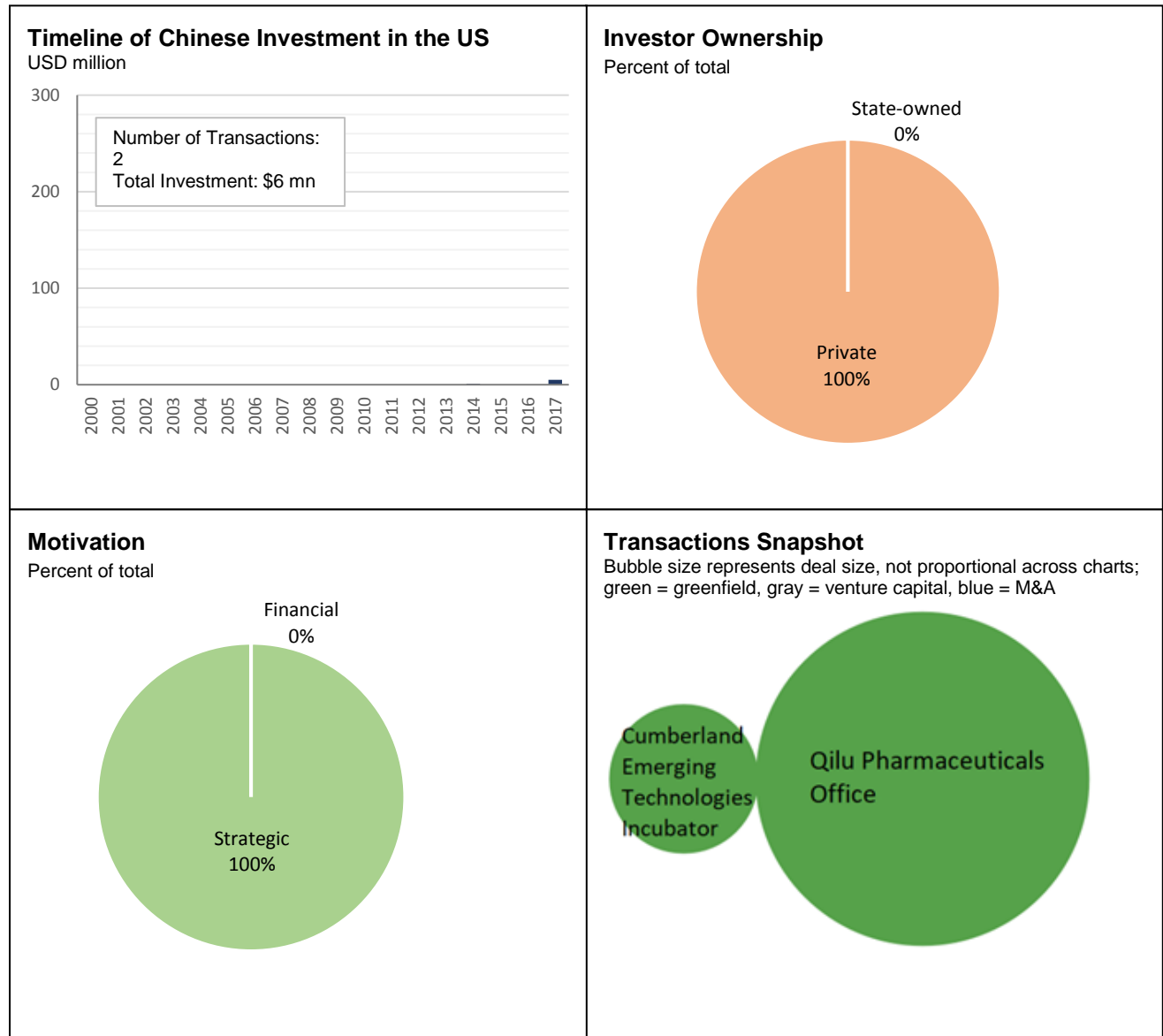
³⁶² "A Strong Foundation," Cumberland Emerging Technologies, <http://www.cet-fund.com/about-cet/a-strong-foundation/>

³⁶³ "CET: Cumberland Emerging Technologies," <http://www.cet-fund.com/>; Note that this incubator exhibits broad life science and biopharmaceutical interests, and is therefore not exclusively biotech-focused, but was included in this category due to its relevance.

³⁶⁴ "Tenants," <http://www.cet-fund.com/life-sciences-center/the-tenants/>

³⁶⁵ Kubis, "Cumberland, Chinese company invest \$2M in incubator," <https://www.nashvillepost.com/business/health-care/article/20476467/cumberland-chinese-company-invest-2m-in-incubator>

Figure 3-17. Summary of Chinese Investments in Biotech Incubators/Accelerators*



Note (*): State-owned entities refer to companies that are at least 20% owned by the government, State-owned Assets Supervision and Administration Commission, and other SOEs; Strategic investments refer to real economy firms making strategic investments in their core areas of business; financial investments refer to those made primarily for financial returns.

Source: Rhodium Group.

3.5. US Regulation of Foreign Investment

The primary mechanism the US has to protect against investments with foreign companies that may pose security risks is review by CFIUS, an inter-agency committee chaired by the Secretary of the Treasury.³⁶⁶ CFIUS has the authority to review “any transaction ... which could result in control of a US business by a foreign person” (also known as a “covered transaction”) and assess the potential national security implications of the transaction. Transactions may be “a proposed or completed merger, acquisition, or

³⁶⁶ "Composition of CFIUS," U.S. Department of the Treasury, updated December 1, 2010, <https://www.treasury.gov/resource-center/international/foreign-investment/Pages/cfius-members.aspx>

takeover."³⁶⁷ Should the Committee find national security threats posed by the proposed transaction, they can specify actions to mitigate them or even recommend blocking the transaction.

In the CFIUS review process, parties to a potential transaction file a voluntary notice, triggering an initial 30-day review period. By the conclusion of the review period, CFIUS can clear the transaction (with or without conditions) or choose to begin an investigation, which can take up to an additional 45 days.³⁶⁸ In clearing a transaction, CFIUS either determines that no national security concerns exist or dictates specific mitigations against identified threats and clears the transaction conditionally on upon their adoption. If the Committee cannot resolve security concerns in the transaction, it may recommend to the President whether to prohibit or suspend the deal, which must occur within 15 days of the recommendation.³⁶⁹ Although filing notice for CFIUS review is voluntary, the Committee can initiate reviews on its own, and can do so at any time even years after closing of a deal.³⁷⁰ From 2009 to 2015, 770 notices were filed with CFIUS.³⁷¹ Mitigation measures resulting from CFIUS reviews have included limiting access to certain technology to authorized persons, limiting handling of certain products and services to US citizens, establishment of a security committee or appointment of a security officer to ensure compliance, and enabling the US government to review certain business decisions.³⁷² When reviewing transactions, CFIUS considers a number of factors, including how the transaction may affect US technological leadership, critical infrastructure, or critical technologies as they relate to national security. Critical technologies are defined as those that fall under specific existing regulations, including the International Traffic of Arms Regulations (ITAR), the US Commerce Control List, and the HHS and USDA Select Agents and Toxins list, plus two nuclear-specific export control regulations.³⁷³ As discussed later in this section, these existing export control measures have limited effect on preventing foreign acquisition of important biotechnology, and likewise the definition of critical technologies used by CFIUS has limited applicability to much of modern biotechnology.

In August 2018, FIRRMA was signed into law, broadening CFIUS' national security criterion and country-based levels of scrutiny.³⁷⁴ A few changes to CFIUS review rules included in the law may have a significant impact on Chinese investments in US biotechnology companies. The first expands the types of covered transactions that are subject to review by CFIUS to include any non-passive investment—not just those that confer control—by a foreign person in US businesses involved in critical infrastructure, critical technologies, or maintenance or collection of sensitive personal data. This new covered transaction allows national security review of even minor ownership transfers in this subset of US businesses. Including companies that hold personal data is a new concept for CFIUS, indicating a shift toward recognizing the value of such data and its importance to national security. Additionally, the definition of critical technologies is expanded by FIRRMA to include emerging and foundational technologies, which will be defined through an interagency process laid out in the Export Control Reform Act of 2018 (ECRA, passed as part of the National Defense Authorization Act for fiscal year 2019).

Due to confidentiality rules, CFIUS does not disclose the transactions it reviews or the outcomes, making it impossible to perform a comprehensive review of the impacts CFIUS has had on biotechnology investments. However, some reports have surfaced that provide examples of decisions the Committee has made in this area. In 2012, CFIUS cleared the acquisition of Complete Genomics by BGI, a deal that

³⁶⁷ Department of the Treasury, "Regulations Pertaining to Mergers, Acquisitions, and Takeovers by Foreign Persons: Final rule," *Federal Register* 73, no. 226 (2008): 70701-29.

³⁶⁸ Latham & Watkins Staff, "Overview of the CFIUS Process," *Latham & Watkins LLP* 2017, <https://www.lw.com/thoughtLeadership/overview-CFIUS-process>

³⁶⁹ "Committee on Foreign Investment in U.S.: Process Overview," U.S. Department of the Treasury, updated December 1, 2010, <https://www.treasury.gov/resource-center/international/foreign-investment/Pages/cfius-overview.aspx>; Latham & Watkins Staff, "Overview of the CFIUS Process," <https://www.lw.com/thoughtLeadership/overview-CFIUS-process>

³⁷⁰ "M&A Guide to CFIUS: Deciding Whether to Submit Voluntarily to CFIUS Review," Cooley LLP, updated February 27, 2018, <https://www.cooley.com/news/insight/2018/2018-02-27-ma-guide-to-cfius>

³⁷¹ Committee on Foreign Investment in the United States. *CFIUS Annual Report to Congress* Washington, D.C.: Committee on Foreign Investment in the United States, 2015.

³⁷² *Ibid.*

³⁷³ 31 CFR § 800.209 – Critical Technologies

³⁷⁴ *Foreign Investment Risk Review Modernization Act of 2018*, S.2098.

brought together two DNA sequencing service providers.³⁷⁵ The approval came despite concerns that BGI would undercut the US sequencing industry with cheaper prices as well as concerns over data privacy.³⁷⁶ CFIUS has also reviewed several biotech deals with targets based outside of the US (which it can if the target has US operations), for example the acquisitions of Sirtex (Australia) or Biotest (Germany).

In addition to CFIUS review of foreign investment, federal and international export control laws may also apply to some investments that could result in a transfer of sensitive, dual-use technology to a foreign country. The export controls system consists of a network of federal agencies and regulations that restrict the export of certain goods and services activities. The most important agency to the biotechnology sector is the Department of Commerce, which maintains the Commerce Control List (CCL). One area covered by this list is agents, equipment, and software that can be used to acquire, create, produce, stockpile, or test biological weapons.³⁷⁷ The ITAR prevent the acquisition of national defense-related information and technologies by adversaries; with respect to biological technologies, ITAR restricts the export of pathogens, toxins, or equipment capable of producing a pathogen or toxin.³⁷⁸ These regulations are relevant to the biotechnology industry insofar as they involve the biological agents that are controlled or if companies have equipment that could be used to produce or manipulate these agents in bulk.

On November 19, 2018, the Department of Commerce's Bureau of Industrial Security (BIS) released an advance notice of proposed rulemaking seeking comment on criteria to identify foundational and emerging technologies to add to the CCL, as directed by the ECRA. Biotechnology, including synthetic biology, genomics, and genetic engineering, is identified in the notice as a general category which may contain sensitive foundational technologies. As this process unfolds, the US may have the authority to control movement of a much broader set of technologies, albeit with a risk of including many technologies and research that may have limited utility in deliberately harming U.S. national security (e.g., genome editing, which was listed as a weapon of mass destruction in 2016 by the Director of National Intelligence).

Given their focus primarily on specific pathogens and equipment, international and national export control policies as they stand now have limited effect on Chinese acquisition of biotechnology from foreign countries. A very small segment of the biotechnology industry works on (or uses) these controlled pathogens and therefore increasing the protection of these few companies would have little effect on the overall health of the biotechnology industry in the US. Moreover, due to the importance of research on these pathogens to US biodefense efforts, funding for these companies is more robust in the US than abroad, which provides a strong incentive not to relocate overseas. As biotechnology continues to expand into the non-medical realms of renewable energy, information storage, and materials, an even smaller portion of US biotechnology will be focused on these few disease-causing agents.

In contrast, many biotechnology companies possess equipment that is controlled under existing export control regimes. For example, large fermenters are extensively used to grow the engineered microbes that are producing biotechnology products, such as biopharmaceuticals and industrial chemicals, but could also be used to produce disease causing microbes for use in a biological warfare program. For this reason, the US and other countries control the trade of this equipment. If a biotechnology company that possesses this equipment is bought by a Chinese firm, an export license would need to be acquired before the regulated industrial equipment could be moved to China. However, Chinese companies can acquire this equipment through other sources (such as domestic manufacturers) and any obstacle to acquiring this equipment from a US company would probably not be a determining factor for any partnership (the intellectual property, not the physical property, is the primary interest).

³⁷⁵ Pollack, "U.S. Clears DNA Firm's Acquisition by Chinese," <https://www.nytimes.com/2012/12/31/health/chinese-firm-is-cleared-to-buy-american-dna-sequencing-company.html>

³⁷⁶ Grant, "Feds Scrutinize Genomics Merger". <https://www.the-scientist.com/?articles.view/articleNo/33567/title/Feds-Scrutinize-Genomics-Merger/>

³⁷⁷ "Commerce Control List (CCL)," U.S. Department of Commerce Bureau of Industrial Security (BIS), <https://www.bis.doc.gov/index.php/regulations/commerce-control-list-ccl>

³⁷⁸ "The International Traffic in Arms Regulations (ITAR)," U.S. Department of State, Directorate of Defense Trade Controls, https://www.pmdtc.state.gov/?id=ddtc_kb_article_page&sys_id=24d528fddbfc930044f9ff621f961987

3.6. Outlook

The outlook for Chinese biotech investment in the US depends on a series of commercial and political factors.

From a high-level perspective, the growth potential of Chinese outbound investment in biotechnology is massive. While China is now the world's second largest economy, its outbound investment catch-up process is just beginning. China's per capita GDP is just \$8,830 and its outbound FDI stock to GDP ratio stood at 12 percent in 2017. This is below that of most advanced economies such as the United States (38 percent), Japan (20 percent), and Germany (46 percent). In other words, most of China's outward FDI boom is still ahead. In the past decade, the United States received on average about 17 percent of global FDI flows. If the United States manages to attract a similar share of China's global outbound FDI, it would receive hundreds of billions of Chinese investment in the coming decade.

Within biotech, Chinese companies appear ready to continue to use outbound FDI as a major tool for technology acquisition. Transactions such as the Dendreon sale suggest that Chinese investors may be looking for opportunities to acquire portfolios of existing, proven products (as opposed to developmental stage technologies) where they can leverage their lower production costs to meet demand, as well as to expand into the US market. The willingness of China to collect personal data on its citizens and those of other countries, coupled with China's advanced positioning in the ICT sector, suggests that genomics and molecular diagnostics applications may also continue to be a target. However, newly passed reforms to CFIUS may dampen outbound FDI in the US, especially with rules that put more scrutiny on foreign access to personal data of US citizens.

While the long-term growth potential is huge, there are serious short-term headwinds to further expansion of Chinese outbound FDI in the US due to deep changes in the policy environment. In 2017, China tightened controls over outbound investment and implemented a crackdown on leveraged private investors. Together this caused China's global outbound FDI to decline for the first time in more than a decade in 2017. At the moment, China is restricting five types of outbound investments in sectors including entertainment, real estate and hospitality.³⁷⁹

While biotech was largely not affected by China's new restrictions on outbound FDI, it could be caught in the cross-fire as China continues to reform the review of foreign investments domestically. China screens for national security issues on a case-by-case basis as part of its inward FDI approval and recording system. A draft foreign investment law that would update the system is in the works. China also made incremental changes in specific areas to refine the system in recent years. For example, for foreign investment in listed companies, China's Ministry of Commerce announced amendments in July 2018 that make clear that strategic stakes will be subject to national security review. In addition, China has recently tightened broader review of technology related deals domestically. In March 2018, China implemented a new measure restricting the export of scientific data. In April, China passed draft rules on restricting external transfers of IPR. The purpose of these new rules is to broadly protect "Chinese innovation and competitiveness", not just to screen for national security risk. But these policies aggravate foreign concerns about FDI reciprocity and could contribute to more actions in the US to limit Chinese M&A in R&D-heavy sectors such as biotechnology.

In the United States, there are regulatory changes that could impact Chinese investment in the biotech sector. In 2017, CFIUS reviewed several deals in which US citizen data privacy and protection is an important issue (Ant Financial's proposed acquisition of Moneygram and Oceanwide's acquisition of Genworth). This new focus on data privacy could impact investments in the biotech and healthcare sector. The decision to block Broadcom's acquisition of US chipmaker Qualcomm illustrates that the US

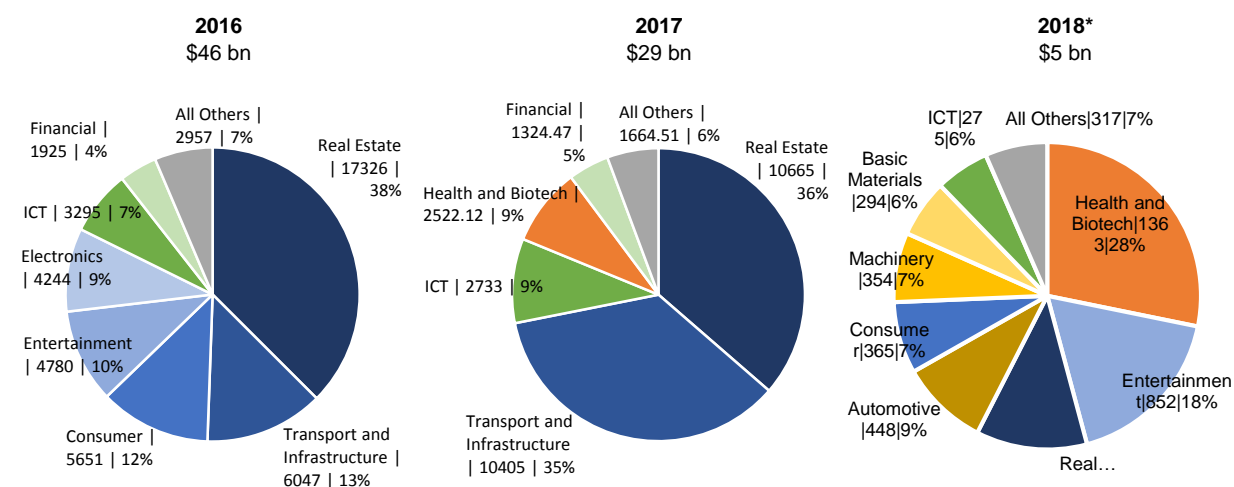
³⁷⁹ The full list of the five types of restricted outbound investments are: investments in regions with no diplomatic relation with China, regions with war or conflicts, and sensitive region with investment restrictions from international agreements; investments in real estate, hospitality, cinemas, entertainment, and sports clubs etc.; equity investment funds or investment platforms with no actual physical project abroad; those employing old equipment not in compliance with the target country's technical standard regulations; and those that are not in compliance with the target country's environmental, energy use, and safety standards.

government is now also applying a broader perspective that analyzes whether foreign acquisitions could threaten technology “ecosystems” in the US. Against the backdrop of China’s non-market economy, this new stance could derail Chinese acquisitions of US technology companies if the transaction is perceived as exporting harmful spillovers from Chinese subsidies and other market distortions. In addition to those execution changes, implementation of FIRRMA will put investment from China and other non-allied nations under additional scrutiny and will tighten screening of R&D related investments in the US, which affects the majority of deals in the biotech sector.

Preliminary data for 2018 suggest that biotech has been more resilient than other sectors. In 2018, overall Chinese FDI dropped sharply to \$5 billion compared to \$29 billion for all of 2017.³⁸⁰ The broader health and biotech sector, however, continued to receive significant Chinese investment: \$1.4 billion in 2018 compared to \$2.5 billion in 2017. This resilience made the health and biotech sector the largest recipient of Chinese FDI in the US last year, although the majority of that investment can be attributed to Shandong Weigao’s acquisition of Argon Medical Devices for \$850 million (which is not at its core a biotech transaction). The same top segments within biotechnology have seen continued investment in 2018, including biologics, genomics, and molecular diagnostics. Despite Chinese capital controls, health and biotech remains an encouraged sector by Chinese policy and one with great commercial incentives for investment.

Figure 3-18. Chinese FDI Transactions in the US by Industry, 2016-2018

Percent of Total



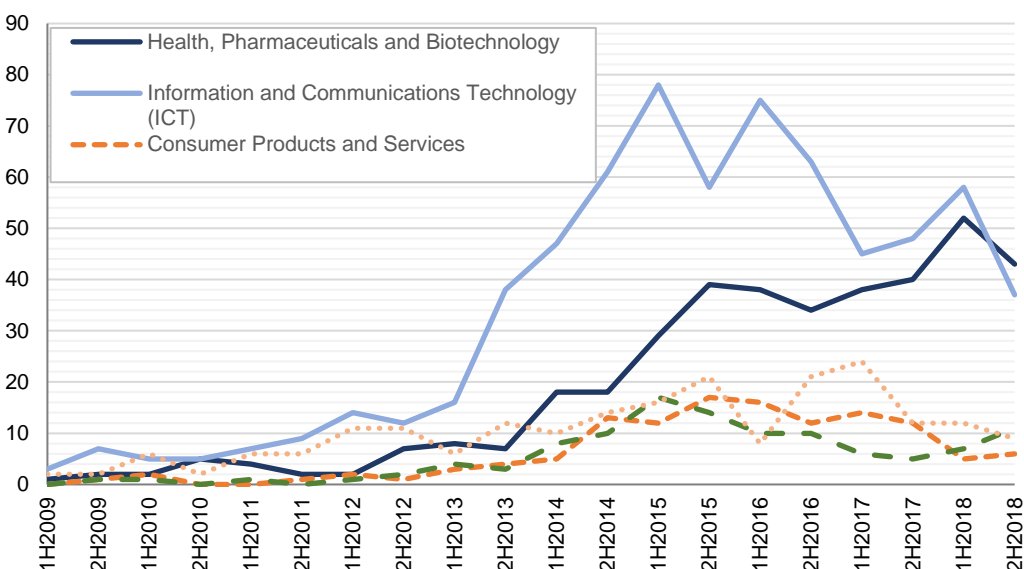
Source: Rhodium Group. *2018 data are preliminary only.

Health and biotech also remained an important sector for Chinese VC investment in the US in 2017 and 2018. The healthcare, pharmaceuticals and biotechnology (health and biopharma) industry, accounting for more than 16 percent of both the number of global VC fundraising rounds and raised capital in 2017. After playing catch-up for several years, in 2018 health and biopharma also overtook ICT as the top recipient of Chinese VC investment in the US by number of transactions. These two sectors receive far more Chinese venture investment than any other sector.

³⁸⁰ A full analysis of the most recent FDI data was not performed, and biotechnology investments were not distinguished from other investments in the healthcare and biotechnology sector for this brief analysis.

Figure 3-19. Chinese VC Investment in the US by Industry, 2000-2018*

Number of Funding Rounds



Source: Crunchbase, Pitchbook, Zero2IPO, Rhodium Group. *Includes all venture capital investments in US-headquartered companies made by Chinese ultimate-owned venture investors; does not include Chinese limited partner investors. 2018 data are preliminary only.

The trajectory of Chinese outbound biotech investments in the US in 2019-2020 will depend on whether the Chinese government will continue to support outbound investment in the biotech industry, and to what extent broader economic and financial volatility could require Beijing to impose additional investment restrictions. On the US side, with the passage of FIRRMA it will be critically important to see to what extent its implementation will put biotechnology on the list of emerging or foundational technologies. First steps by the US government to implement FIRRMA suggest that biotech will be heavily scrutinized: Biotech R&D is one of the 27 industries singled out for specific scrutiny under a first pilot program by the US Treasury Department that came into effect in November 2018.³⁸¹ Biotechnology—including nanobiology, synthetic biology, genomic and genetic engineering and neurotech—has also made it onto the list of emerging technologies issued by the Department of Commerce in November 2018.³⁸²

³⁸¹ "Determination and Temporary Provisions Pertaining to a Pilot Program To Review Certain Transactions Involving Foreign Persons and Critical Technologies," (31 CFR Part 8012018).

³⁸² "Review of Controls for Certain Emerging Technologies," (15 CFR Part 7442018).

4. China's Involvement in U.S.-Based Research Organizations

Key Findings

- **Chinese companies and researchers play an important role in in US biotechnology innovation through US-based R&D centers and incubators, corporate and academic partnerships, and a large cohort of Chinese researchers in US academic institutions and companies.**
- **China's biotech companies attempt to benefit from the US biotechnology innovation pipeline by creating US-located R&D centers and incubators.** They are attracted to the concentration of elite biotech companies and academic research institutes in major centers like Boston and the San Francisco Bay area. Some locales offer financial incentives for biotechnology that the companies are also looking to leverage.
- **The Chinese government is trying to recruit students and researchers trained in the US to relocate to China.** Over 360,000 Chinese students are studying in the US today. Through programs offering incentives such as high salaries, laboratories, and startup financing, China has recruited thousands of researchers, both Chinese-born and foreign, to relocate to China since the programs began in 1994; the Thousand Talents Program alone has recruited over 2,600.
- **Research partnerships between US and Chinese academic institutions or biotech firms spur scientific advancement and are generally beneficial to the US economy.** Partnerships are often designed to leverage expertise in specific fields, such as cancer therapeutics or precision medicine.
- **Such partnerships also marginally increase the potential for theft of IP and trade secrets.** Close research collaboration can offer opportunities to individuals and companies to illegitimately or illicitly obtain and transfer US IP to China.
- **The US has limited regulations on foreign involvement in US research.** Open collaboration is a cornerstone of scientific research and innovation, and foreign-born researchers are an integral part of US biotechnology. The United States must maintain a balance between open collaboration and access to foreign talent with the potential losses due to leakage or theft of IP and technologies.

This chapter reviews non-investment engagement of Chinese companies and institutions in the United States. It first discusses partnerships (including R&D centers, biotechnology incubators and other types of arrangements) and then describes academic collaborations. It concludes with a discussion of benefits and risks from a US perspective.

4.1. Types of Partnerships

Apart from VC and FDI, biotech firms can use a number of other mechanisms of partnership to gain access to foreign technology and data, including licensing or R&D partnerships, incubators and other arrangements to enable sharing of expertise and technology, corporate partnerships with research institutions or universities, and founding of research institutions in foreign locations. We found that Chinese biotechnology companies have utilized all of these channels in expanding their relationships with US entities. Apart from wholesale acquisitions of companies, though, determining the meaning of a transaction in terms of IPR transfer and other risks is difficult, but we have identified some specific relevant cases.

4.1.1. Research and Development Centers

Numerous Chinese biotechnology companies have started new R&D facilities in the US, generally focused in major biotech hubs such as Boston, San Francisco, or the Research Triangle area in North Carolina. Establishing R&D centers in the US is a strategy Chinese companies may use to gain access to new technologies that they can then bring back to the mainland.³⁸³ By locating in major biotech regions, Chinese companies get access to a wealth of expertise not found elsewhere in the world plus a large, well-educated workforce and top-tier research universities. Local governments from many of these areas provide financial incentives to attract globally innovative, high-tech companies as well.

Many Chinese biotechnology companies have opened their doors in the US with research centers in the Boston area. A couple of high profile companies have opened R&D centers jointly with incubators to foster product development by startups: Qilu Pharmaceutical opened QLB Biotherapeutics, its US operation, alongside their QBIC incubator,³⁸⁴ and VcanBio Cell & Engineering Corporation—the self-claimed largest biotech company in China—simultaneously opened VcanBio USA and the VcanBio Center for Translational Biotechnology, both located near Boston.³⁸⁵ Both companies develop cancer immunotherapy products and related technologies. Other research centers from Chinese companies in the Boston area include the Luye Boston R&D Center by Luye Life Sciences Group for cancer immunotherapy development, and Biocytogen's facility for preclinical pharmacological animal studies.³⁸⁶ Other major biotechnology regions in the US are also attractive to Chinese companies as well. Sihuan Pharmaceutical set up an R&D Center in the San Francisco Bay area for their immuno-oncology work.³⁸⁷ Novogene, a provider of genomics services, established a genome sequencing center in the Sacramento area on the campus of UC Davis.³⁸⁸ Genetron Health Co. Ltd opened their molecular diagnostics and precision medicine center, Genetron Health Technologies, in Research Triangle Park, NC.³⁸⁹ While both Boston and San Francisco areas are considered the top two biotechnology hubs in the US, Boston is viewed as arguably the premier biopharma hub, leading the country in NIH funding, laboratory space, and, in 2016, VC funding for biopharmaceutical companies;³⁹⁰ Boston's primacy may explain its draw for foreign investors.

When asked why they chose these biotech hub locations for their new operations, company executives repeatedly referred to the innovation ecosystem that can be found nowhere else, relationships with biotech entrepreneurs, and access to US talent (including Chinese-Americans located in the US). John Lu of VcanBio cited access to advanced technologies and talented scientists in Boston. Qilu's Larry Cai also

³⁸³ William C. Hannas, James Mulvenon, and Anna Puglisi, "Chinese Industrial Espionage," (New York, NY: Routledge, 2013).

³⁸⁴ Xiao, "Biotechnology incubator opens doors in Boston," http://usa.chinadaily.com.cn/world/2017-05/22/content_29449554.htm; Weisman, "China likes what it sees in Boston biotech," <https://www.bostonglobe.com/business/2017/05/26/china-likes-what-sees-boston-biotech/ToXpTLMyatPKIX11LPLwoN/story.html>

³⁸⁵ Mark Terry, "There's No Place Like Massachusetts for China's Largest Biotech Vcanbio," *BioSpace* September 14, 2016, <https://www.biospace.com/article/there-s-no-place-like-massachusetts-for-china-s-largest-biotech-vcanbio/>; Stephen Hansen, "Bridge to Innovation," *Biocentury*(2017), <https://www.biocentury.com/biocentury/strategy/2017-09-29/why-chinese-biopharmas-are-building-beachheads-boston>

³⁸⁶ "Luye Life Sciences Expands Global Reach as New Boston R&D Center Opens," Luye Life Sciences Group, updated July 17, 2017, <https://www.prnewswire.com/news-releases/luye-life-sciences-expands-global-reach-as-new-boston-rd-center-opens-300489083.html>; Hansen, "Bridge to Innovation". <https://www.biocentury.com/biocentury/strategy/2017-09-29/why-chinese-biopharmas-are-building-beachheads-boston>; Angus Liu, "Gene-targeted animal model CRO Biocytogen nets \$65M series C, eyes global expansion," *Fierce Biotech* April 12, 2018, <https://www.fiercebiotech.com/cro/gene-targeted-animal-model-cro-biocytogen-nets-65m-series-c-eyes-global-expansion>

³⁸⁷ "Sihuan Pharmaceutical : Voluntary Announcement - Establishment of United States Research and Development Centre," Sihuan Pharmaceutical, updated August 15, 2017, <http://www.4-traders.com/SIHUAN-PHARMACEUTICAL-HOL-6797640/news/Sihuan-Pharmaceutical-Voluntary-Announcement-Establishment-of-United-States-Research-and-Develop-24947699/>

³⁸⁸ "Novogene Establishes First U.S. Genomic Sequencing Center Located at UC Davis; Acquires Second Illumina Hi-Seq X Ten System," Novogene Corporation, updated April 14, 2016, <https://www.prnewswire.com/news-releases/novogene-establishes-first-us-genomic-sequencing-center-located-at-uc-davis-acquires-second-illumina-hi-seq-x-ten-system-300251077.html>

³⁸⁹ Barry Teater, "Cancer Diagnostics Firm with NC Lab Lauded in China," *North Carolina Biotechnology Center* October 26, 2016, <https://www.ncbiotech.org/news/cancer-diagnostics-firm-nc-lab-lauded-china>

³⁹⁰ "Top 10 U.S. Biopharma Clusters," Alex Phillippidis, updated June 5, 2017, <https://www.genengnews.com/the-lists/top-10-us-biopharma-clusters/77900917>

referenced local government support as a reason for locating in Boston.³⁹¹ In 2008, Massachusetts passed a bill to provide \$1 billion to the life sciences industry over 10 years via discretionary investment and grants, investments in life sciences infrastructure, and tax incentives to life sciences companies.³⁹² In 2018, the state authorized a \$623 million bill to continue this initiative.³⁹³ In addition, the establishment of US-based facilities allows firms more direct access to their customers and further expand the company's customer base.

4.1.2. Biotechnology Incubators

Startup incubators refer to a range of commercial facilities and organizations that provide infrastructure and support to help new companies grow and develop. The simplest biotechnology incubators provide laboratory space and equipment, allowing fledgling companies to share and distribute those startup costs, which are high in biotechnology.³⁹⁴ Incubators also frequently provide business support, including leveraging their expertise and networks to facilitate expansion and marketing, as well as providing basic legal and accounting support. Incubators are often linked to or sponsored by investors in the companies within the incubator, thereby increasing the probability that those investments result in a successful company and a positive return to those investors.

Large corporations have also entered the incubator arena, though on a much larger scale than the simple incubators described above. US biotech firms have created large centers that combine R&D, data analysis, preclinical and clinical trial support, and other functions to speed up product development. By sponsoring incubators, the larger companies have inside access to witness the technologies being developed by the early-stage startup companies they support. In the US, both types of incubators for startup biotechnology companies are popular—a 2015 article in *Genetic Engineering and Biotechnology News* listed 65 biotech incubators in the US.³⁹⁵ We identified several examples of Chinese biotech firms creating such incubators and partnerships in the US, a seemingly preferred way for these Chinese to advance their biotechnology development via connections with US partners.

In May 2018, the cities of Houston, TX, and Suzhou signed a memorandum of understanding to spur biomedical and biotechnology research and investment between the two cities. Through this agreement, the Jiangsu Industrial Technology Research Institute (JITRI) will open the China US Biotechnology Innovation Center (CUBIC) at the Texas Medical Center in Houston.³⁹⁶ JITRI, a major nonprofit research institute founded and supported by the Jiangsu provincial government, specializes in IT, biomedicine, and nanotechnology with an R&D budget of \$300 million.³⁹⁷ CUBIC will provide an opportunity for US startups and companies to work at the Center and access Chinese collaborators and investors. By locating CUBIC at the Texas Medical Center, one of the nation's most prominent biomedical research campuses, both US startups and Chinese collaborators can take advantage of the expertise and resources of this growing research area.

The QBIC is another Chinese biotech incubator collocated with a R&D facility of its parent company (see QLB Biotherapeutics, above). As a biotech incubator, QBIC aims to support biotech startups to further develop their products into successful therapeutics. Its sister company, QLB Biotherapeutics, intends to

³⁹¹ Hansen, "Bridge to Innovation". <https://www.biocentury.com/biocentury/strategy/2017-09-29/why-chinese-biopharmas-are-building-beachheads-boston>

³⁹² "Life Sciences Initiative," Massachusetts Executive Office for Administration and Finance, <http://budget.digital.mass.gov/bb/h1/fy10h1/prnt10/exec10/pbudbrief23.htm>

³⁹³ "Baker-Polito Administration Signs Life Sciences Initiative," Massachusetts Governor's Office, updated June 15, 2018, <https://www.mass.gov/news/baker-polito-administration-signs-life-sciences-initiative>

³⁹⁴ For example, highly specialized analytical equipment can cost a million dollars or more for a single instrument.

³⁹⁵ Philippidis, "65 U.S. Biotech and Pharma Incubators," <https://www.genengnews.com/the-lists/65-us-biotech-and-pharma-incubators/77900440>

³⁹⁶ Chris Teale, "Houston to partner with Chinese city Suzhou on biotech research," *Smart Cities Dive* May 17, 2018, <https://www.smartcitiesdive.com/news/houston-chinese-city-suzhou-partner-biotech-research/523764/>

³⁹⁷ Paul Takahashi, "Houston, China to partner on biotech innovation," *Houston Chronicle* May 15, 2018, <https://www.houstonchronicle.com/business/article/Houston-China-to-partner-on-biotech-innovation-12914224.php#photo-15555468>

make investments in the startups at QBIC and acquire the rights to any therapeutics that come out of the center.³⁹⁸ QBIC and QLB Biotherapeutics are owned by Qilu Pharmaceutical, a Chinese pharmaceutical giant producing drugs and biologics with over \$2 billion in annual sales.³⁹⁹ Senior leadership of QBIC and QLB Biotherapeutics have touted the importance of locating in Boston due to the “connectivity” to biotech elites in the area and the value of having a local partner.⁴⁰⁰

4.1.3. Other partnerships

Apart from creating new research facilities and startup incubators, Chinese biotech firms have entered into a variety of traditional and non-traditional agreements and partnerships to further development of biotech products and research.

In January 2017, iCarbonX announced the Digital Life Alliance, a new collaborative effort designed to give people a deeper understanding of the medical, behavioral, and environmental factors that can accelerate disease or optimize health. iCarbonX was founded in China in 2015 by the former CEO of BGI and aims to build an internet-based ecosystem of digital life based on artificial intelligence (AI) and a combination of an individual's biological, behavioral, and psychological data.⁴⁰¹ The Digital Life Alliance brings together leading bio, health networking, sequencing, and AI technology and application companies around the world. An initial seven companies, including the US-based companies SomaLogic, HealthTell, PatientsLikeMe, AOBiome, and GALT, joined the alliance and received \$400 million in total investment from iCarbonX. The participating companies bring a wide variety of expertise in protein measurement, microbial detection and isolation, human health modeling, enzymatics, and the study of immune system regulation and probiotic therapies. Additionally, iCarbonX brings its own vast expertise in data analysis and mining. The consortium ultimately aims to merge comprehensive biological and patient-generated data with AI technology and predictive algorithms to provide data-based insights into an individual's health, disease progression, and aging and deliver a personalized guide for living well. The system could also be leveraged by the healthcare industry to improve precision medicine.⁴⁰²

Since 2012, Chinese sequencing giant BGI has partnered with the Bill and Melinda Gates Foundation to advance global health and agricultural biotechnology research. In 2012, a memorandum of understanding was signed between the two organizations to collaborate on genetics studies tied to global health and agricultural breakthroughs as part of the United Nations Millennium Development Goals.⁴⁰³ Two recent projects have leveraged BGI's genomics capabilities to identify biomarkers for enteropathy in malnourished children and to study immunization against malaria.⁴⁰⁴

While we identified several examples, no data are available to comprehensively review and assess the quantity or quality of other existing partnerships between Chinese firms and US institutions.

³⁹⁸ Weisman, "China likes what it sees in Boston biotech," <https://www.bostonglobe.com/business/2017/05/26/china-likes-what-sees-boston-biotech/ToXpTLMyatPKIX11LPLwoN/story.html>

³⁹⁹ Xiao, "Biotechnology incubator opens doors in Boston," http://usa.chinadaily.com.cn/world/2017-05/22/content_29449554.htm

⁴⁰⁰ Weisman, "China likes what it sees in Boston biotech," <https://www.bostonglobe.com/business/2017/05/26/china-likes-what-sees-boston-biotech/ToXpTLMyatPKIX11LPLwoN/story.html>; Xiao, "Biotechnology incubator opens doors in Boston," http://usa.chinadaily.com.cn/world/2017-05/22/content_29449554.htm

⁴⁰¹ "iCarbonX Expands Digital Life Alliance to Accelerate Development of Global Health Ecosystem," iCarbonX, updated January 5, 2017, <https://www.businesswire.com/news/home/20170105005285/en/iCarbonX-Expands-Digital-Life-Alliance-Accelerate-Development>

⁴⁰² Ibid.

⁴⁰³ Bio-IT World, "BGI and Gates Foundation Collaborate," *Bio-IT World*(2012), <http://www.bio-itworld.com/2012/09/25/bgi-gates-foundation-collaborate.html>

⁴⁰⁴ "BGI Collaborates with the Bill & Melinda Gates Foundation," Beijing Genomics Institute, http://www.genomics.cn/communication_newsletter/2017-Aug-PC-E/page-en/detail-en-hezuo.html

4.2. Chinese Students and Academic Research in the US

Academic science and technology research in the US is fueled primarily by graduate students and post-graduate doctoral researchers. Graduate research assistants are masters and doctoral students paid by their institutions through training grants acquired by research faculty. In addition to providing needed training and a living stipend for the grantees, these training grants are essential to supporting academic research programs. In 2015, there were 115,000 US graduate students in Science and Engineering receiving research assistantships and 45,000 postdoctoral researchers, many of whom are foreign-born.⁴⁰⁵ Of the foreign-born students in the US, one-third are from China.⁴⁰⁶

Chinese students have for decades been travelling to the United States for higher education. During the middle of the 20th century, Chinese students studying abroad were not celebrated, but Chinese attitudes changed in the 1980s and '90s and studying internationally was encouraged. As early as 1978, Chinese leader Deng Xiaoping stated that sending students abroad is one of the most important ways to improve Chinese science and education. Hoping for a high rate of return, he suggested money invested in sending students abroad was cost effective.⁴⁰⁷ Since then, the numbers of Chinese students travelling abroad for higher education has climbed, and it is now widely accepted in China as an important milestone of a successful academic career. In the US alone, there were more than 360,000 Chinese students studying in universities during the 2017-2018 academic year.⁴⁰⁸

4.2.1. China's Talent Programs

In 1994, the first Chinese talent development program, the Hundred Talents Program, was started by the CAS to attract top foreign scientists to research positions in China. Awardees were paid relocation costs, startup funds, and a competitive salary; the most recent award packages range from 800,000 yuan (\$124,000) for young talent to 7 million yuan (\$1.1 million) for academic leaders (employers may pay extra on top of those figures).⁴⁰⁹ Other national talent development programs have been established, including the Thousand Talents Program and the National Science Fund for Distinguished Young Scholars, which focus on repatriating Chinese scientists abroad but also accept non-Chinese applicants.⁴¹⁰ Most of these programs aim to bring in talent in science and engineering fields.

In 2014, President Xi Jinping announced the development of human talent would be the highest priority in science and technology innovation. As part of Made in China 2025 and the 13th FYP, these programs receive a significant amount of government funding (although specific numbers are not reported).⁴¹¹

By many accounts, Chinese talent programs have been very successful. According to Chinese estimates, 58,000 recruits have come back because of these programs, including 7,000 they would qualify as top-tier recruits. By comparison, the US recruitment program for the Manhattan Project brought in 300 foreign scientists, and Operation Paperclip—a secret program to recruit scientists following World War II—netted 1,600 to 2,000 talented, mostly German scientists and engineers. Talent programs are not just targeting Chinese nationals, either—roughly 10 percent of all program participants now are not Chinese-born.⁴¹²

⁴⁰⁵ National Science Board, *Science and Engineering Indicators*; A breakdown of graduate research assistants and postdocs by nationality is not available.

⁴⁰⁶ Institute of International Education. *International Student Totals by Place of Origin, 2012/13-2017/18* Open Doors Report on International Educational Exchange: <http://www.iie.org/opendoors>, 2018.

⁴⁰⁷ Cao, "China's Brain Drain at the High End," 331-45.

⁴⁰⁸ Alice Shen, "Chinese students still drawn to US universities, but growth rate slowing," *South China Morning Post* November 14, 2017, <https://www.scmp.com/news/china/society/article/2119903/chinese-students-still-drawn-us-universities-growth-rate-slowing>

⁴⁰⁹ Chinese Academy of Sciences, "Chinese Academy of Sciences launches the Hundred Talent Program of the Pioneer Initiative," (2017), <http://international-talent.cas.cn/front/index.html#/bicsite/pifilntroduce/hundred>

⁴¹⁰ Cao, "China's Brain Drain at the High End," 331-45.

⁴¹¹ Huiyao Wang, "China's National Talent Plan: Key Measures and Objectives," (2010), <https://www.brookings.edu/research/chinas-national-talent-plan-key-measures-and-objectives/>

⁴¹² Authors' discussion with confidential federal law enforcement source.

For the past few years, biotechnology has been a major focal point of China's talent programs. Highlighted in both Made in China 2025 and the 13th FYP, biotechnology is a focal point of Chinese industrial development, and talent development programs are a major mechanism toward achieving those goals. Out of the estimated 2,629 current recruits in the Thousand Talents program as of June 2018, 44 percent specialize in life sciences or medicine.⁴¹³ Within the sector, however, there is no concerted effort to target specific technologies. Instead, the programs cast a wide net and look for top talent across the biomedical and life science fields, correctly realizing that recruiting a critical mass of top scientists will necessarily result in representation from the most important and advanced fields. Indeed, common areas of study by talent program participants include cancer therapeutics and genomics, two of the most active areas of biotechnology research in China and worldwide.

Despite these recruitment programs, most Chinese students frequently opt to stay in the US after the receipt of a graduate degree. According to the National Science Foundation, for temporary visa holders receiving science and engineering doctorates in the US in 2010, the five-year stay rate (i.e., the percent remaining in the US in 2015), was highest for students from China, at 85 percent, followed closely by India at 83 percent (Figure 4-1). The five-year stay rate for students of European origin was 64 percent.⁴¹⁴ The five-year stay rate for Chinese students in the US has remained steady in recent years and was also 85 percent for science and engineering doctoral students graduating in 2006 and remaining in the US in 2011.⁴¹⁵ Ten-year stay rates are similar to five-year stay rates; of Chinese science and engineering doctoral students graduating in 2005, 90 percent remained in the US in 2015.⁴¹⁶ It is unclear why these rates differ significantly from those reported by China's MOE, though one speculative possibility is that science and engineering doctorate return rates differ from other types of students; National Science Foundation-reported rates refer only to recipients of S&E doctorates in the US, while MOE's reported rates would include students at all levels in all fields and would include those abroad but outside the US. Another possibility is that doctoral students are much more likely to stay in the US than undergraduate students. Overall, Chinese students have historically returned from abroad at lower rates than students from many other countries, and closing this gap may be the more immediate aim of China's repatriation efforts.

⁴¹³ Anthony Capaccio, "U.S. Faces 'Unprecedented Threat' From China on Tech Takeover," *Bloomberg*(2018), <https://www.bloomberg.com/news/articles/2018-06-22/china-s-thousand-talents-called-key-in-seizing-u-s-expertise>

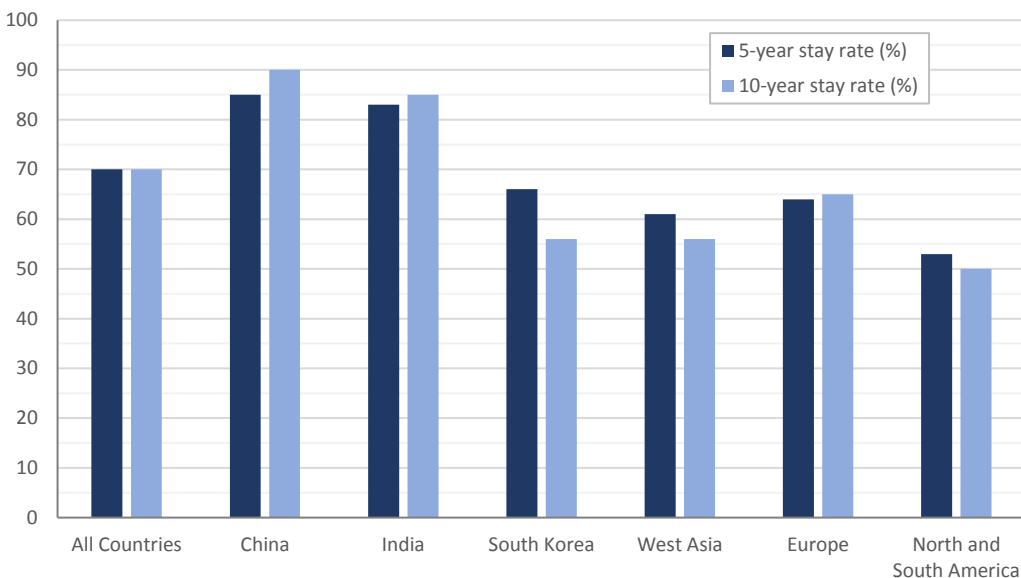
⁴¹⁴ National Science Board, *Science and Engineering Indicators*.

⁴¹⁵ Michael G. Finn, "Stay Rates of Foreign Doctorate Recipients from U.S. Universities, 2011 ", *Oak Ridge Institute for Science and Education*(2014), <https://orise.orau.gov/stem/reports/stay-rates-foreign-doctorate-recipients-2011.pdf>

⁴¹⁶ National Science Board, *Science and Engineering Indicators*.

Figure 4-1. Five- and 10-Year Stay Rates for Science and Engineering Doctorate Temporary Visa Holders by Country, 2015*

Stay rate, Percentage



Note (*): Five- and 10-year stay rates refer to temporary visa holders receiving S&E doctorates in 2010 and 2005 who were in the United States in 2015.

Source: NSF.

US immigration policies have played a significant role in the number of Chinese students staying in the country after graduation. Following the student protests in Tiananmen Square in 1989, President Bush issued an executive order that provided several benefits for Chinese student visa holders, including extension of immigration status, work authorization, and waiver of home country residence requirements. The Chinese Student Protection Act, passed in 1992, authorized permanent residence status to be granted to Chinese nationals who were in the US between June 4, 1989 and April 11, 1990. Together, these policies enabled 40,000-80,000 Chinese students to remain in the US. In the decades following, the number of Chinese students returning to China increased. While the lapse of policies enabling retention of students likely played a role, so did the economic development that was occurring in China. A 2002 survey of Chinese immigrant engineers in the US indicated that the most frequently cited factor in whether to return to China (78 percent of respondents) was professional opportunities in their home country. Fewer than half (44 percent) of survey respondents indicated that limits on professional advancement in the US would factor into their decision to leave.⁴¹⁷ The results of this survey suggest that as China's bioeconomy continues to develop, more US-based biotechnology researchers may leave to return home, regardless of Chinese policy. At the same time, favorable immigration policies (e.g., portable work authorizations or a simplified path to permanent residency), could incentivize more highly skilled researchers to remain in the US.⁴¹⁸

4.2.2. University partnerships

Official partnerships between universities are a popular way to expand collaboration, especially in science and technology. Currently, the US appears not to track these formal partnerships in a comprehensive way, so identifying them requires searching individual institutions for their presence. Based on our investigation of top US research universities, six of the top 10, according to Nature Index, have at least

⁴¹⁷ AnnaLee Saxenian, Yasuyuki Motoyama, and Xiaohong Quan. *Local and Global Networks of Immigrant Professionals in Silicon Valley*: Public Policy Institute of California, 2002.

⁴¹⁸ National Economic Council and Office of Science and Technology Policy, *A Strategy for American Innovation: Securing Our Economic Growth and Prosperity*.

one life science or biotechnology partnership with Chinese institutes (Table 4-1). This high prevalence among the institutions we investigated suggests these types of partnerships are common.

Speaking with persons who have participated in similar partnerships revealed that these partnerships are motivated by the increased scientific productivity that results from a larger group of collaborative partners. In some instances, these partnerships also serve to foster US interests by enabling US access to Chinese experts in certain fields. They can also serve as a form of diplomatic “soft power” by fostering links between US and Chinese nationals.

In our conversations, participants noted that partnering with China has largely the same benefits and same risks (see next section) as partnering with other nations, with perhaps a more acute IP risk when partnering with China. The US federal government appears to have historically maintained a “hands-off” approach to scientific and research collaborations in nations beyond China, having neither closely tracked them nor demonstrated a pattern of intervention. Until a specific economic or national security threat emerges from such partnerships (be it with Chinese institutions or those of other countries), the US government is unlikely to intervene.

Table 4-1. Chinese Partnerships with Top 10 US Universities

US University	Collaboration
Harvard University	Collaborative Innovation Center for Targeting Tumor Diagnosis and Therapy
MIT	Avian Phylogenomics Project
	MOE Joint International Research Laboratory of Metabolic Developmental Sciences
UC Berkeley	Avian Phylogenomics Project
	SIBS-UC Berkeley Center of Molecular Life Sciences
	Tsinghua-Berkeley Shenzhen Institute (TBSI)
University of Michigan	MOE Joint International Research Laboratory of Metabolic Developmental Sciences
	University of Michigan - Shanghai Jiao Tong University Joint Institute
University of California at Los Angeles (UCLA)	Avian Phylogenomics Project
	Fujian Agriculture and Forestry University-UCLA Joint Research Center on Plant Proteomics
	UCLA-PKU Joint Research Institute in Science and Engineering (JRI)
	UCLA-ZJU Joint Center for Medical Education and Research
Yale	Collaborative Innovation Center for Genetics and Development
	Fudan-Yale Biomedical Research Center
	Peking-Yale Joint Research Center for Plant Molecular Genetics and Agrobiotechnology (PYC)

Source: Nature Index. The top 10 institutions are according to the Nature Index Fractional Count, a weighted count of peer-reviewed article authorship.

4.3. Benefits and Risks

Chinese companies and researchers play an important role in in US biotechnology innovation through US-based R&D centers and incubators, corporate and academic partnerships, and a large cohort of Chinese researchers in US academic institutions and companies. The scientific advantages of these relationships are bi-directional—both China and the US benefit from the exchange of ideas and information that is fostered. In a 2017 post for *Scientific American*, former White House Science Advisor

John Holdren argued not only that international collaboration is important to advance science and technology around the globe, but that many advances, such as those in public health, provide benefits to the whole world and even that scientific collaboration can lay groundwork for beneficial diplomatic relationships.⁴¹⁹

Foreign students and researchers provide a wealth of talented individuals to US institutions, individuals that then contribute significantly to US innovation and growth. The system of US academic science depends on this international workforce. According to the National Science Foundation's Science and Engineering Indicator 2018 report, more than 45 percent of doctorate researchers in the biological, agricultural, and environmental life sciences are foreign-born, and 22 percent of all science and engineering doctorates are from China, the largest foreign source of workers.⁴²⁰ Immigrants provide direct benefit to US innovation and economic growth, too. In 1998, executives of Chinese or Indian descent led 24 percent of Silicon Valley businesses started in 1980 or later,⁴²¹ and the number doubled the following decade.⁴²² Three billion-dollar startups in the US had Chinese founders as of January 2016.⁴²³ A report released in 2012 found that 20 percent of patents at the top 10 US research universities had an inventor from China. Foreigners appear especially significant in biotechnology-related patents, with 79 percent of drug or drug-related patents having a foreign-born inventor.⁴²⁴

But with this heavy reliance on foreign scientists come fears that Chinese scientists practicing or training in the US are stealing IP and creating at least an economic drain and at worst compromising national security. As discussed in Chapter 2 of this report, there have been a handful of publicly known cases where Chinese researchers have been caught trying to steal either information or materials from their place of employment in the US. Examples include theft of genetically engineered seeds, experimental proteins and antibodies, and trade secrets. Compared to the number of Chinese-born researchers working the US, though, such instances are rare and represent considerable risk to the individual. Unauthorized transfer of IP does not have to be as overt, however. The concept of "two bases," which was introduced by China's National Natural Science Foundation in 1992 and expanded by the Ministry of Personnel in 1994, describes Chinese researchers operating abroad as a mechanism for sharing knowledge and expertise gained from a host institution with China. Through activities such as participating in conferences, returning to China to lecture, and maintaining positions at Chinese institutions while abroad, Chinese researchers in the US may share information and know-how with colleagues in China.⁴²⁵

IP considerations are paramount in formal collaborations between institutions. The ownership status of any IP developed out of a formal partnership may be in question unless agreements are put in place to determine to whom rights belong, which is true whether the partnership is wholly US, between the US and China, or between the US and other nations. China, like many nations in the development phase, has faced challenges meeting international IP norms, making IP concerns even more acute when China participates in a partnership. Chinese officials have frequently downplayed concerns about actions seen as violating IP norms or agreements abroad, such as reverse-engineering a product or software, plagiarism, counterfeiting, and the unauthorized use of components. Addressing these concerns may require solutions developed on an individualized basis, with each partnership addressing the specific IP risks accordingly.

⁴¹⁹ John P. Holdren, "How International Cooperation in Research Advances Both Science and Diplomacy," Guest Blog, *Scientific American* (2017), <https://blogs.scientificamerican.com/guest-blog/how-international-cooperation-in-research-advances-both-science-and-diplomacy/>

⁴²⁰ National Science Board, *Science and Engineering Indicators*. [Figure 3-32 and Figure 3-33]

⁴²¹ AnnaLee Saxenian, "Silicon Valley's New Immigrant Entrepreneurs," *Public Policy Institute of California* 1999, http://www.pplic.org/content/pubs/report/R_699ASR.pdf

⁴²² Vivek Wadhwa, "Boost visas for foreign entrepreneurs," *Nature* 2017, <https://www.nature.com/news/boost-visas-for-foreign-entrepreneurs-1.21544>

⁴²³ Ibid.

⁴²⁴ The Partnership for a New American Economy, "Patent Pending: How Immigrants Are Reinventing the American Economy," 2012, <https://www.newamericaneconomy.org/sites/all/themes/pnae/patent-pending.pdf>

⁴²⁵ Hannas, Mulvenon, and Puglisi, "Chinese Industrial Espionage."

The potential loss of IP to China presents an economic risk when researchers return to their home country, bringing technologies and know-how with them and fostering innovation and commercial success outside of the US. When foreign researchers develop technologies at US institutions, they utilize significant private and public capital investments. US public institutions, such as the NSF and NIH, provide vast amounts of funding to train graduate and doctoral researchers, and when some of those investments end up supporting innovation in other countries, the effective return on the investment is reduced. Furthermore, the start of companies in foreign countries rather than the US represents a loss of potential domestic economic activity.

While concerns over loss of IP have long existed, the increase in Chinese scientists training in the US along with expansion of programs such as the Thousand Talents Program have caused tensions to rise recently, especially in the biomedical research field. In August 2018, the NIH announced it was tightening oversight of grantees and grant applicants with respect to foreign collaborations, including international sources of funding, and set up an advisory group to facilitate the process. As part of the move, the NIH is investigating a handful of researchers with undisclosed funding from foreign governments.⁴²⁶ And in November 2018, Johns Hopkins University School of Medicine announced it was not accepting any more visiting scientists out of fears of IP loss.⁴²⁷

Clearly, a balance must be maintained to ensure the US biotechnology industry can benefit from foreign talent and a free, international exchange of ideas while mitigating potential losses due to leakage or theft of technologies. In the rest of this section, we describe the regulatory mechanisms available to the US to protect against loss of IP to foreign collaborators.

4.3.1. Role of U.S. government in regulating international research

There is no single governing body regulating international research collaborations with US scientists. Instead the agency sponsor determines, on a case-by-case basis, if the researchers and collaborators are qualified to conduct funded research. Most of the policies of the funding sources are based off of government regulations (e.g., the Export Administration Regulations from the Commerce Department and the Foreign Corrupt Practices Act from the Justice Department).

The regulation of research that is done for legitimate scientific purposes but also could be used by those wishing to create weapons of mass destruction (called “dual use” research) has a long history that will only be briefly summarized here. National Security Decision Directive (NSDD)-189, issued in 1985, specifically exempts many types of academic research from regulation. It established policy for federally-funded research that is performed with the intent of publication (whether basic or applied), known as “fundamental research.”⁴²⁸ In this policy, broad sharing of research results with the scientific community is encouraged rather than restricted. Moreover, researchers in laboratories that are seeking to publish their research are exempt from deemed export requirements that would otherwise restrict the roles that non-US citizens can have in the laboratory. This early policy, established with nuclear technologies in mind, was soon found to be unable to adequately control the publication or conduct of legitimate research in the life sciences that could be misused by those with hostile intent.

In 2004, the National Research Council published “Biotechnology Research in an Age of Terrorism” which outlined seven types of studies that have a potential for misuse yet argued strongly for self-governance

⁴²⁶ Lev Facher, "NIH is investigating researchers who might have failed to disclose contributions from foreign governments," *STAT News*(2018), <https://www.statnews.com/2018/08/23/nih-is-investigating-researchers-who-might-have-failed-to-disclose-contributions-from-foreign-governments/>

⁴²⁷ Alice Shen, "US medical school Johns Hopkins bars foreign scientists over intellectual property risk," *South China Morning Post*(2018), <https://www.scmp.com/news/china/science/article/2171823/us-medical-school-bars-foreign-scientists-over-intellectual>

⁴²⁸ "National Security Decision Directive 189: National Policy on the Transfer of Scientific, Technical and Engineering Information," (1985).

by the scientific and science publishing communities.⁴²⁹ As a response to a recommendation in the 2004 report, in 2005, the National Science Advisory Board on Biosecurity was established to advise the government on appropriate oversight guidance for biological research; however, they too called for self-regulation.⁴³⁰ The continued publication of dual-use research (specifically, several instances where viruses were manipulated to be more pathogenic or more transmissible than natural strains) in the open literature spurred the creation of additional regulations: US Government Policy for Oversight of Life Sciences Dual Use Research of Concern in 2012, and US Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (DURC) in 2014.⁴³¹ While these policies establish an approach to assess the potential risks of accidental or intentional misuse of this research, they are explicitly not concerned with the potential of published research to undermine US competitiveness in biotechnology.

Recently, the US government has taken steps to limit student visas in STEM. As stated in the 2017 *National Security Strategy*, the US "will consider restrictions on foreign STEM students from designated countries to ensure that intellectual property is not transferred to our competitors."⁴³² In June 2018, the first such policy was announced, shortening from five years to one year the duration of visas for those planning to study aviation, robotics, and advanced manufacturing. Students who remain in the US will not be forced to leave, but those who travel abroad after one year, for instance to present their work at international conferences, would need to reapply.⁴³³ While these fields mostly fall outside of biotechnology, additional policies could still be released that directly affect biotechnology research. Such policies could significantly hinder the ability of the US to attract and retain top foreign talent and meet the workforce needs of a growing biotechnology industry.

4.3.1.1. National Security and Export Control

International and national export control policies have a limited effect on Chinese acquisition of biotechnology from foreign countries. The biotechnology-related portions of the US commerce control policies, which are aligned with the Australia Group list, are focused on agents, equipment, and software that can be used to create, produce, stockpile, and test pathogen-based biological weapons. Similarly, the US government policies on dual-use life sciences research are focused on specific pathogens and experiments of concern. While these policies may help protect against the development of biological weapons, they do not prevent, nor are they intended to prevent, acquisition by foreign states of technologies with commercial or medical applications that are critical to our country's economic development.

Sharing of biological samples and genetic data internationally is dependent on international agreements and specific national policies. The World Health Organization passed two resolutions to facilitate viral sample sharing of influenza strains to promote preparedness activities, development of vaccines, and surveillance efforts. The Convention on Biodiversity passed the Nagoya Protocol, which calls for the sharing of genetic data of organisms in a manner that promotes equitable and fair benefit-sharing.

The US has a number of policies to facilitate sharing of and access to data from federally funded research. In 2008, the NIH began requiring intramural and extramural researchers to make their published articles publicly accessible within 12 months after publication.⁴³⁴ The 2010 America COMPETES Act called upon the US Office of Science and Technology Policy (OSTP) to establish a working group to coordinate among federal agencies the policies for dissemination of publications and

⁴²⁹ National Research Council, *Biotechnology Research in an Age of Terrorism* (Washington, DC: The National Academies Press, 2004).

⁴³⁰ National Science Advisory Board for Biosecurity, "Enhancing Responsible Science: Considerations for the Development and Dissemination of Codes of Conduct for Dual Use Research," (2012).

⁴³¹ United States Government Policy for Oversight of Life Sciences Dual Use Research of Concern (2012). ; United States Government Policy for Institutional Oversight of Life Sciences Dual Use Research of Concern (2014).

⁴³² United States and Donald Trump. *National Security Strategy of the United States of America 2017*.

⁴³³ Mervis, "Stricter Chinese student visas raise alarm," 1161.

⁴³⁴ Richard Van Noorden, "White House announces new US open-access policy," *Nature News Blog* February 22, 2013, <http://blogs.nature.com/news/2013/02/us-white-house-announces-open-access-policy.html>

digital data resulting from agency-funded research. In 2013, in response to that act, OSTP released a policy on public access of scientific research, which requires U.S. government agencies to develop policies to promote public access to federally-funded research within 12 months of publication. In 2017, Representatives Kevin Yoder (R-KS-3), Mike Doyle (D-PA-14), and Zoe Lofgren (D-CA-19) and Senators John Cornyn (R-TX) and Ron Wyden (D-OR) introduced the Fair Access to Science and Technology Research Act, which would require that US government departments and agencies with annual extramural research expenditures of over \$100 million make manuscripts produced from that research publicly available online.⁴³⁵ To date, this legislation has not been enacted into law, but it has been introduced into the last two sessions of Congress.⁴³⁶

⁴³⁵ "FAQ for the Fair Access to Science and Technology Research Act (FASTR)," SPARC, <https://sparcopen.org/our-work/fastr/faq/>

⁴³⁶ Roy Kaufman, "Recent Developments in US Federal Open Access Policies: FASTR Moves Slower," *Copyright Clearance Center* December 5, 2017, <https://www.copyright.com/blog/us-federal-open-access-policies-fastr/>

5. China's Access to U.S. Healthcare-Related Data

Key Findings

- **The Chinese government has formulated policies to support the use of big data and modern techniques to drive new discoveries and cures by analyzing large healthcare, genomic, and other personal health data sets.** China's State Council recognizes the importance of big data to health and medicine as a national priority, and China is building national and regional health and big data centers in Fuzhou, Xiamen, Nanjiang, and Changzhoi. China has also launched a 60 billion yuan (\$9.3 billion) precision medicine initiative.
- **China's biotech companies have access to healthcare and genomic data on US persons through various channels,** including investments and partnerships. At least 23 companies with a nexus to China are CLIA/CAP accredited, giving them direct access to US medical and health data via their participation in our healthcare system.
- **Compared to other nations, the US has lower protections on medical and healthcare data, facilitating access to data on US persons.** The EU's General Data Protection Regulation protects identifiable information more strongly than US regulations. China's laws go even further, preventing export of data on Chinese persons and requiring a permit for each research use of genomic information.
- **China's efforts to acquire US health data combined with limited protections raise questions about national security.** Theoretically, access to private information on security-sensitive US persons creates a risk of blackmail and may reveal health conditions exploitable in a targeted attack, although no public reports suggest this has yet happened or is a current aim of the Chinese Government or industry.
- **China has numerous laws requiring or authorizing access to private-sector data by the central government,** ostensibly for national security reasons. While it is difficult to discern the level of access afforded to the Chinese government through these laws, their vagueness when it comes to oversight could allow collection of data to go relatively unchecked.
- **The US is not moving as aggressively as China to advance big data in healthcare, and that could, over time, open an innovation gap.** The US can prevent this outcome by re-investing in our own infrastructure, knowledge base and scientific enterprise to compete with China.

This final chapter first reviews the nexus between healthcare data and biotechnology, then discusses recent Chinese initiatives to modernize data collection in this area and reviews how Chinese companies could gain access to US healthcare data through various channels. The chapter concludes with a discussion of data protection and security concerns related to this situation.

5.1. Healthcare Data and Biotechnology

In the past several years, key advances in the field of healthcare biotechnology have been driven by the collection, management, and analysis of large data sets (a.k.a. big data) to improve diagnostic capabilities, provide more effective therapies, and discover new determinants of disease. Large medical data sets can also be used to make drug discovery and clinical trials more reliable and cost-efficient, while predictive models based on patient profiles can inform diagnosis or treatment strategies. These big data approaches require access to high-quality, large data sets to ensure that discoveries are valid and reproducible and to allow for advances that cross traditional disciplines.

The biotech industry has recognized the value of these data for several years. In fact, healthcare data have become a commodity—a product with value of its own to be bought and sold—as the ability to collect and analyze data sets on a massive scale has become easier. Over the past decade, the cost of genomic sequencing has dropped precipitously—from \$10 million per genome in 2007 to close to \$1,000 today—allowing the generation of massive volumes of data.⁴³⁷ At the same time, the rise of cloud computing has made possible the computationally intensive analyses required to process thousands of samples and gain new insights. As a result, the amount of healthcare data that will be produced in 2020 is estimated to be 15 times what it was in 2013.⁴³⁸ The market for healthcare data has grown as well; worth about \$14.25 billion in 2017, it is expected to be worth over \$68.75 billion by the end of 2025.⁴³⁹

5.1.1. Genomic Data

Broadly, genomics is the study of the entirety of an individual's DNA sequence information (the genome). While doctors and scientists have been able to use information from single genes to inform healthcare decisions for decades (e.g., BRCA testing for breast cancer risk), the advent of high-throughput and next generation DNA sequencing technology enabled the analysis of large portions of or even entire human genomes with relative ease, opening new avenues of research and discovery that can inform the development of treatments and improve patient care.

By collecting and comparing the genomes of many individuals, medical researchers can identify new genetic determinants of disease to inform drug development. For example, in 2017, US genomics company 23andMe, along with US biotech giant Genentech and the National Institute on Aging, published a meta-analysis of Parkinson's disease using data from more than 425,000 people, identifying 17 new genetic variants associated with Parkinson's and confirming genetic mutations already associated with the disease.⁴⁴⁰ Additionally, 23andMe and the University of Edinburgh used data from the UK Biobank and 23andMe customers (who consented to participate in research) to identify over a dozen new genetic variants associated with depression.⁴⁴¹ Beyond research uses, genomic data can also be used in direct clinical applications, including molecular diagnostics and precision medicine, each of which is discussed below.

On an individual level, genomic sequencing allows for the screening of hundreds of known genetic determinants or risk factors of disease. Molecular diagnostics refers to the use of DNA (or RNA) sequences to diagnose a disease or condition. The first molecular diagnostics detected disorders caused by genetic mutations, including α -thalassemia, phenylketonuria, and cystic fibrosis.⁴⁴² Today, newer techniques are being used to diagnose a broader range of genetic disorders as well as diseases such as cancer. While molecular diagnostics were possible before the advent of next-generation sequencing, the technology has enabled a greater number of diseases to be screened at a time, and for more sequence-based diagnostic methods to be developed. As of 2015, there were approximately 600 different genetic diagnostic tests available, with the number increasing at a rate of around 40 new tests per year.⁴⁴³

⁴³⁷ "The Cost of Sequencing a Human Genome," National Human Genome Research Institute, updated July 6, 2016, <https://www.genome.gov/27565109/the-cost-of-sequencing-a-human-genome/>

⁴³⁸ Stanford Medicine. *Stanford Medicine 2017 Health Trends Report: Harnessing the Power of Data in Health* Stanford, CA: Stanford Medicine, 2017.

⁴³⁹ BIS Research, "Global Big Data in Healthcare Market to Reach \$68.75 Billion by 2025, Reports BIS Research," *Cision PR Newswire*(2018), <https://www.prnewswire.com/news-releases/global-big-data-in-healthcare-market-to-reach-6875-billion-by-2025-reports-bis-research-678151823.html>

⁴⁴⁰ Alexa Lardieri, "23andMe is Using Your DNA for Genetics Research," *U.S. News and World Report*(2017), <https://www.usnews.com/news/health-care-news/articles/2017-09-13/23andme-is-using-your-dna-for-genetics-research>

⁴⁴¹ 23andMe, "Study Finds New Genetic Associations for Depression," (2018), <https://blog.23andme.com/23andme-research/study-finds-new-genetic-associations-for-depression/>

⁴⁴² G. P. Patrinos, P. B. Danielson, and W. J. Ansorge, "Molecular Diagnostics: Past, Present, and Future," in *Molecular Diagnostics*, ed. George P. Patrinos (Academic Press, 2017).

⁴⁴³ Rossa W. K. Chiu, Y. M. Dennis Lo, and Carl T. Wittwer, "Molecular Diagnostics: A Revolution in Progress," *Clinical Chemistry* 61, no. 1 (2015): 1.

Sequence data can also be used to predict the efficacy of certain treatments or for diagnosis of conditions ranging from cancer to chromosomal abnormalities. Precision (or personalized) medicine refers to the use of genetic information to tailor the treatment of an illness to the individual, compared to classical medicine where treatment is by and large the same for all patients with the same disease. For an increasing number of treatments, knowledge of specific gene sequences from an individual provides information about which treatment strategy will be most effective in that individual by selecting a specific drug or combination of drugs or by tailoring drug dosage appropriately. Most strikingly, personalized medicine is critical in modern cancer care, where clinicians use genomic information from cancer cells to identify chemotherapies that are likely to be the most effective. In the US, more than 200 FDA-approved drugs contain this so-called pharmacogenomic information on their labels, and many more are being studied.⁴⁴⁴ Post-treatment, additional whole-genome sequencing allows for the identification of ever more pharmacogenomic determinants by correlating sequences of individuals with their responses to specific therapies, continuously improving treatment outcomes for future patients.

Genomic data are also being used for outside of the clinic, most commonly by “ancestry” services where individuals can send in a sample (usually saliva or a cheek swab) to a company who will sequence large portions of the DNA and, by comparing the sequence against a database of sequences of individuals with known ancestry, provide a report detailing the customer’s ancestral lineage.⁴⁴⁵ Such analyses are enabled by the ability to sequence genomes of a large, highly diverse pool of individuals combined with powerful data analysis tools. These genomic data can also be used to tailor diets, exercise regimens, or other lifestyle choices to an individual. However, the accuracy of the predictions by these companies is questionable, as the volume of scientific literature correlating genomic data to such outputs is scant compared to the more established medical links discussed above. But because these products are marketed as consumer products and not medical services, regulators have less oversight over the claims made by providers. Additionally, the handling of the data is not covered by the Health Insurance Portability and Accountability Act (HIPAA) healthcare data protection law, raising concerns about privacy and data security (see Section 5.4 for a discussion on data protection).

5.2. China’s Investments in Modernizing Collection of Healthcare Data

The Chinese government recognizes the importance of healthcare-related data in a cutting-edge biotechnology industry and has made the use of data in medicine a national priority while investing in building the capabilities necessary for China to play a major role in the field. In 2016, China’s State Council released a notice entitled Guidance on Promoting and Developing the Application and Development of Big Data in Healthcare Industry, recognizing the importance of big data applications in the health and medical sectors.⁴⁴⁶ The notice called for national and regional health information platforms to be built as well as 100 regional clinical medicine data demonstration centers. Moreover, the Guidance called for efforts to unify and connect platforms on population health, promote sharing and open resources, and regulate and promote intelligent medical care and Internet Plus (an initiative to integrate cloud computing and the Internet of Things into a wide range of industries).⁴⁴⁷

Also in 2016, the National Health and Family Planning Commission announced a pilot program to establish four new national and regional centers focused on big data in health and medicine. The cities of Fuzhou, Xiamen, Nanjiang, and Changzhou (all in the East China provinces of Fujian and Jiangsu) were

⁴⁴⁴ "Table of Pharmacogenomic Biomarkers in Drug Labeling," U.S. Food & Drug Administration, updated February 8, 2018, <https://www.fda.gov/Drugs/ScienceResearch/ucm572698.htm>

⁴⁴⁵ Because every human cell contains an entire genome, a relatively small number of cells from a cheek swab or saliva sample is all that is needed to perform genomic analyses. Companies may sequence the entirety of the genome or only portions, but the amount of data collected is very large: AncestryDNA claims to examine 700,000 different locations across autosomal chromosomes ("Types of DNA Testing," AncestryDNA, <https://www.ancestry.com/lp/types-of-dna-testing>)

⁴⁴⁶ The State Council of the People's Republic of China, "Guidance on Promoting and Developing the Application and Development of Big Data in Healthcare Industry," (2016), http://www.gov.cn/gongbao/content/2016/content_5088769.htm [Chinese Language Source]

⁴⁴⁷ "China to boost big data application in health and medical sectors," The State Council of the People's Republic of China, updated June 24, 2016, english.gov.cn/policies/latest_releases/2016/06/24/content_281475379018156.htm

chosen as pilot locations.⁴⁴⁸ The goal of the centers is to integrate data sets, including genetic sequence data, regional health data (e.g., claims data from the national basic health insurance), administrative data from local health offices, public health data from the Chinese Center for Disease Control and Prevention (CCDC), birth and death registries, and electronic medical records. These interconnected healthcare services and products are part of the Internet Plus initiative. The National Health and Medicine Big Data Center under construction in Nanjiang aims to build a genetic database containing the genomes of one million ethnic Chinese and use that information to study the relationship between genetics, disease, and the environment, with focuses on population genetics, cancer, rare diseases, newborns, and childhood cognitive development.⁴⁴⁹

There are currently two major regional data health centers in China—in Shanghai and Ningbo. In 2015, the Ningbo Cloud Hospital opened, providing cloud computing, big data analytics, and internet-connected devices to support healthcare services. The Ningbo Cloud Hospital platform connects hospitals, primary healthcare centers, community doctors, pharmacies, health insurance companies, and other healthcare institutions in the greater Ningbo region with the goal of improving health information management and the patient experience. Patients can utilize online diagnostic “rooms” connected to a doctor via the internet and access their personal health data through a smartphone app; the entire consultation process can be done through the online platform from home. This cloud hospital platform aims to improve healthcare access to its approximately 3.5 million local residents, as well as the people in the surrounding metropolitan area. Shortly after opening, the Ningbo Cloud Hospital was connected to 100 healthcare organizations and 226 doctors.

China is already utilizing medical data for research outside of the major data centers. A database covering 600 million people (50 percent of China's population) has been assembled from claims data from the national social insurance system. While these data are not publicly accessible, they are available to researchers who apply, and have been used for several medical and public health research projects.⁴⁵⁰

The Chinese government is also investing in private companies and researchers to expand access to genomic data. In 2010, the China Development Bank provided a \$1.5 billion 10-year loan to DNA sequencing giant BGI.⁴⁵¹ This loan enabled BGI to purchase 128 high-end Illumina-brand sequencers and in one act, BGI gained the world's largest sequencing capacity.⁴⁵² In 2016, China launched its 60 billion yuan (\$9.3 billion) precision medicine initiative with plans to fund many separate projects in genome sequencing and clinical data acquisition.⁴⁵³

In addition to direct Chinese government funding, global and domestic private investment capital is flowing toward genomics companies, and these companies are using this capital to amass large genomic data sets. HaploX Biotechnology has initiated two sequencing projects for the study of lung cancer and colorectal cancer, with the aim of sequencing 100,000 patients for each project, supported by a \$32 million VC funding round.⁴⁵⁴ WuXi NextCODE, formed by the Chinese acquisition of a US-based company (see Section 5.3.1), has partnered with many of the world's biggest pharmaceutical companies, including Novartis, Abbvie and Bristol-Myers Squibb, as well as medical institutions such as Boston Children's

⁴⁴⁸ Jiang Xingguang, "China to build health care big data centers, industrial parks," *National Health Commission of the People's Republic of China* October 24, 2016, en.nhfpc.gov.cn/2016-10/24/c_70420.htm

⁴⁴⁹ Ibid.; Xinhua News Agency, "China to create gigantic DNA database," *China Daily* (2017), www.chinadaily.com.cn/china/2017-10/31/content_3390020.htm; Claudia Geib, "A Chinese Province Is Sequencing One Million of Its Residents' Genomes," *Futurism* (2017), <https://futurism.com/chinese-province-sequencing-1-million-residents-genomes/>; Dou Shicong, "Jiangsu Government Unveils Plans to Sequence Genes of 1 Million Subjects," *Yicai Global* October 30, 2017, <https://www.yicai.com/news/jiangsu-government-unveils-plans-sequence-genes-1-million-subjects>

⁴⁵⁰ Luxia Zhang et al., "Big data and medical research in China," *BMJ* 360(2018).

⁴⁵¹ Chen, "Genomic Dreams Coming True In China". <https://www.forbes.com/sites/forbesasia/2013/08/28/genomic-dreams-coming-true-in-china/>

⁴⁵² Dennis Normile, "China's Sequencing Powerhouse Comes of Age," *Science* 335, no. 6068 (2012): 516-19.

⁴⁵³ Cyranoski, "China embraces precision medicine on a massive scale," 9-10.; Perez, "China's 'precision medicine' initiative gets lift from latest genomics company funding," <https://www.scmp.com/tech/china-tech/article/2092362/chinas-precision-medicine-initiative-gets-lift-latest-genomics>

⁴⁵⁴ GenomeWeb, "Chinese Firm HaploX Biotechnology Raises \$32M in Financing". <https://www.genomeweb.com/informatics/chinese-firm-haplox-biotechnology-raises-32m-financing>

Hospital and Peking Union Medical College Hospital. Section 5.3 provides more discussion on how Chinese firms may access genomic and other healthcare-related data through US investments and partnerships.

5.2.1. China's Improvements in Data Infrastructure

To effectively harness the power of massive healthcare and genomic data collections, proper internet and data infrastructure are required. Genomic databases require large amounts of computer storage; a single human genome requires around 25 GB of computer storage. More intensive than storage needs, however, is computing power. To analyze one human genome sample requires around 300 hours of computer processing.⁴⁵⁵ In order to efficiently process these large amounts of data, genomics researchers turn to cloud computing, where they can run analyses across hundreds or even thousands of computers connected on a cluster accessible over the internet. Large genomic sequencing projects like the ones being developed in China, therefore, require not only large cloud computing centers but also a robust internet infrastructure capable of supporting large-scale cloud computing efforts.

China is working toward rapid advancement of IT infrastructure with the goal of being a major market for data centers and cloud computing. China has built the largest next-generation network in the world, the IPv6-based ChinaNet Next Carrying Network (CN2), through an effort involving eight government agencies including the Ministry of Science and Technology, Ministry of Information Industries (MII, whose functions have since been assumed by the Ministry of Industry and Information Technology, or MIIT),⁴⁵⁶ Chinese Academy of Sciences, and Chinese Academy of Engineering.⁴⁵⁷ The three state controlled carriers in China, China Mobile, China Telecom, and China Unicom, have been building optical cable networks on an international scale to make cross-border connections with China. The companies have also advanced IP infrastructure in China; China Mobile has made network restructuring efforts to convert to IPv6 systems, and China Unicom developed plans to invest in commercial IPv6 projects in 10 Chinese cities.⁴⁵⁸ China Telecom also deployed a plan to replace its public switched telephone network infrastructure with IP Multimedia Subsystem infrastructure in 2012. In 2015, these three companies also created China Tower to make telecommunications infrastructure construction more efficient; by June 2018, China Tower operated 1.9 million telecommunications tower locations.

In 2015, China launched the Internet Plus action plan, which will integrate mobile networks, cloud computing, big data and the Internet of Things with a variety of industries including manufacturing, commerce and internet banking.⁴⁵⁹ The Internet Plus action plan has several goals for China to reach by 2020 including access to 100 megabits per second (Mb/s) internet connections for people in large cities, broadband connectivity for 98 percent of the population, and increased funding for R&D and business development and innovation.⁴⁶⁰ Furthermore, the plan calls for decreasing dependency on foreign technology to achieve these goals.⁴⁶¹ This plan indeed is playing out, as the cloud computing market in China—including cloud services and data center hardware and software—is dominated by Chinese companies, which is a striking anomaly, as US-based companies are the major players in this space

⁴⁵⁵ B. Langmead and A. Nellore, "Cloud computing for genomic data analysis and collaboration," *Nat Rev Genet* 19, no. 4 (2018): 208-19.

⁴⁵⁶ "Ministry of Industry and Information Technology (MIIT)," The US-China Business Council, updated July 2016, <https://www.uschina.org/sites/default/files/MIIT%202016.07.pdf>

⁴⁵⁷ William Foster and Xiangyu Liu. *China's Next Generation Internet: The Adoption of IPv6* Institute for Next Generation Internet, 2006.

⁴⁵⁸ Laura Luo, "China: Racing ahead with IPv6," *DatacenterDynamics* June 28, 2012, <http://www.datacenterdynamics.com/content-tracks/servers-storage/china-racing-ahead-with-ipv6/66334.fullarticle>

⁴⁵⁹ "China unveils Internet Plus action plan to fuel growth," The State Council of the People's Republic of China, updated July 4, 2015, http://english.gov.cn/policies/latest_releases/2015/07/04/content_281475140165588.htm

⁴⁶⁰ Lulu Chang, "China outlines its latest Five Year Plan, called Internet Plus," *Digital Trends*(2016), <https://www.digitaltrends.com/web/china-internet-plus/>

⁴⁶¹ "Everything You Need to Know About China's "Internet Plus" Future," China Telecom Americas, <https://www.ctamericas.com/chinas-internet-plus-future/>

around the rest of the world, with Amazon Web Services, Microsoft, IBM, and Google together capturing over half of the global cloud computing revenue in 2017.⁴⁶²

5.3. Channels of Access to US Healthcare Data

Chinese companies are entering the US healthcare market in two major ways: via mergers, acquisitions, and other investment vehicles and through partnerships with US healthcare providers and research institutes. While some companies use these partnerships to access facilities with the licensing and accreditation necessary to perform clinical tests on patients in the US, others have acquired that accreditation directly. Through these partnerships and accreditations, Chinese firms gain access to US medical and healthcare data, which may create security and scientific risks. Globally, these types of data are protected at varying levels, and the US appears to protect data less rigorously than the EU or China. This section describes some of the relationships Chinese firms have formed with US institutions to access healthcare data. Following (in Section 5.4) is a discussion of data protection laws and the implications of such access.

5.3.1. Chinese Investment in US Healthcare Data Companies

Chapter 3 describes some of the M&A and VC investments Chinese firms have made in US genomic sequencing companies and other firms that handle healthcare-related data. Such investments provide the Chinese investing firms with rich sources of healthcare-related information. Prominent examples include:

- In 2013, BGI acquired US sequencing company Complete Genomics and through that gained a proprietary sequencing technology and a base of operations in the US (see Box 3 earlier in this report for more details).
- In 2015, WuXi PharmaTech acquired the US firm NextCODE Health for \$65 million, then merged NextCODE Health and the WuXi Genome Center into a new subsidiary company called WuXi NextCODE Genomics, headquartered in Shanghai with operations in Cambridge, Massachusetts and Reykjavik, Iceland.⁴⁶³ Through the acquisition, the genome sequence analysis platform of NextCODE Health was brought together with the next-generation sequencing capabilities of the WuXi Genome Center, greatly increasing WuXi's access to CLIA-certified facilities and enabling them to broaden their customer base to US doctors and patients.⁴⁶⁴
- Also in 2015, WuXi Healthcare Ventures contributed \$10.45 million to a \$115 million venture capital round E financing of 23andMe. The funding allowed 23andMe to expand operations, maximize their direct-to-consumer product, and invest in new laboratory spaces.⁴⁶⁵ However, WuXi Healthcare Ventures and WuXi PharmaTech are not listed as research collaborators with 23andMe, meaning they would not have access to the genomic database as per 23andMe's research participation policies.⁴⁶⁶

⁴⁶² "Chinese Data Center & Cloud Market Remains Dominated by Local Companies," Synergy Research Group, updated October 25, 2017, <https://www.srgresearch.com/articles/chinese-data-center-cloud-market-remains-dominated-local-companies>; Mike Robuck, "Report: Amazon Web Services still rules the cloud roost for market share," *Fierce Telecom* April 27, 2018, <https://www.fiercetelecom.com/telecom/report-amazon-web-services-still-rules-cloud-roost-for-market-share>

⁴⁶³ "WuXi PharmaTech Acquires NextCODE Health to Create Global Leader in Genomic Medicine," WuXi PharmaTech (Cayman) Inc., updated January 9, 2015, <https://www.prnewswire.com/news-releases/wuxi-pharmatech-acquires-nextcode-health-to-create-global-leader-in-genomic-medicine-300018311.html>

⁴⁶⁴ Ibid.

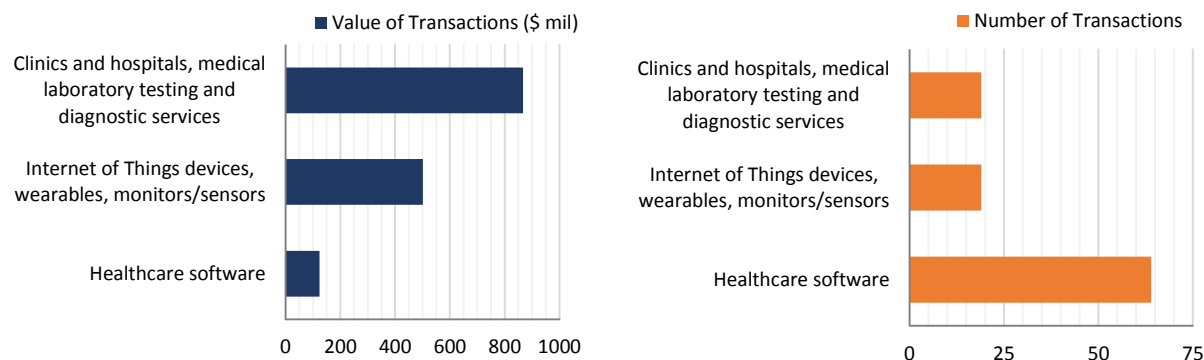
⁴⁶⁵ Reuters, "Funding values genetics company 23andMe at \$1.1 billion," *Reuters* October 14, 2015, <https://www.reuters.com/article/genetics-23andme-idUSL1N12E2EN20151014>

⁴⁶⁶ "Research Consent Document," 23andMe, <https://www.23andme.com/about/consent/>

- In 2017, Chinese AI firm iCarbonX made an equity investment in US-based SomaLogic, one of several investments that expanded the iCarbonX Digital Life Alliance. The investment helped fuel use of SomaLogic's proteomics platform and data.⁴⁶⁷
- Also in 2017, PatientsLikeMe received \$100 million in funding from iCarbonX to contribute to its Digital Life Alliance.⁴⁶⁸ The US-based company provides an online network where over 600,000 individuals can share information on their health conditions and treatments to crowdsource new insights into healthcare. While data may be shared to build iCarbonX's biological ecosystem, PatientsLikeMe reports that its data are anonymized and are kept on servers within the US.⁴⁶⁹

We additionally investigated Chinese investment in companies outside the biotechnology sector (and thus not represented in that data) but that still may collect, analyze, or otherwise have access to healthcare and related data. Such companies include health insurance companies, clinics and hospitals, medical testing laboratories, and companies that develop consumer devices (such as fitness trackers and other wearable sensors) and software. The majority of investments identified (64 of 103 investments tracked) were in software companies. These investments included software for analytics and clinical management, patient engagement and appointments, records and claims, and telemedicine and care management, as well as consumer-oriented software. Collectively, however, the total Chinese investment value was very low—only \$124 million, or an average of \$1.9 million per investment compared to close to \$20 million on average per investment across all biotech investments—and all but one of them were VC transactions (Figure 5-1). Relatively small transactions are expected, as software VC deals tend to be smaller than in other sectors, and VC investments are typically smaller than M&A. Although not completely risk-free, VC from Chinese investors generally does not present economic or security risks to the US, as the investors typically do not have access to sensitive data or technologies.

Figure 5-1. Chinese Investment in US Healthcare Companies, 2000-2017



Source: Rhodium Group.

One of the largest investments identified was the 2016 acquisition of Nipro Diagnostics by Sinocare. Nipro Diagnostics (now Trividia Health, Inc.) is a health and wellness company based in Fort Lauderdale, FL, and a leading developer, manufacturer and marketer of advanced performance products for people with diabetes, selling products under TRUE and store brand labels. No investments in health insurance companies were found. We found 13 investments for wearable medical devices, many of which manage diabetes, as well as five developers of activity monitors designed for personal use (the largest of which was the acquisition of Misfit Wearables Corp. by a group of Chinese investors for \$15 million). Of the software companies receiving Chinese investment, 13 were consumer-oriented, six were for patient engagement and appointments, 12 for records and claims, 19 for telemedicine and care monitoring, and 14 for other types of clinical management.

⁴⁶⁷ "SomaLogic announces that it has joined the iCarbonX Digital Life Alliance," SomaLogic, <https://somallogic.com/somallogic-joins-icarbonx-alliance/>

⁴⁶⁸ Heather Mack, "PatientsLikeMe secures \$100M, partners with health data company iCarbonX," *Mobi Health News*(2017), <https://www.mobihealthnews.com/content/patientslikeme-secures-100m-partners-health-data-company-icarbonx>

⁴⁶⁹ David J Lynch, "Biotechnology: the US-China dispute over genetic data," *Financial Times* (2017)

Data collected from wearable devices could give insight into population health trends that could be used to develop targeted interventions. Certainly, medical records, claims management, and telemedicine products could generate specific enough medical data to observe disease trends. However, given the large number of device and software developers and manufacturers, acquiring a data set of significant size would require acquisition of many different companies. Since the value in healthcare-related data is derived from the ability to analyze patterns across a large population, small datasets are much less attractive than the massive data sets managed by large genomics and molecular diagnostics companies (or the large health record databases that have been accessed through cyberattacks). The limited amount of investment activity in the healthcare companies identified here suggests that Chinese companies are indeed looking elsewhere to access US healthcare data.

5.3.2. Chinese-US Partnerships

Chinese companies are now forming partnerships with medical biotech companies, universities, and hospitals in the US to provide sequencing and analytical services for health research projects. These partnerships provide access to US patient data through testing labs certified according to CLIA, a requirement for processing clinical samples in the US (see Section 5.3.3 for more on CLIA-certified labs). While the research performed through these partnerships could lead to medical breakthroughs that benefit US citizens, the collection of genetic data on US citizens by Chinese companies may also present economic or even national security risks.

One Chinese company stands out in its penchant for forming partnerships with US healthcare providers and research organizations that enable access to US healthcare data: BGI (see Box 4). The Chinese sequencing giant has formed numerous partnerships with US healthcare providers and research organizations to provide large-scale genetic sequencing to support medical research efforts. In each case, US institutions or companies benefitted by expanding their research capabilities and capacity, while BGI gained access to genetic sequence data as well as clinical data on people within the US. Because BGI was providing sequencing and analysis services, they necessarily had access to health records and genetic data on individual patients; to what extent those data were de-identified is unknown. By collecting data across many efforts, BGI may be amassing a database of genomic and healthcare data on US persons that is greater than that achieved through any single research endeavor. Provided that the data are de-identified, current US regulations (see section 5.4.1) do not appear to prohibit such activity (the extent to which a Chinese firm can be held accountable in that regard is another matter). While collections of such data may not present obvious national security risks, they could be used to develop medical biotechnology breakthroughs in China and create greater competition and potential economic loss (see section 5.4.2 for a thorough discussion of these issues).

Box 4: BGI Partnerships with US Healthcare Research Institutions

- October 2011:** BGI and UC Davis announced a collaboration to establish a BGI sequencing facility at the UC Davis Health System Campus in Sacramento, called BGI@UCDavis, which opened in 2013.⁴⁷⁰ It later closed by mutual agreement in September 2015, with the University stating the closure was due to unspecified changes in the business model at BGI.⁴⁷¹ The BGI@UCDavis was intended to increase UC Davis' DNA sequencing capacities tenfold and to contribute to research in human and animal health and medicine, food safety and security, biology, and the environment.⁴⁷²

⁴⁷⁰ Andy Fell, "UC Davis and BGI announce partnership to establish state-of-the-art genome center in Sacramento," *UC Davis* (2011), <https://www.ucdavis.edu/news/uc-davis-and-bgi-announce-partnership-establish-state-art-genome-center-sacramento/>

⁴⁷¹ Dale Kasler, "Major UC Davis genetics partnership with Chinese firm ends," *Sacramento Bee* November 11, 2015, <https://www.sacbee.com/news/business/article44277492.html>; "What happened to the BGI@UC DAVIS?," UC Davis Genome Center, <http://dnatech.genomecenter.ucdavis.edu/faqs/uc-davis-genome-center-and-the-bgiuc-davis/>

⁴⁷² Fell, "UC Davis and BGI announce partnership to establish state-of-the-art genome center in Sacramento". <https://www.ucdavis.edu/news/uc-davis-and-bgi-announce-partnership-establish-state-art-genome-center-sacramento/>

- **November 2011:** The Children's Hospital of Philadelphia (CHOP) and BGI formed a collaborative genome center titled BGI@CHOP, which appears to be still in operation.⁴⁷³ This center is intended to conduct large-scale human genome sequencing and bioinformatics analysis at a new, state-of-the-art Joint Genome Center, and to focus on the discovery of genes underpinning pediatric diseases using NGS.⁴⁷⁴
- **October 2011:** Autism Speaks and BGI announced a two-year partnership to build on the work of the Autism Speaks' Autism Genetic Resource Exchange and create the world's largest library of sequenced genomes of individuals with autism spectrum disorders (ASD). The collaboration aimed to perform whole genome sequencing of 10,000 genomes from participating US and Chinese families with children on the autism spectrum, hoping to gain new insights into the genomics of ASD to guide diagnosis and treatment.⁴⁷⁵
- **September 2013:** BGI (through its subsidiary BGI Tech Solutions) partnered with South Texas Accelerated Research Therapeutics to work on the San Antonio 1000 Cancer Genome Project (SA1kCGP) to study genetic alterations underlying various cancers and link genomic information to clinical outcomes.⁴⁷⁶ Under the terms of the partnership, BGI Tech Solutions agreed to provide next-generation sequencing as well as data analysis and storage for all genetic and clinical data generated through the tumor sequencing and clinical analyses.⁴⁷⁷

5.3.3. CLIA Certification of Chinese Companies

As demonstrated by BGI's partnerships with US healthcare researchers, Chinese companies may gain access to data on US patients by offering diagnostic services to the US healthcare market, and CLIA certification is an important requirement for access to the US market. CLIA specifies requirements for laboratories to produce or collect healthcare-related data, including the diagnosis or treatment of disease.⁴⁷⁸ The requirements are in place to ensure the analytical validity of results, (i.e., that they are performed and interpreted correctly). Notably, CLIA does not address the clinical validity of tests (e.g., that a positive result from a diagnostic test in fact means the patient has the condition being tested for);⁴⁷⁹ in this sense, CLIA can be seen as analogous to the Good Manufacturing Practices standards, which ensure quality during production of pharmaceuticals but do not ensure the pharmaceuticals are efficacious as treatments for the targeted disease. Laboratories performing moderate- and high-complexity tests, which include most molecular diagnostics and other genetic testing, must acquire a Certificate of Compliance from the Center for Medicare and Medicaid Services (CMS) or accreditation through an approved organization.⁴⁸⁰ There are seven approved accreditation organizations under CLIA, the most prominent being CAP.⁴⁸¹ In the case of CAP accreditation, the standards ensured go above and beyond those required by CLIA.

⁴⁷³ "High-Throughput Sequencing Center," Children's Hospital of Philadelphia, <https://hts.research.chop.edu/index.php>

⁴⁷⁴ "CHOP and BGI Partner for Human Genome Sequencing," updated November 9, 2011, <https://www.chop.edu/news/chop-and-bgi-partner-human-genome-sequencing>; "High-Throughput Sequencing Center," <https://hts.research.chop.edu/index.php>

⁴⁷⁵ "Autism Speaks and BGI Collaboration to Generate World's Largest Library of Sequenced Genomes of Individuals With Autism Spectrum Disorders," Autism Speaks, updated October 13, 2011, <https://www.autismspeaks.org/about-us/press-releases/autism-speaks-bgi-library-sequenced-genomes>

⁴⁷⁶ W. Scott Bailey, "START to team up with China's BGI Tech on San Antonio cancer genome project," *San Antonio Business Journal*(2013), http://www.startthecure.com/news_detail.php?uid=91

⁴⁷⁷ Asian Scientist Newsroom, "BGI Tech To Collaborate On San Antonio 1000 Cancer Genome Project," *Asian Scientist*(2013), <https://www.asianscientist.com/2013/09/tech/bgi-tech-collaborate-san-antonio-1000-cancer-genome-project/>

⁴⁷⁸ "Clinical Laboratory Improvement Amendments (CLIA)," U.S. Department of Health and Human Services, Food and Drug Administration, updated March 22, 2018, <https://www.fda.gov/medicaldevices/deviceregulationandguidance/ivdregulatoryassistance/ucm124105.htm>

⁴⁷⁹ "What Health Information Is Protected by the Privacy Rule?," National Institutes of Health, updated February 2, 2007, https://privacyruleandresearch.nih.gov/pr_07.asp

⁴⁸⁰ H. L. Stang and N. L. Anderson, "Use of Proficiency Testing as a Tool to Improve Quality in Microbiology Laboratories," *Clin Microbiol News* 35, no. 18 (2013): 145-52.

⁴⁸¹ "Accreditation Organizations/Exempt States," U.S. Department of Health and Human Services, Centers for Medicare and Medicaid Services, updated August 18, 2017, https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Accreditation_Organizations_and_Exempt_States.html

Under US regulations, any testing of materials from human specimens collected in the US is subject to CLIA. If an international lab, performs tests for the assessment of human health and tests are referred by, and results returned to, a facility in the US, those international labs are also subject to CLIA.⁴⁸² Thus, without a CLIA certification, domestic and international labs cannot perform testing for the diagnosis or treatment of any disease or condition for human patients.⁴⁸³ Few, if any, health insurance plans, including Medicare and Medicaid, will pay for tests performed by labs without CLIA certification, effectively closing off uncertified labs from the US market. Conversely, gaining CLIA certification would enable access to the US healthcare market, and, as a result, access to US-associated human specimens and related medical data, including genetic sequence data for those labs that provide molecular diagnostics and genetic testing.

We identified 23 companies associated with China that have CLIA/CAP accreditation and perform molecular diagnostics or other genetic testing, including whole genome sequencing (Table 5-1). In total, there were eight US-headquartered companies with a location in China, five China-headquartered companies with a location in the US, and 10 wholly Chinese companies. Each of these companies can perform genetic testing or sequencing on patients in the US healthcare system, and therefore has access to individual patients' genetic data.

Table 5-1. Companies Associated with China that have CLIA/CAP Accreditation and Perform Molecular Diagnostics or Other Genetic Testing

Company	Location	Description
Cancer Genetics, Inc.	US with Chinese presence	Developer of personalized medicines for cancer diagnostics.
Fulgent Genetics	US with Chinese presence	Provider of cancer drug research services, personalized cancer treatments, genetic testing and genetic diagnostic services.
Illumina Clinical Services Laboratory	US with Chinese presence	Uses DNA sequencing to help in disease research, drug development and the development of molecular tests in the clinic.
Veritas Genetics	US with Chinese presence	Provider of a genetic testing platform.
ACM Global Central Lab China Pte. Ltd.	US with Chinese presence	Performs diagnostic tests spanning all disciplines including pathology, microbiology, molecular diagnostics, toxicology, and more.
AccuraGen	US with Chinese presence	Developer of a liquid biopsy technology (diagnosis from cancer DNA circulating in the blood) designed to facilitate personalized cancer treatment.
Hangzhou Veritas	US with Chinese presence	Provider of a genetic testing platform.
Q Squared Solutions (Beijing) Co., Ltd.	US with Chinese presence	Testing services include genomics, biomarkers, and precision medicine.
Kingmed Center for Clinical Lab Co., Ltd.	Chinese with US presence	Operator of a third-party medical laboratory group. The company's main business includes medical testing, clinical trials, food and hygiene testing, and scientific research service.

⁴⁸² "How to Apply for a CLIA Certificate, Including International Laboratories: International Laboratory CLIA Certification Process (PDF)," Centers for Medicare & Medicaid Services, updated November 9, 2017, https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/How_to_Apply_for_a_CLIA_Certificate_International_Laboratories.html

⁴⁸³ J. Cello, A. V. Paul, and E. Wimmer, "Chemical synthesis of poliovirus cDNA: generation of infectious virus in the absence of natural template," *Science* 297, no. 5583 (2002): 1016-8.

Company	Location	Description
Kingmed Diagnostics (Shanghai)	Chinese with US presence	Operator of a third-party medical laboratory group. The company's main business includes medical testing, clinical trials, food and hygiene testing, and scientific research service.
WuXi AppTec	Chinese with US presence	Operator of pharmaceutical, biopharmaceutical and medical equipment business based in China and the United States.
WuXi NextCODE Genomics	Chinese with US presence	Provider of a global genomics platform created to provide genomic sequence data.
Novogene	Chinese with US presence	Provider of genomic services intended to blend NGS and bioinformatics with genomic science.
3DMed Clinical Laboratory, Inc.	Chinese	Medical company focusing on cancer. Platforms include NGS and the world's largest PDC bank for liver cancer.
Adicon Clinical Laboratories	Chinese	Provider of clinical reference lab services to the healthcare community in China. Testing services include pathology, genetics, biochemistry, and molecular diagnostics. Part of the first batch of CAP accredited labs in China.
Chengdu Gaoxin-Daan Medical Laboratory Co., Ltd.	Chinese	Offers clinical diagnostic testing services and laboratory services.
Genetron Health (Beijing) Co., Ltd.	Chinese	Developer of precision medicine products designed to provide cancer patients with molecular clinical services and professional cancer genetic risk assessment.
Guangzhou DAAN	Chinese	Offers clinical diagnostic testing services and laboratory services.
Nanjing Shihe Jiyin Biotech, Inc.	Chinese	Core facility for NGS analysis.
Shanghai Daan Med Laboratory	Chinese	Offers clinical diagnostic testing services and laboratory services.
Shanghai Dian Medical Testing Lab	Chinese	Provider of medical agency services, including the sale, outsourcing, research and development of medical diagnostic products and services.
Shanghai Liwen Diagnostics	Chinese	Provides molecular diagnostic services to help doctors and patients with precision and personalized medicine.
Teddy Clinical Research Laboratory	Chinese	Result of a merger between Tigermed and DiAn Diagnostics. Tigermed is a provider of full clinical trial services; DiAn Diagnostics is a provider of medical agency services, including the sale, outsourcing, research and development of medical diagnostic products and services.

Source: Author's Compilation from NCBI Genetic Testing Registry, CAP Laboratory Directory for Chinese laboratories.

5.4. Data Protections and Security Concerns

The recent actions of Chinese firms providing access to US healthcare-related data, especially genomic data, have naturally raised questions about the extent of China's access and their use of these data. A major concern is whether Chinese access to healthcare data of Americans raises security and misuse issues. Another concern is whether data sharing, especially if not reciprocal, hurts American scientific and economic interests by hindering US competitiveness in the burgeoning areas of genomics and personalized medicine.

In this section, we will investigate both questions, but first we provide a short overview of the major relevant laws and policies that regulate access to and protect healthcare data, especially genetic information. Though a comprehensive review is beyond the scope of this report, we cover salient rules in both the US and China and compare them to data protection laws in the EU, which may serve as a model for any future US policy or regulatory actions.

5.4.1. Data Oversight and Protection Laws

5.4.1.1. United States

Unlike many countries, the US does not have a single, overarching data protection policy. Instead, data protection is implemented piecemeal at the sector level or for special circumstances. For instance, the Fair and Accurate Credit Transactions Act (FACTA), which amended the Fair Credit Reporting Act (FCRA), protects credit information when used by credit-reporting agencies or lenders.⁴⁸⁴ The Electronic Communications Privacy Act and the Computer Fraud and Abuse Act create penalties for the unauthorized interception of transmitted electronic data and for computer tampering, respectively.⁴⁸⁵ While not tied to a specific sector, the Children's Online Privacy Protection Act (COPPA) protects the sharing of information from children under 13, including requiring parental consent for the collection of data.⁴⁸⁶

Table 5-2. US Personal Data Privacy Laws

Legislation	Year	Data Protection
Fair and Accurate Credit Transactions Act	2003	Regulates the use of credit information by credit-reporting agencies or lenders to protect against identity theft
Financial Services Modernization Act (Gramm–Leach–Bliley Act)	1999	Requires financial institutions to disclose to customers how data are shared and to protect sensitive information
Children's Online Privacy Protection Act	1998	Creates privacy requirements for online collection of personal information of individuals under the age of 13
Health Insurance Portability and Accountability Act	1996	Provides privacy protections for personally identifiable healthcare data when collected, stored, and transmitted by healthcare providers and institutions
Electronic Communications Privacy Act	1986	Protects against the interception of data while in transmission, including telephonic communications and computer-based transfers
Computer Fraud and Abuse Act	1984	Prohibits unauthorized access of computer systems
Federal Trade Commission Act	1914	Prohibits unfair and deceptive acts affecting commerce; has been used to prosecute undisclosed data collection or sharing

The Health Insurance Portability and Accountability Act provides the primary legal protection of healthcare data in the US.⁴⁸⁷ HIPAA provides for privacy protections for the collection, storage, and transmission of personal healthcare data by healthcare providers and institutions.⁴⁸⁸ It creates a class of

⁴⁸⁴ "Fair Credit Reporting Act -- Revised May 2016," Federal Trade Commission, https://www.ftc.gov/system/files/fcra_2016.pdf

⁴⁸⁵ "Electronic Communications Privacy Act of 1986 (ECPA), 18 U.S.C. § 2510-22.," US Department of Justice, Office of Justice Programs, Bureau of Justice Assistance, updated July 30, 2013, <https://it.ojp.gov/PrivacyLiberty/authorities/statutes/1285>

⁴⁸⁶ "Children's Online Privacy Protection Rule ("COPPA")," Federal Trade Commission, <https://www.ftc.gov/enforcement/rules/rulemaking-regulatory-reform-proceedings/childrens-online-privacy-protection-rule>.

⁴⁸⁷ "HIPAA for Professionals," US Department of Health and Human Services, Office of Civil Rights, updated June 16, 2017, <https://www.hhs.gov/hipaa/for-professionals/index.html>

⁴⁸⁸ "Covered Entities and Business Associates," updated June 16, 2017, <https://www.hhs.gov/hipaa/for-professionals/covered-entities/index.html>

Protected Health Information (PHI), information that is both personally identifiable and relates to a health condition.⁴⁸⁹ The Privacy Rule of HIPAA delineates permitted disclosures of PHI (e.g., for the purposes of treatment or healthcare payment), while the Security Rule specifies the protections that must be in place (e.g., protection against impermissible disclosure and workforce compliance measures). Compliance with HIPAA is enforced through corrective actions and civil monetary penalties. The primary intent of HIPAA is to maintain the privacy of patients; it does not provide restrictions on sharing data, either domestically or internationally, provided the rules for privacy and security are followed.

In 2013, the HIPAA Omnibus Rule amended the Privacy, Security and Enforcement Rules of HIPAA to strengthen them as directed by the Health Information Technology for Economic and Clinical Health (HITECH) Act of 2009, by, for example, prohibiting the sale of protected health information without individual authorization and increasing civil penalties for non-compliance.⁴⁹⁰ The 2013 amendments also modified HIPAA as required by the Genetic Information Nondiscrimination Act (GINA) to prohibit most health plans from using or disclosing genetic information for underwriting purposes, though the GINA-specific modification did not further restrict sharing of de-identified information of this type for research and other purposes.

Importantly, HIPAA protects health information only if collected by a covered entity or a business associate of a covered entity. Covered entities are defined in HIPAA rules as (1) health plans, (2) healthcare clearinghouses, and (3) healthcare providers.⁴⁹¹ Collection of healthcare data by entities other than the covered entities or their business associates, or solely for research purposes, is not subject to HIPAA. Notably, consumer genetic testing firms that provide results for purposes other than healthcare (for example, ancestry, lifestyle factors, or even health risk factors) are typically not subject to HIPAA.⁴⁹² Some firms that purport to offer information about a person's risk of a specific disease based on genetic information operate in a gray area and have been scrutinized by the FDA for potentially offering diagnostic services, which would be under FDA's regulatory authority.⁴⁹³

Data that have been de-identified such that the identity of the person or people in the data set cannot be determined are also no longer subject to the privacy protections afforded by HIPAA. Under the HHS Safe Harbor Rule, data are considered de-identified when all of a set of eighteen identifiers have been removed and the entity in possession of the data has no "actual knowledge" that what remains could be used to identify an individual in the data set.⁴⁹⁴ This rule, then, offers institutions a set of well-defined and straightforward steps to take that ensure data meet the de-identification standard under HIPAA, and thus holders of data need not interpret the meaning of the law or terms within. Notably, genetic sequence information, though unique to an individual, is not considered identifiable under the Safe Harbor Rule. Thus, sharing a data set of human genomic sequence information appears not to be covered under the HIPAA privacy rule unless other identifying information is included.

In addition to HIPAA, research involving human subjects (which includes research that uses identifiable private information, including health information) is often covered by The Federal Policy for the Protection

⁴⁸⁹ National Institutes of Health, "What Health Information Is Protected by the Privacy Rule?,"

https://privacyruleandresearch.nih.gov/pr_07.asp; "What is the Computer Fraud and Abuse Act (CFAA)?," Corey Varma, updated January 3, 2015, <http://www.coreyvarma.com/2015/01/what-is-the-computer-fraud-and-abuse-act-cfaa/>

⁴⁹⁰ Department of Health and Human Services, "Modifications to the HIPAA Privacy, Security, Enforcement, and Breach Notification Rules Under the Health Information Technology for Economic and Clinical Health Act and the Genetic Information Nondiscrimination Act; Other Modifications to the HIPAA Rules; Final Rule," *Federal Register* 78, no. 17 (2013): 5565-702.

⁴⁹¹ "HIPAA Privacy Rule: To Whom Does the Privacy Rule Apply and Whom Will It Affect?," National Institutes of Health, updated February 2, 2007, https://privacyruleandresearch.nih.gov/pr_06.asp

⁴⁹² Linnea Laestadius, "Transparency and Direct-to-Consumer Genetic Testing Companies," *Bill of Health* November 22, 2016, <http://blogs.harvard.edu/billofhealth/2016/11/22/transparency-and-direct-to-consumer-genetic-testing-companies/>

⁴⁹³ "Inspections, Compliance, Enforcement, and Criminal Investigations: 23andMe, Inc. 11/22/13," U.S. Food & Drug Administration, updated March 28, 2014, <https://www.fda.gov/ICECI/EnforcementActions/WarningLetters/ucm376296.htm>; Andrew Pollack, "F.D.A. Faults Companies on Unapproved Genetic Tests," *The New York Times* June 11, 2010, <https://www.nytimes.com/2010/06/12/health/12genome.html>

⁴⁹⁴ "Guidance Regarding Methods for De-identification of Protected Health Information in Accordance with the Health Insurance Portability and Accountability Act (HIPAA) Privacy Rule," Department of Health and Human Services, updated November 6, 2015, <https://www.hhs.gov/hipaa/for-professionals/privacy/special-topics/de-identification/index.html>

of Human Subjects (known as the "Common Rule").⁴⁹⁵ This policy applies to all research (a) conducted or supported by a federal department or agency or (b) research subject to regulation by a federal agency (for example, IND research subject to regulation by FDA). The policy also applies to research outside the United States that is conducted, supported, or otherwise subject to regulation by the federal government. Under the rule, institutions undertaking human subject research must convene an institutional review board to review the research to ensure, among other things, informed consent is given to all subjects, including consent to use personal data and health information for research purposes.

Notably, however, and similar to HIPAA, research that uses existing data or specimens is exempt from the policy if the sources are publicly available or the information has been recorded such that subjects have been de-identified.⁴⁹⁶ In addition, under a recent update to the Common Rule, seeking informed consent for broad future use of data and samples is allowable, such that an individual can be asked for informed consent to allow data gathered in one study to be re-used for unspecified future studies.⁴⁹⁷ Given this ability to broadly gather consent in the US, informed consent requirements are unlikely to protect or prevent sharing of data sets that contain personal health information, including genomic information, for research purposes. Like HIPAA, the Common Rule does not specify unique requirements for sharing identifiable private information or biospecimens with researchers in third countries, and regulations describing the role of IRBs under the Common Rule do not distinguish between domestic and foreign research.⁴⁹⁸

As described in the following sections, China has much stricter controls than the US on sharing personal data internationally, creating an imbalance in data access between the US and China. While a review of all countries' data sharing laws is outside the scope of this report, we additionally review the EU's regulations on the topic as a new and noteworthy development.

5.4.1.2. China

China has promulgated numerous policies governing healthcare-related data access, many of which restrict the transfer of data to foreigners or foreign countries by necessitating domestic storage and processing of data, as well as necessitating restrictive security checks on businesses that transfer data to foreign countries.⁴⁹⁹ Genetic data collected from Chinese citizens are subject to multiple regulations, and recent policies have strengthened central control and protection for Chinese genetic and health data. While individual interests and privacy are an important motivation for data protection policies, China has placed growing emphasis on national interests associated with genetic data, and regulatory frameworks treat healthcare and genetic data as resources for national advancement and collective good.⁵⁰⁰

In 2017, a comprehensive cybersecurity law went into effect in China, integrating several national policies into a single framework and highlighting China's interest in information and communication technology for economic development and the importance of countering cyber threats. The law (and its supplemental guidelines) identify three types of protectable data:

- Personal data, which can be used to identify an individual, including name, address, birth date, etc.;

⁴⁹⁵ "New Chinese Requirements on Management of Health Information," *World Data Protection Report by BNA International Inc.* 14, no. 7.

⁴⁹⁶ *Ibid.*

⁴⁹⁷ Haley Bavasi et al. *Using Biospecimens Collected Abroad in Future Research: Key Considerations* Arlington, VA: The Bureau of National Affairs, Inc., 2017. ; "Attachment C - Recommendations for Broad Consent Guidance," Office for Human Research Protections, updated August 2, 2017, <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-august-2-2017/index.html>

⁴⁹⁸ M. A. Majumder, "United States: law and policy concerning transfer of genomic data to third countries," *Hum Genet* 137, no. 8 (2018): 647-55.

⁴⁹⁹ Nigel Cory, "Cross-Border Data Flows: Where Are the Barriers, and What Do They Cost?," *Information Technology & Innovation Foundation*(2017), <https://itif.org/publications/2017/05/01/cross-border-data-flows-where-are-barriers-and-what-do-they-cost>

⁵⁰⁰ Y. Chen and L. Song, "China: concurring regulation of cross-border genomic data sharing for statist control and individual protection," *Hum Genet* 137, no. 8 (2018): 605-15.

- Sensitive personal data, which if misused would endanger the health, safety, or security of an individual (including health records and biometric data); and
- Important data related to national interests or economic or national security.

Under the law, these types of data collected or generated in China may not be stored overseas. Further, cross-border transfer of personal data is prohibited if the owner of the data has not given consent to international transfer or if international transfer may harm personal interests or negatively affect national security or economic or public interests.⁵⁰¹

Another key Chinese data protection policy is the National Health and Family Planning Commission's Administrative Measures on Management of Population Health Information. Published in 2014, the measure aims to protect population health information—defined as that which is collected during the provision of medical, health care, and family planning services—in part because of its value as a resource. The measure prohibits the export of personal information by health organizations in China and mandates the domestic storage of medical information. The term “population health information” includes not only individual medical records but also aggregated or derivative data, potentially even if de-identified, though the specifics are unclear.⁵⁰² Under US HIPAA regulations, PHI that has been de-identified may be shared, and aggregated data (for example population statistics) where individual persons cannot be identified are not considered PHI. For that reason, the Chinese rule appears to create a broader set of protections than HIPAA.

With respect to genetic information, any research involving genetic resources in China is subject to the Interim Measures for the Administration of Human Genetic Resources, China's foundational policy on protection of genetic data.⁵⁰³ These measures were implemented for the purpose of “efficiently protecting and rationally utilizing human genetic resources in the People's Republic of China.”⁵⁰⁴ Under the measures, any sampling, collecting, trading or exporting of human genetic resources performed in China is subject to government approval via a permitting and registration process. Only a Chinese entity may apply for such a permit; therefore, the only lawful way for international entities to access Chinese genetic data is through collaboration with a Chinese institution. All collaborations involving genetic data must be approved by the participating institutions and by the China Administration of Human Genetic Resources.⁵⁰⁵ Chinese entities partnered with a foreign institution must state the purpose of the collaboration, the duration of the collaboration, and any plans for sharing and ownership of IP.⁵⁰⁶

Applications to collect genetic data are reviewed to ensure that the proposed collection and/or export will not cause harm to China's national security, national interests, or public safety. This explicit link to national interests and national security is a unique facet of China's oversight of genetic data collection not present in US oversight or regulatory frameworks and may give the Chinese government wide latitude to deny foreigners, including US companies, access to Chinese genetic information. Additionally, and unlike the US, a permit must be sought for each additional research use of the genetic information; once collected for one purpose, the same information cannot be reused for a new one without re-applying for a new permit.

Although we have not directly studied the effects of these policies, the additional security and permitting requirements as applied by China may hinder scientific research, due to the requirements for re-

⁵⁰¹ Whitaker P, Wang D, Andreeva K. (2018) Data Transfers in the EU, Russia and China. Prepared for Morgan, Lewis & Bokius LLP

⁵⁰² Carlson and Livingston, "New Chinese Requirements on Management of Health Information."

⁵⁰³ "Administrative License: Collection, collection, sale, export, and exit approval of human genetic resources," Ministry of Science and Technology of the People's Republic of China, <http://www.most.gov.cn/bszn/new/rlyc/cjw/index.htm> [Chinese Language Source]

⁵⁰⁴ Harvard School of Public Health. *Guidance on Conducting Research Involving Human Genetic Resources in People's Republic of China (China)* Cambridge, MA: Harvard School of Public Health, 2012.

⁵⁰⁵ Chen and Song, "China: concurring regulation of cross-border genomic data sharing for statist control and individual protection," 605-15.

⁵⁰⁶ Ministry of Science and Technology of the People's Republic of China. *Collection, collection, sale, export, and exit approval of human genetic resources: Administrative License Matters Service Guide* 2016.

application. As the uses of medical data for innovation and discovery may not be obvious far in advance, the future research uses of medical data are difficult to predict. In addition, tracking an individual over a long period of time in order to re-obtain consent is likely to be time consuming and difficult, leading to a degradation of data over time as subjects fall out of the data set. However, except for rare conditions where identifying other persons with the same medical information may be difficult, or for longitudinal studies where collecting years of data is challenging and expensive, new people may be added to replace those that are lost. Thus, while the policies may hinder research and innovation, they do so via a resource and paperwork burden, not a scientific or technological one. Through these policies, China places strict controls on the sharing of healthcare and genetic data to protect not only individual privacy but also to safeguard the data as a valuable resource. This approach seems unique as most countries and regions, including the US and EU (as described in the following section) focus on protecting individuals' rights and privacy while enabling data sharing in order to facilitate R&D.

5.4.1.3. European Union

Unlike the US, the EU has passed comprehensive laws protecting the data rights of EU citizens and recognizes protection of personal data as a basic human right. In 2016, the EU issued its General Data Protection Regulation (GDPR),⁵⁰⁷ which came into force in 2018 and significantly expanded data protections with an eye toward addressing the data security challenges created by new technologies.⁵⁰⁸ Notably, the GDPR expanded the concept of "sensitive personal data" beyond health-related data covered in prior data protection laws to specifically include genetic and biometric data.⁵⁰⁹ Under these regulations, persons have rights to control the uses of their personal data, and sensitive personal data extends these protections to include "fair processing," prohibits the processing of sensitive data except in specified circumstances, such as explicit consent.⁵¹⁰ The regulations include exemptions for certain types of research, and some governance of scientific data is the responsibility of the national government rather than the EU.⁵¹¹

In addition, data that have been anonymized (akin to de-identified under HIPAA) are exempt from the GDPR,⁵¹² and data that have been psuedoanonymized (data coded such that individuals cannot be identified without a "key", like coded medical data) can be used for purposes beyond those for which it was originally collected.⁵¹³ Unlike HIPAA, however, the GDPR does not contain published guidance or a HIPAA-like Safe Harbor rule for organizations to follow to ensure that data are de-identified or anonymized under the regulation. As a result, firms must determine what de-identification means for the data they hold and remain liable for the inadvertent release of identifiable or re-identifiable information. The lack of guidance, in effect, subjects EU data holders to stricter de-identification standards than those that apply under HIPAA.⁵¹⁴

Under the GDPR, transfers of personal data to places outside the EU are subject to regulations to ensure that personal data are processed only in environments where they will be sufficiently protected, and the data protection laws in third countries are not automatically assumed to be adequate. The European Commission does recognize some countries and dependencies outside of the EU as providing adequate levels of protection for personal data: Andorra, Argentina, Canada (only commercial organizations), Israel, New Zealand, Switzerland, Uruguay and the US (if the recipient belongs to the Privacy Shield, a

⁵⁰⁷ A. M. Kilpatrick et al., "Predicting the global spread of H5N1 avian influenza," *Proc Natl Acad Sci U S A* 103, no. 51 (2006): 19368-73.

⁵⁰⁸ Aisling de Paor, *Genetics, Disability and the Law: Towards an EU Legal Framework* (Cambridge, UK: Cambridge University Press, 2017).

⁵⁰⁹ *Ibid.*

⁵¹⁰ *Ibid.*

⁵¹¹ Editorial, "Science needs clarity on Europe's data-protection law," *Nature* 557, no. 7706 (2018): 467.

⁵¹² Gauthier Chassang, "The impact of the EU general data protection regulation on scientific research," *ecancermedalscience* 11(2017): 709.

⁵¹³ A. Bouma et al., "Estimation of transmission parameters of H5N1 avian influenza virus in chickens," *PLoS Pathog* 5, no. 1 (2009): e1000281.

⁵¹⁴ Matt Wes, "Looking to comply with GDPR? Here's a primer on anonymization and pseudonymization," *The Privacy Advisor* April 25, 2017, <https://iapp.org/news/a/looking-to-comply-with-gdpr-heres-a-primer-on-anonymization-and-pseudonymization/>

specific program developed to promote secure transfer of data between the EU and US).⁵¹⁵ Data transfer to these countries is expressly permitted. China is not among these countries; therefore, data transfer is not expressly permitted, and appropriate data safeguards must be implemented before personal data on EU citizens can be transferred to Chinese entities, which can be accomplished by:

- Ensuring the European Commission's standard contractual clauses that ensure appropriate data safeguards are in place;
- Adopting binding corporate rules that control intra-group international transfers, which requires approval by data protection authorities; or
- Implementing an approved code of conduct or certification mechanism with binding and enforceable commitments to apply appropriate safeguards.⁵¹⁶

However, in limited circumstances data transfer may occur even if the recipient country does not have adequate data protection measures in place: data may be transferred if the data subject has explicitly given consent after being informed of the potential risks of the absence of adequate data protection⁵¹⁷

Overall, the EU GDPR appears to take a middle ground between the US, which maintains a patchwork of rules and relatively open sharing of healthcare information, especially for research purposes, and China, which heavily restricts foreign export and storage of healthcare data, requires explicit government consent for each collection and export effort of human genetic resources, and explicitly considers national interests in its permit-making processes. The GDPR appears to prioritize patient and consumer privacy, while valuing data sharing for scientific collaboration, allowing mechanisms for data sharing where privacy and security can be reasonably assured. While EU member states are allowed to enact national laws or regulations that place further conditions and limitations on the processing of sensitive data, the GDPR specifically states that such policies should not hamper cross-border processing or the exchange of personal data within the EU.⁵¹⁸

5.4.2. Access to US Personal Data by China

This report has detailed several instances of private Chinese firms generating or accessing clinical and other healthcare-related data on US persons, through direct investment in genomics and precision medicine companies, partnerships with US researchers, and CLIA/CAP accreditation of Chinese sequencing and molecular diagnostics firms. These activities provide the companies with access to large databases of healthcare and genetic data as well as data on individuals. Given the multiple Chinese investments in US genomics and molecular diagnostics companies and the many CLIA/CAP-accredited laboratories with ties to China, the US appears to take a policy stance that does not dissuade foreign access to US healthcare data and perhaps even encourages it.

Although none of the investments or partnerships detailed appear to involve state-owned enterprises, the possibility remains that the Chinese government may still be able to force or compel private companies in China to disclose the data they have collected (or surreptitiously take the data). While there are no known instances of biotechnology companies handing over patient or customer data to the Chinese government, such a move would not be unprecedented. Both foreign and domestic companies have been required to disclose personal data to the Chinese government: in events that led to the 2004 imprisonment of Chinese dissident Shi Tao, Yahoo! provided email data specific to Shi's account at the request of the

⁵¹⁵ Articles 44-49, General Data Protection Regulation (2016).

⁵¹⁶ Tina Brøgger Sørensen, "How will the new European data protection reform impact Chinese companies?," (2017), <https://www.kromannreumert.com/Insights/2017/How-will-the-new-European-data-protection-reform-impact-Chinese-companies>

⁵¹⁷ Ibid.

⁵¹⁸ Article 9, General Data Protection Regulation (2016).

Chinese government.⁵¹⁹ Another case, from 2013, revealed that Chinese police appeared to have access to messages on WeChat, the world's fifth-largest smartphone app.⁵²⁰ According to an analysis by the Center for Democracy and Technology, "the Chinese government maintains almost unlimited and unfettered access to private sector data, through a variety of regulatory requirements."⁵²¹ Furthermore, private companies may voluntarily allow government access to data with the hopes of receiving beneficial treatment in the future, whether through favorable policies, regulatory decisions, or investments.⁵²²

China has numerous laws requiring or authorizing access to private-sector data by the central government. Many of these laws, such as the Law of Guarding State Secrets (2010) and the Criminal Procedure Law (2012) are ostensibly intended to facilitate investigation into crimes or national security issues, but are loosely worded and contain vague exemptions, providing broad opportunities for the central government to exert its will.⁵²³ The State Security Law of the People's Republic of China, enacted in 1993, describes the rights of the central government to private information during the course of investigations: Article 8 dictates the state may have access to files and materials for examination with approval and after producing a certificate; Article 10 allows the state to conduct technological reconnaissance after going through approval processes; Article 11 allows state inspection of communication equipment; and Article 18 states citizens and organizations may not refuse to furnish information requested by the state.⁵²⁴ None of the certification or approval process required are described in the law, however. Both the State Security Law and the Criminal Procedures Law state that government searches and seizures must be authorized, but do not say by which entity nor detail procedures for approval. According to one source, approval is obtained through various state entities, such as the People's Procuratorate (prosecutor general) or the Public Security Bureau.⁵²⁵

Recently, China has increased its focus on national security with the passage of several laws, including the National Security Law (2015), the Counter-Terrorism Law (2015) and the Cybersecurity Law (2016). These new laws appear largely aimed at internet and telecommunications companies, but their broad scope of does not preclude their application to a wider range of companies such as those harboring genomic or other personal data. Many cybersecurity experts have written about the powers these new laws grant the state and the lack of clarity on mechanisms for compelling access to important data.⁵²⁶ For example, the Counter-Terrorism Law requires internet service providers and telecommunications providers to assist officials conducting investigations, including technical support in decryption, yet does not specify how these requirements will be implemented.⁵²⁷ Additional provisions issued jointly in 2016 by the Supreme People's Court, Supreme People's Procuratorate, and the Public Security Bureau provide clarification on the types of data that can be collected (broad categories including information on the web, communications data, user registration information, and electronic documents) and establish handling procedures to maintain data integrity and chain of custody, but do not address authorization procedures.⁵²⁸ The provisions also allow remote collection of data by the state over the internet (Article 29), and while they state "strict standards" must be followed, no further definition of the term is provided.⁵²⁹ Overall, it is difficult to discern the level of access afforded to the Chinese government

⁵¹⁹ Nate Anderson, "Chinese dissident e-mails: what did Yahoo know, and when did it know it?," *Ars Technica*(2007), <https://arstechnica.com/tech-policy/2007/07/chinese-dissident-e-mails-what-did-yahoo-know-and-when-did-it-know-it/>

⁵²⁰ Anne Henochowicz, "Beware the WeChat Spy," *China Digital Times*(2013), <https://chinadigitaltimes.net/2013/08/beware-the-wechat-spy/>

⁵²¹ Ira S Rubinstein, Gregory T Nojeim, and Ronald D Lee, "Systematic government access to personal data: a comparative analysis," *International Data Privacy Law* 4, no. 2 (2014): 96-119.

⁵²² Zhizheng Wang, "Systematic government access to private-sector data in China," *ibid.*2, no. 4 (2012): 220-29.

⁵²³ *Ibid.*

⁵²⁴ "State Security Law of the People's Republic of China," (1993).

⁵²⁵ Howard Wu and Chris Jiang, "Baker MacKenzie 2017 Surveillance Law Comparison Guide," (2017).

⁵²⁶ Yuxi Wei, "Chinese Data Localization Law: Comprehensive but Ambiguous," (2018), <https://jsis.washington.edu/news/chinese-data-localization-law-comprehensive-ambiguous/>; Jyh-An Lee, "Hacking into China's Cybersecurity Law," *Wake Forest Law Review* 53(2018).

⁵²⁷ "Cybersecurity Law of the People's Republic of China," (2016); Marissa (Xiao) Dong, "China," in *The Privacy, Data Protection and Cybersecurity Law Review - Edition 4*, ed. Alan Charles Raul (London, UK: 2017).

⁵²⁸ Supreme People's Court, Supreme People's Procuratorate, and Ministry of Public Security, "Provisions on Handling Criminal Law Cases for Extracting and Examining and Judging Electronic Data," (2016).

⁵²⁹ Susan Hennessey and Chris Mirasola, "Did China Quietly Authorize Law Enforcement to Access Data Anywhere in the World?," *Lawfare*(2017), <https://www.lawfareblog.com/did-china-quietly-authorize-law-enforcement-access-data-anywhere-world>

through its national security laws, but their vagueness when it comes to oversight could allow collection of data to go relatively unchecked.

Meanwhile, healthcare-related data, whether stored in China, the US, or elsewhere, are vulnerable to cybersecurity breaches. Despite these risks and the knowledge that healthcare is one of the most targeted sectors globally,⁵³⁰ healthcare cybersecurity in the US appears to be inadequate currently.⁵³¹ More than 90 percent of healthcare institutions report having been victims of cyberattacks, and only half of providers believe they are capable of defending against these attacks.⁵³² Given the recent well-known and large data breaches of tens of millions of healthcare organizations in the US, including Community Health,⁵³³ Quest Diagnostics,⁵³⁴ Anthem,⁵³⁵ UCLA,⁵³⁶ and Premera,⁵³⁷ (breaches that some have attributed to Chinese state-sponsored groups⁵³⁸), the healthcare industry remains vulnerable to cybersecurity attacks and much must be done to guard against the risks inherent in the loss of these data. For this reason, data stored in China may be only marginally less secure against acquisition by the Chinese government than data stored in the US.

Utilizing only publicly available information, there is no way of knowing how much access to US data the Chinese government actually has, either from private Chinese companies or through cyber espionage. Regardless, the possibility exists, and the risks of such access include both the potential for damage to US national security and the prospect of economic losses. We examine both risks in the following sections.

5.4.2.1. National Security Risks

Most of the risks to national security that could arise from Chinese access to personal data on US persons, including genomic and healthcare-related data, stem from the dual-use nature of biotechnology information. The promise of genomics and precision medicine includes the abilities to tailor treatments to individuals or populations and to identify new disease determinants and risk factors, for which therapies can be developed. However, the same analyses that lead to those discoveries could be used for malicious purposes in the hands of a foreign state government, such as China.

National security risks that may arise from Chinese access to US healthcare data would require identified records of individuals. Foreign states such as China could target vulnerabilities in specific individuals brought to light by genomic data or health records. For example, healthcare data may contain private information that persons may feel is embarrassing if revealed publicly, creating a blackmail risk. Alternatively, health conditions themselves could be used in a targeted attack; for example, allergy information could be misused to induce an allergic reaction or a fatal injury. Individuals targeted in such

⁵³⁰ G. Martin et al., "Cybersecurity and healthcare: how safe are we?," *BMJ* 358(2017): j3179.

⁵³¹ C. S. Kruse et al., "Cybersecurity in healthcare: A systematic review of modern threats and trends," *Technol Health Care* 25, no. 1 (2017): 1-10.

⁵³² E. D. Perakslis, "Cybersecurity in health care," *N Engl J Med* 371, no. 5 (2014): 395-7; Martin et al., "Cybersecurity and healthcare: how safe are we?," j3179.

⁵³³ Him Finkle and Caroline Humer, "Community Health says data stolen in cyber attack from China," *Reuters*(2014), <https://www.reuters.com/article/us-community-health-cybersecurity-idUSKBN0G16N20140818>

⁵³⁴ David J Lynch, "Biotechnology: the US-China dispute over genetic data," *Financial Times*(2017), <https://www.ft.com/content/245a7c60-6880-11e7-9a66-93fb352ba1fe>

⁵³⁵ Reed Abelson and Matthew Goldstein, "Millions of Anthem Customers Targeted in Cyberattack," *The New York Times*(2015), <https://www.nytimes.com/2015/02/05/business/hackers-breached-data-of-millions-insurer-says.html>

⁵³⁶ Chad Terhune, "UCLA Health System data breach affects 4.5 million patients," *Los Angeles Times* July 17, 2015, <http://www.latimes.com/business/la-fi-ucla-medical-data-20150717-story.html>

⁵³⁷ Reuters, "Premera Blue Cross Says Data Breach Exposed Medical Data," *The New York Times* March 17, 2015, <https://www.nytimes.com/2015/03/18/business/premera-blue-cross-says-data-breach-exposed-medical-data.html>

⁵³⁸ Ellen Nakashima, "Security firm finds link between China and Anthem hack," *The Washington Post* February 27, 2015, https://www.washingtonpost.com/news/the-switch/wp/2015/02/27/security-firm-finds-link-between-china-and-anthem-hack/?utm_term=.5a7bea7e30fb; Finkle and Humer, "Community Health says data stolen in cyber attack from China". <https://www.reuters.com/article/us-community-health-cybersecurity-idUSKBN0G16N20140818>

attacks would likely be strategically identified persons, such as diplomats, politicians, high-ranking federal officials, or military leadership.

Genomic sequence data, due to the growing body of literature linking genetic sequence to traits, may also create a security risk by revealing information useful for gaining leverage over an intelligence target. Like with health records, knowledge of genetic traits may increase the potential for blackmail (e.g., genetic markers associated with mental illness or addiction). As more genetic traits are linked to health conditions, more opportunities for directed attacks at individuals will arise. In the future, the genetic link to more complex personality traits—such as loyalty, susceptibility to flattery, etc.—may be known and these links could be exploited by foreign intelligence officials.

While the national security threats discussed above are, at this point, theoretical, they are not implausible. In fact, recent events and activities could contribute to the data access necessary for these types of attacks. China has been accused by White House National Security Adviser John Bolton of perpetrating the 2015 data breach at the United States Office of Personnel Management (OPM)—which involved approximately 21.5 million stolen records—and a Chinese national was arrested in 2017 in connection with the attack.⁵³⁹ While this breach does not contain healthcare-related data, it could be used in combination with such databases to identify government employees or officials with healthcare or genetic information of interest provided such data included personal identifiers. In addition, the access by Chinese biotechnology companies to US healthcare and genetic data through M&A, research partnerships, and CLIA/CAP accreditation could contribute significantly to population-level analyses to support military or covert attacks if provided to the Chinese government.

Current US protections on access to healthcare data are not sufficient to guard against these risks by a hostile actor, especially a state actor or state-supported actor. While no US law would prevent an actor with criminal intent from accessing data, the US has no general data protection laws that could prevent sharing of personal data with entities whose data security practices may be inadequate. HIPAA, which attempts to prevent unauthorized disclosure of healthcare information, appears to have no foreign enforcement mechanism except to ban future access to protected data by foreign entities. In addition, HIPAA relies on the good and legitimate intentions of the holders of healthcare information to maintain privacy and security. Given the potential Chinese state nexus to Chinese firms with access to healthcare data, relying on good and legitimate intentions may not be protective enough. In addition, though US laws prevent unnecessary sharing of identifiable genomic information, security researchers have demonstrated that genomic data can be combined with publicly available searches to de-identify the genomic data and determine from which individual it likely derives, exacerbating the future security risk of genomic data sharing.⁵⁴⁰

Given the national security risks inherent in foreign access to US healthcare and genomic data, the US should consider these risks when authorizing access. As discussed in Chapter 4, scientific collaboration and discovery are fostered by open access, including to these types of data sets, while national security interests are furthered by limiting access, creating a natural tension between these two concerns. This tension has been present and discussed for decades and continues to be a hotly debated topic.⁵⁴¹ (See Section 4.3.1 for further discussion.) Given the longstanding debate, resolving this tension is beyond the scope of this report. However, the scientific value of these data sets comes from their size and breadth, while a portion of the national security concerns arise from the detailed information potentially available about *specific individuals* (for example, key political officials and members of the intelligence community). This difference allows an opportunity to potentially address some of the risk without compromising

⁵³⁹ Ian Smith, "Bolton Confirms China was Behind OPM Data Breaches," *FedSmith*(2018), <https://www.fedsmith.com/2018/09/21/bolton-confirms-china-behind-opm-data-breaches/>; Evan Perez, "FBI arrests Chinese national connected to malware used in OPM data breach," (2017), <https://www.cnn.com/2017/08/24/politics/fbi-arrests-chinese-national-in-opm-data-breach/index.html>

⁵⁴⁰ B. Malin and L. Sweeney, "How (not) to protect genomic data privacy in a distributed network: using trail re-identification to evaluate and design anonymity protection systems," *J Biomed Inform* 37, no. 3 (2004): 179-92.

⁵⁴¹ Committee on Science Engineering and Public Policy (U.S.). Panel on Scientific Communication and National Security., *Scientific communication and national security : a report* (Washington, D.C.: National Academy Press, 1982).

scientific progress, by merely focusing any attempts to limit access to those individuals whose data are related to national security.

5.4.2.2. Scientific and Technological Risk Considerations

Because of the importance of big data collections to healthcare discoveries, Chinese access to US health and genomic data, whether by private companies or the central government, raises the potential for serious threats to the long-term health of the US biotechnology industry as well as the security of the US medical supply chain. Should China use its access to these data sets to outpace US companies and develop new and important therapeutics or technologies, they would not only capture the subsequent economic gains, but could create a scenario where the US depends on Chinese innovation and drug development for its cures. In fact, a similar type of risk may already exist in the biomedical enterprise, as many critical antibiotics and other drugs are made exclusively in China.⁵⁴² For example, in 2008, stocks of heparin (an anticlotting agent) imported by Baxter International from China were discovered to be contaminated with a closely related, but artificial, substance, suggesting that the contamination was intentional.⁵⁴³ Baxter recalled the affected lots, but the only other major supplier of heparin to the US, APP Pharmaceuticals, also imported their product from China, raising concerns that the US had become over-reliant on Chinese manufacturing.⁵⁴⁴

The FDA holds the primary responsibility for ensuring quality of drugs entering the US market, both from foreign and domestic producers, but is under resourced and struggles to inspect facilities. Following the heparin incident, the FDA opened foreign offices in countries around the world to aid in inspections. A December 2016 report from the Government Accountability Office indicated that while FDA's foreign inspections are increasing, many facilities still have not been inspected, and no assessment has been performed to determine if the activities of the FDA's foreign offices have had a positive effect on drug safety in the US.⁵⁴⁵

Currently, the US has relatively few restrictions on sharing personal data, even de-identified, either domestically or with foreign entities; conversely, China has much stronger restrictions on access to these types of data by foreign entities, as discussed earlier in this chapter. As Chinese firms have formed partnerships with US institutions for the purpose of generating and collecting health and genomic data about Americans, over time China will gain access to a considerable amount of this data on persons in both China and the US, while the US may not have reciprocal access to data from China. This inequity is not as concerning as it may appear, however. Genetic information is a renewable resource; the US can develop the same data sets about US persons that China may be developing, and US researchers can analyze them using the same technologies and techniques to develop the same cures and treatments provided the scientific, entrepreneurial, and political will remains. In addition, data on US persons are likely to be significantly more relevant and valuable for developing new therapies and cures most needed in the US, and the ethnic and racial diversity of the US population may mean that data on US persons are more valuable for developing therapies and cures globally. These two facets call into question the need for US entities to gain access to Chinese data to be competitive. Unlike for security risks, where mere access to US healthcare data is enough to create a risk, China's access to US healthcare and genetic

⁵⁴² Annie Wu and Joshua Philipp, "China Manufacturing of Most US Medicine and Vitamins Poses Security Threat, Researchers Say," *The Epoch Times* April 22, 2018, https://www.theepochtimes.com/china-manufacturing-of-most-us-medicine-and-vitamins-poses-security-threat-researchers-say_2497862.html; Gardiner Harris, "Medicines Made in India Set Off Safety Worries," *New York Times* (2014), <https://www.nytimes.com/2014/02/15/world/asia/medicines-made-in-india-set-off-safety-worries.html>

⁵⁴³ "Drug Making's Move Abroad Stirs Concerns," *New York Times* (2009), <https://www.nytimes.com/2009/01/20/health/policy/20drug.html>; Walt Bogdanich, "Heparin Find May Point to Chinese Counterfeiting," *ibid.* (2008), <https://www.nytimes.com/2008/03/20/health/20heparin.html>

⁵⁴⁴ Gardiner Harris, "Drug Making's Move Abroad Stirs Concerns," *ibid.*, <https://www.nytimes.com/2009/01/20/health/policy/20drug.html>

⁵⁴⁵ United States Government Accountability Office, *FDA Has Improved Its Foreign Drug Inspection Program, but Needs to Assess the Effectiveness and Staffing of Its Foreign Offices.*

data is not, in and of itself, a scientific or technological risk *unless the US chooses not to compete with China*.

We are still at the dawn of the machine learning and artificial intelligence age, with the most transformative discoveries likely yet to come. Large healthcare and health data sets are likely to drive new discoveries and cures. Today, the US appears to undervalue healthcare data when compared to the major efforts underway in China and by Chinese firms—not only in analyzing these data sets but also building and gathering them.⁵⁴⁶ Still, the US maintains a lead in science and technology activity and holds a strong, if not leading position in machine learning and AI, with more than half of all big data revenue expected to come from the US.⁵⁴⁷ Given these advantages, the US appears well-positioned to compete for the lead in future innovation in healthcare data analytics should it choose to prioritize it.

⁵⁴⁶ Mariya Yao, "U.S. Falls Behind China & Canada In Advancing Healthcare With A.I.," *Forbes* June 1, 2017, <https://www.forbes.com/sites/mariyayao/2017/06/01/u-s-falls-behind-china-canada-in-advancing-healthcare-with-ai/#c74b28b206a3>

⁵⁴⁷ National Science Board, *Science and Engineering Indicators*.; Reva Goujon, "AI and the Return of Great Power Competition," *Stratfor Worldview*(2018), <https://worldview.stratfor.com/article/ai-and-return-great-power-competition>; Ron Davies, "Big data and data analytics: The potential for innovation and growth," *European Parliamentary Review Service* 2016

Conclusions and Recommendations

US firms and research institutions have played a critical role in the development of the Chinese biotech industry, and investment and cooperation with US partners continues to help Chinese firms gain access to technologies and data that bolster their current capabilities. Mechanisms for Chinese access to US biotechnologies span many different channels, including two-way capital flows such as M&A, VC, and greenfield FDI; corporate and academic partnerships; transfer of IPR, including patent acquisition and licensing; establishment of US-based R&D centers and incubators; and recruitment of US-trained researchers, both foreign- and Chinese-born. The flow of capital, people and ideas between the Chinese and US biotech industries reflects the reality of increasing economic globalization, which creates benefits to both sides. Correlation between Chinese investment and the level of existing domestic activity in the target biotech segments indicates that Chinese investment is focused on reinforcing existing capacities back home rather than expanding into newer fields. As in other industries, US-China biotechnology collaboration also brings specific national security and economic risks to the US (e.g., theft of IP, dual-use concerns, or increased dependence on foreign products) that US policymakers must mitigate against. We find that current mechanisms are largely adequate, but some areas require updating.

Overall, the US maintains a superior biotechnology innovation capacity through world-class research training and strong governmental support of R&D, but China is seeking to close that gap with its top-down government strategy and coordination, talent recruitment programs, high R&D spending across the industry, and capacity for high-tech R&D. As evidenced by the influx of foreign researchers, large domestic biotech market, and strong federal and private support of innovation, the US is clearly still a global leader in biotechnology. While China has made significant gains in a few fields (e.g., CAR-T, CRISPR, and genomics), continued investment by the US in its own biotechnology industry will ensure its dominance well into the future, obviating the need for drastic interventions.

China has grown to be a global biotechnology player largely through dominance in the production and development of biologic therapeutics. Most Chinese companies have operated in the high-tech but low-innovation segments of contract research/manufacturing and development and production of biosimilars (generic biologics). The future of these companies depends on demand for new therapies to treat serious and complex conditions such as cancer and autoimmune diseases. Recently, however, a push towards more advanced innovation has occurred, with development of new therapies that make use of cutting-edge biotechnology like CAR-T and CRISPR. Moreover, Chinese companies in the fast-growing fields of genomics, molecular diagnostics, and personalized medicine have begun to contribute to China's biotechnology capabilities. Companies like BGI and WuXi NextCODE have grown tremendously, partially through foreign acquisitions and low-cost offerings, to become worldwide leaders in the field.

China's biotechnology growth reflects a combination of policy and market forces. Chinese growth in the sector was driven by a number of commercial factors, including strong global growth and China's comparative advantage of a large domestic market, abundance of talent, and competitiveness in certain activities. A massive political push also played a role; Chinese leaders drove biotechnology with policies including Made in China 2025 and the 12th and 13th Five Year Plans, as well as many provincial and local policies supporting biotechnology ventures. Chinese government spending on biotech has been strong, from R&D programs such as the National Technology Research and Development Plan (863 Program) and the 973 Program as well as government projects like the \$9.3 billion Precision Medicine Initiative.

Recommendation #1: China's approach to the development of its biotechnology sector mirrors the state- and industrial policy-driven approaches causing concerns in other high-tech sectors, thus **it is important for the US to analyze the potential long-term risks from those non-market interventions and formulate appropriate policies to respond to these challenges.** The liberal US market approach can only be sustained if the US has adequate policies in place to mitigate against economic and security risks posed by China's statist approach to innovation without stifling US innovation. While a comprehensive investigation of policy options needs to be performed, for example, through an interagency effort led by the White House, the subsequent recommendations provide some specific avenues to focus on.

Economically, a major concern with China's industrial policies and lack of market access reciprocity is that subsidies and other distorting factors cause Chinese firms to crowd foreign firms that would be more competitive on purely market terms out of the global market, harming innovation and marketplace efficiency. Market exclusivity for biologics first developed in China is a prime example. Currently, China's biotechnology revenues are only around six percent of those of the US, so there is still time for the US to get policy right. In the long run, the first best outcome for the US is a China that converges with liberal approaches to innovation in biotechnology. Since that is just as true for other advanced economies, multilateral approaches to encouraging that Chinese course correction are advisable, and less likely to invite gamesmanship from China in market access.

Recommendation #2: Increase international efforts to bring China's approach to innovation policy and market access more in line with standards in other major biotech markets. Given the small number of regions with major stakes in biotechnology, and the US's current global leadership in the industry, international coordination to address potential security and economic concerns requires just a few nations to participate, increasing the prospects for success. Potential remedies range from incentives (e.g., free-trade agreements or industry-wide standards setting) to deterrents (e.g., tariffs). Identifying appropriate economic or diplomatic interventions requires a thorough assessment that factors in the rapidly evolving nature of biotech as well as the broader suite of policies currently being deployed or considered by the US across all industries.

There are legitimate national security concerns related to the rise of China as major player in the global biotech industry. Recent changes to the process by which the US government reviews inbound foreign investment transactions for potential threats to national security have created additional avenues for the US to scrutinize transactions by broadening the definition of critical technologies to include emerging and foundational technologies and by covering more transaction types for businesses dealing with critical technologies and/or with access to personal data. These expanded rules will allow CFIUS, should it so choose, to review more biotechnology-related transactions and will also facilitate expanded export control of US biotechnologies and related equipment as directed in the ECRA. However, the stronger restrictions on foreign involvement in the US biotechnology industry that may result from these changes could hinder growth of the sector if not implemented carefully. Preventing access to capital from foreign markets could dampen the growth of the US biotech sector if domestic investors do not meet demand. Meanwhile, defining foundational and emerging technologies too broadly could result in export controls that limit the international collaborations that help drive innovation. Identification of critical technologies, therefore, must proceed carefully and deliberately, be informed by data, and involve significant input from the private sector.

Recommendation #3: Ensure that CFIUS and export control reform implementation results in a measured approach toward biotechnology that is based on careful deliberation and data gathering, not broad inclusion of all biotech R&D activity. The FIRRMA and ECRA laws created a process to identify emerging and foundational technologies that are important to US national security and will be subject to special scrutiny. The process to identify these technologies must be underpinned by deliberative work that systematically collects data on the technologies emerging from US biotechnology companies and the relationship those technologies have to national security and the future growth of the US biotechnology industry. Otherwise, these efforts will fall short of their aims, or worse, be counterproductive to innovation and long-term US competitiveness. During this process, delineating fundamental research from foundational and emerging technologies will be difficult yet critical; we propose three potential criteria for defining fundamental and emerging technologies that permit continued basic research:

- a) The technology has been reduced to marketable commercial practice in at least one application, clearly distinguishing it from current definitions of fundamental research (see NSDD-189);
- b) The technology has some plausible, if not demonstrable, link to a specific risk to national security, reducing the potential for inadvertent inclusion of technologies with limited or no feasible national security contributions; and

- c) The technology can be controlled such that embargoed countries are unlikely to acquire it or a technology with the same end-use easily through sharing of fundamental research, minimizing the potential for ineffective regulation.

China's reach into the US biotech industry goes beyond the marketplace and includes US institutions of higher education training Chinese scientists as well as Chinese companies working with US institutions to collect genomic and other healthcare-related data on individuals in the US. Such international partnerships have developed because of the value offered by Chinese services and personnel to US institutions, including skilled labor and inexpensive data processing services. While these arrangements come with some risks, those risks have historically been outweighed by the benefits of high-skilled jobs and lower-cost services. But this balance is not a given.

The US research and innovation engine, especially at the university level, relies heavily on foreign talent, a third of which comes from China. China has invested significant resources into so-called talent programs, which aim both to repatriate citizens who have traveled to the US and other countries for education and training as well as to recruit top international scientists not of Chinese origin. Despite their efforts, China still lags many countries in the rate at which its students return. Indeed, loss of US-trained talent to China is minor in comparison to other, more developed countries about which the US has shown relatively little concern, and the economic gains in the US enabled by foreign technology students and workers far outweigh potential losses due to exportation of technologies. Theft of IP by such individuals—a concern frequently raised within the national security community—is relatively rare given the number of foreign workers in the US. Still, further protection of US biotechnologies can be achieved with manageable hinderance to the R&D environment through two measures:

Recommendation #4: Enhance ethics and IPR programs to prevent theft of US intellectual property. US institutions in both academia and the private sector can better protect themselves from economic threats with a strengthened understanding of IPR, research ethics, and the risk of IP theft, as well as education on how to recognize and report threats. US government agencies such as NIH, BIS, and the State Department should produce guidance for universities and companies engaging in S&T research and international collaboration that support scientific advancement while protecting IPR. Expanding access to this knowledge will enable academic and private institutions to better weigh the risks and benefits of foreign talent and to prevent loss of data or technology through theft by foreign nationals of any country.

Recommendation #5: Provide incentives to retain foreign-born students in technological fields. Professional opportunity is the primary driving factor for Chinese students remaining in the US after training. The US biotech sector is vibrant enough to provide that opportunity despite challenges foreigners may face in trying to stay in the US, but as China's biotechnology sector continues to develop, the balance may shift. Expanded investment by the US government in basic and applied biotechnology research would help ensure that the best opportunities for professional development are on US soil, either in academia or industry. Simultaneously, modifications to US immigration policy, such as expanding H-1B visas, creating portable work authorizations, and easing the path to permanent residency of foreigners trained at the best US research institutions, would help ensure that talented workers who wish to stay can continue to innovate and conduct research in the United States.

China is banking on technologies that leverage big data in healthcare, including genomics and precision medicine, as a major component of its expanded biotech industry. Through direct investments in US companies and research partnerships with US institutions, Chinese biotechnology companies are acquiring critical and foundational technologies necessary for continued industry and sector growth as well as amassing large collections of clinical and genetic data on US residents. The ability to provide services at low cost has been a major driver of these partnerships, and allows US institutions to make more efficient use of their resources for R&D. As long as US institutions maintain access to the data generated, the risk of China using the data to overtake the US's standing in the global health-related biotech field is low; the US maintains a significant lead over China and has a superior ability to innovate. Still, international data sharing agreements and strong cybersecurity measures are required to protect the

data collected from unauthorized access. Governmental guidance on how to structure partnerships with China to ensure continued equitable access to the personal data on US citizens that are generated could go a long way toward mitigating the potential risks without placing limits on the ability of US institutions to access low-cost services which could help reduce healthcare costs.

Recommendation #6: Develop federal guidance for international data agreements. Access to aggregated data on US citizens by Chinese or other foreign firms does not inherently disadvantage the US unless data access is not shared equitably among all partners. Washington should develop specific guidance on how to structure such partnerships so that US interests are maintained. This approach is preferable over more stringent prohibitions on foreign access to data, which could raise costs for R&D in the US; with access to the same data, US entities are collectively more capable of innovating than their Chinese counterparts.

National security risks due to access to US citizens' personal data by China are still theoretical at this stage—specific examples of using such data in a strategic and hostile way have not been found, and the extent the Chinese government is compelling access to data collected by private Chinese firms is unclear. Conversely, evidence points to China as a leading originator of cyberattacks on the US, with many of these attacks targeting personal healthcare-related data, suggesting that data uninvolved in transactions with China are still at risk. Strong cybersecurity practices are therefore crucial to prevent unauthorized access by the Chinese government to personal data maintained in the US.

Recommendation #7: Enhance cybersecurity measures to protect personal data on US citizens. Legal protections on data access, no matter how stringent, will not prevent unauthorized access by China or other foreign governments. Recent healthcare cybersecurity breaches in the US suggest that enhanced measures to protect personal data from hacking are necessary. Yet, while the healthcare industry is receiving increasing numbers of cyberattacks, we see no particularities that suggest protecting genomic and healthcare-related data requires unique cybersecurity measures.

In the current environment, several risks to US and economic security are clear, and the recommendations above provide a starting point for addressing them. However, as biotechnology continues to grow and develop, new risks and opportunities will emerge, and the US government must be prepared to adequately and proactively address them. The US developed a National Bioeconomy Blueprint in 2012 which outlined strategic goals for growing the US biotechnology industry, but it is far out of date compared to current technology trends, and failed to foresee risks to US competitiveness that are now arising. Updating and expanding this document would provide a strategic framework by which the US could ensure the vitality and competitiveness of its biotechnology industry in the face of a dramatically changing global industry landscape.

The original National Bioeconomy Blueprint described the importance of biotechnology to the US economy and highlighted how federal programs have encouraged development of the industry—by strengthening R&D, translating research advances into commercial products, reducing regulatory barriers, creating a skilled workforce, and fostering public-private partnerships. Revisiting and expanding this strategy could help ensure that the US biotechnology industry continues to grow and does not lose ground to an advancing China. While the current Blueprint demonstrates how biotechnology programs can contribute to US economic success, it lacks milestones and forecasts of sector growth by which future progress can be measured. Furthermore, it does not address dependence on or competition from foreign industries, which are clear realities as demonstrated in this report.

Recommendation #8: Update and Expand the National Bioeconomy Blueprint. A refresh of this high-level, executive document would underscore the importance of the biotechnology industry to the greater US economy and illustrate how the federal government can support its future growth. A new Bioeconomy Blueprint should accomplish the following:

- a) Measure the productivity of the US biotechnology industry and draw forecasts and goals for the expected growth of the sector;

- b) Provide an updated view of biotechnology as the global industry it is, including an assessment of US dependence on foreign industries and recognition of rising players on the world stage; and
- c) Perform an analysis of the health and stability of the US biotechnology sector, including identifying which segments are strong, which are vulnerable to foreign competition, and which may be key to future growth of the sector.

There are larger debates about the advisability of an expanded American embrace of industrial policy at home to confront industrial policy abroad; importantly, our recommendations here do not require a wholesale change of mindset on this weighty question—important support for the health of the industry can be accomplished with a limited, catalytic role for government coordination of assessment for the industry, without prejudice to larger industrial policy questions.

The recommendations in this report reflect the need to secure the growth of the US biotechnology industry by addressing threats from China while limiting intervention that could stifle innovation and growth. These recommendations should not be viewed in isolation but rather as a set of complementary actions that together will help maintain a vibrant US biotech sector. An updated and expanded National Bioeconomy Blueprint is an important piece that can serve as a guiding document to support implementation of each of the recommendations and by which future progress can be measured.

Methodology Appendix

Investment Data

Chapter 3 of this report is based on a series of data sets covering Chinese investment transactions in the US biotechnology industry developed and maintained by Rhodium Group (RHG). This section describes the various data sets, their coverage and their application.

Data Coverage

Foreign Direct Investment

Official statistics from both the Chinese and US side are not suitable for an in-depth and real-time analysis of Chinese outbound foreign direct investment (FDI) patterns. Data are only available with a significant time lag and suffer from other distortions such as the extensive use of offshore financial centers. Moreover, official statistics do not provide detailed data on the biotechnology sector.

We therefore rely on a transactional data set on Chinese outbound FDI in the United States developed and maintained by Rhodium Group. The data set covers acquisitions and greenfield projects by ultimately Chinese-owned companies in the US from 2000 to 2017.⁵⁴⁸ This approach allows an in-depth assessment of Chinese outbound direct investment patterns in the US biotechnology sector.

The data set is compiled from tracking individual investments by mainland-Chinese companies in the US utilizing a mixture of channels including commercial databases, online search algorithms, media reports, regulatory filings, company reports, industry associations, official sources, investment promotion agencies, industry contacts, and other sources. The data set only includes transactions that qualify as FDI under common international definitions, i.e. new establishments (greenfield projects) or acquisitions of stakes in existing companies that exceed 10 percent of equity or voting shares. Services contracts, procurement and other elements not defined as investment in the International Monetary Fund's Balance of Payments Manual are not counted. The minimum value for individual deals to be included in the database is \$500,000. Acquisitions over 10 percent are only included if they are completed and they are recorded at the date of completion. Greenfield projects must have been started to be included and they are recorded at the time they have broken ground or begun. Expenditures for multi-year greenfield projects are logged incrementally over time as they occur. The deal values are added based on either the officially announced value or estimates based on variables such as the number of employees, annual revenue, or the value of similar projects. The values for the over 10 percent M&A transactions include equity investment as well as debt assumption.

Venture Capital

The outbound FDI data set is augmented with a new data set that covers Chinese venture capital investment in the US from 2000 to 2017. The data set includes investments made by Chinese nationals, corporations and other entities in US-headquartered biotechnology startups as part of venture capital fundraising transactions.

The venture capital data set covers equity investments from the angel and seed stages through all later-stage, pre-IPO funding rounds. It includes direct transactions made by mainland-Chinese investors as well as investments by Chinese entities through subsidiary firms domiciled outside of mainland China. Where partnership structures are used as investment vehicles, investments are counted based on the ownership of the general partner, which is typically the entity with the sole decision-making authority over fund capital deployment.

⁵⁴⁸ Full methodology of the RHG foreign direct investment data sets is available at <http://cim.rhg.com/notes/china-investment-monitor-methodology-update>

Venture capital investments are recorded at the closing date of the relevant investment or fundraising round, with each fundraising round comprising a single transaction having potentially multiple investors. Where only total fundraising round values are publicly disclosed and individual investment sizes are unknown, a Chinese investment total is estimated by assigning a pro-rata share of the total fundraising round value to all Chinese participants based on the total number of known fundraising round investors. Transactions with no known investment totals are included in the data set at zero value.

The data set does not include venture investments made by entities domiciled in mainland China that are ultimately non-Chinese owned. It does also not include investments in biotechnology firms headquartered in other countries that have operations in the United States.

While venture investments sometimes include stakes of more than 10 percent in a target company and may therefore qualify as direct investments, to avoid double counting all venture capital investments are confined to this data set.

Other Portfolio Investments

The third data set included in our analysis of Chinese investment includes publicly-disclosed investments by Chinese-owned companies in US assets for stakes of less than 10 percent (non-venture portfolio stakes).

This includes acquisitions of minority stakes in US assets where the total stake size is unknown. Disclosure requirements for these types of investments in private companies are very limited, so most transactions in the data set involve US-listed biotech firms where investors owning at least 5 percent of shares must disclose their ownership to the Securities and Exchange Commission. Transactions are counted at the date of completion and assigned a zero value if the investment size is unknown.

Qualifications and Caveats

Given the lack of available official statistics, the transactions data we present in this report are the only way to analyze Chinese investment in the US biotech sector. The transactions approach also allows us an in-depth analysis of Chinese activity by sub-sector, which is based on coding each transaction with a sub-segment of activity within biotechnology. We coded segments thusly:

- **Biologics:**
 - Antibody and protein therapeutics: Companies developing therapeutic protein and antibody products,⁵⁴⁹ including protein/antibody biosimilars and biobetters
 - Gene and cellular therapy: Companies developing gene therapy and cellular therapy products
 - Other, or Multiple Categories: Companies that are either: (1) developing any other biologic product that is not described by the two categories above, such as vaccines, (2) working on biologics formulation, or (3) working in a combination of the categories above such that a primary focus could not be identified
- Contract Research or Manufacturing: Companies providing research and development or manufacturing services to biologics companies, particularly on a contract basis, with biotechnology-specific capabilities
- Genomics and Related Technologies: Companies developing/providing genomics platforms and software, performing genomic-based medical research on the population level,

⁵⁴⁹ Peptides are not included, as these are often considered to be small molecule pharmaceuticals.

- developing/providing genomic sequencing technologies including whole-genome sequencing or next generation sequencing (WGS/NGS), and offering other genomics services⁵⁵⁰
- Molecular Diagnostics and Precision Medicine: Companies developing and offering molecular diagnostic tests for patients and providing diagnostic information intended to shape therapeutic decisions for the individual patient
 - Research/Discovery Platforms, Tools, and Support Products: Companies that support biotechnology research and development by providing commoditized services, research products, specialized discovery platforms, and other tools facilitating biotechnology research
 - Industrial Bioproduction and Bioprocessing: Industrial biotechnology companies working on bio-based production and processing of materials and development of microbes for this purpose⁵⁵¹
 - Agricultural or Agriculture-Applicable Biotechnology: Companies developing genetically-modified crops and companies developing any other biotechnology product with a focus on agriculture applications
 - Biotech Incubators/Accelerators: Technology incubators and accelerators with a biotechnology or life science focus

At the same time, the resulting data are not directly comparable to investment statistics compiled according to balance of payments principles and cannot be used to analyze balance of payments-related questions. Annual investment values represent the simple aggregation of single investments, which is different from the “stock” concept in official statistics, which are often adjusted for market price fluctuations in equity or for depreciation.

The combined annual investment values in a transactional database are generally higher than annual flows from official statistics due to two major reasons: First, it traces investments back to the ultimate beneficiary owner, whereas balance of payment data largely miss investments routed through offshore entities. Second, definitions and accounting used for the RHG data set slightly differ from balance of payment principles. For example, the RHG data set counts the full value of M&A transactions (including assumed debt) and does not account for reverse flows back to China through, for example, intracompany transactions or divestitures.

Bibliometric Analysis

Bibliometric analyses were performed using the Scopus database. All searches were performed in the English language, as English is generally the standard language for publication in scientific journals. Searches were performed for various keywords and phrases relevant to biotechnology. The search term used for each analysis is indicated in a footnote for the applicable figure in the text. Results were not manually filtered; the full set of citations generated by each search, over a selected set of years, was included in the analysis. Search results were sorted by geographic region of author affiliations:

- Publications with at least one author affiliated with a US institution and no authors affiliated with Chinese institutions were labelled “US”;
- Publications with at least one author affiliated with a Chinese institution and no authors affiliated with US institutions were labelled “China”;

⁵⁵⁰ There may be overlap between the Genomics and Related Technologies category and the Molecular Diagnostics and Precision Medicine category. Companies were classified based on their primary focus and capabilities as determined from available information.

⁵⁵¹ Manufacturing of biologics is included in the Contract Research and Manufacturing category or the Biologics category, as applicable, rather than the Industrial Bioproduction and Bioprocessing Category.

- Publications with authors affiliated with both US and Chinese institutions were labelled “US & China”; and
- Publications with all authors affiliated with institutions that are neither in the US nor in China were labelled “Other Countries.”

Identification of CLIA Certified Genetic Testing Laboratories in the US and China

The Clinical Laboratory Improvement Amendments Act of 1988 specifies requirements for laboratories to produce or collect healthcare-related data, including the diagnosis or treatment of disease.⁵⁵² The requirements are in place to assure the analytical validity of results, i.e., that they are performed and interpreted correctly (CLIA does not address the clinical validity of tests).⁵⁵³ Laboratories performing moderate- and high-complexity tests, which includes most molecular diagnostics and other genetic testing, must acquire a Certificate of Compliance from CMS or accreditation through an approved organization.⁵⁵⁴ There are seven approved accreditation organizations under CLIA, including CAP.⁵⁵⁵

To identify US genetic testing laboratories with CLIA certification/accreditation, we searched the Genetic Testing Registry, created by the National Center for Biotechnology Information.⁵⁵⁶ This database includes the types of accreditation received by each laboratory and the types of genetic tests that are performed by each laboratory. To identify Chinese genetic testing laboratories with CAP accreditation, we searched the CAP Laboratory Directory for Chinese laboratories. Then, for each testing company, its description from Pitchbook or the company's website was used to determine whether it performs some type of genetic or molecular diagnostic testing (most companies did not explicitly state the tests they perform).⁵⁵⁷

Next, for each certified genetic testing laboratory identified, we determined whether the company is solely US-based versus solely Chinese-based versus US-based with a Chinese presence or vice-versa. For companies listed on Pitchbook, the primary office location listed was first used to determine whether the company is US- or Chinese-based. Then, to determine if a US company has a Chinese presence, other locations were identified by searching the business's website or by using Rhodium Group data to determine if the laboratory has Chinese investors. Similarly, to determine if a Chinese company has a US presence, the business' website was searched to determine if it has US laboratory locations or if it merged with a US company. For companies not listed on Pitchbook, the business' website was used to determine if their main headquarters is US- or China-based and if it has satellite sites in the other country.

University Partnerships

To find US-Chinese university partnerships, we looked at the top US research universities in Nature Index.⁵⁵⁸ For each university, we collected all affiliated joint institutions and consortia in China and filtered the results to remove non-biotechnology related programs (e.g., aerospace engineering or nanotechnology).

⁵⁵² U.S. Department of Health and Human Services, "Clinical Laboratory Improvement Amendments (CLIA)," <https://www.fda.gov/medicaldevices/deviceregulationandguidance/ivdregulatoryassistance/ucm124105.htm>

⁵⁵³ National Institutes of Health, "What Health Information Is Protected by the Privacy Rule?," https://privacyruleandresearch.nih.gov/pr_07.asp

⁵⁵⁴ Stang and Anderson, "Use of Proficiency Testing as a Tool to Improve Quality in Microbiology Laboratories," 145-52.

⁵⁵⁵ U.S. Department of Health and Human Services, "Accreditation Organizations/Exempt States," https://www.cms.gov/Regulations-and-Guidance/Legislation/CLIA/Accreditation_Organizations_and_Exempt_States.html

⁵⁵⁶ "GTR: Genetic Testing Registry," National Library of Medicine, National Center for Biotechnology Information, [https://www.ncbi.nlm.nih.gov/gtr/all/labs/?term=all\[&filter=location:840](https://www.ncbi.nlm.nih.gov/gtr/all/labs/?term=all[&filter=location:840)

⁵⁵⁷ "Accredited Laboratory Directory," College of American Pathologists, http://www.cap.org/apps/cap.portal?_nfpb=true&_pageLabel=acclabsearch_page&hideNavFrame=Y; "Pitchbook," Pitchbook, <https://pitchbook.com/>

⁵⁵⁸ "Nature Index," Nature Index, <https://www.natureindex.com/>

List of Abbreviations

AI	Artificial Intelligence
ASD	Autism Spectrum Disorders
BGI	Beijing Genomics Institute
BIS	Bureau of Industrial Security
BMBF	Federal Ministry of Education and Research (Germany)
CAP	College of American Pathologists
CAR-T	Chimeric Antigen Receptor T Cell
CAS	Chinese Academy of Sciences
CEO	Chief Executive Officer
CET	Cumberland Emerging Technologies
CDE	Center for Drug Evaluation
CFDA	China Food and Drug Administration
CFIUS	Committee on Foreign Investment in the United States
CHOP	Children's Hospital of Philadelphia
CIC	China Investment Corporation
CLIA	Clinical Laboratory Improvement Amendments
CMO	Contract Manufacturing Organization
CMS	Center for Medicare and Medicaid Services
COFCO	China National Cereals, Oils and Foodstuffs Corporation
COPPA	Children's Online Privacy Protection Act
CRISPR	Clustered Regularly Interspaced Short Palindromic Repeats
CRO	Contract Research Organization
CUBIC	China U.S. Biotechnology Innovation Center
DNA	Deoxyribonucleic Acid
ECRA	Export Control Reform Act
EU	European Union
FACTA	Fair and Accurate Credit Transactions Act
FCRA	Fair Credit Reporting Act
FDA	Food and Drug Administration
FDI	Foreign Direct Investment
FIRB	Foreign Investment Review Board
FIRRMA	Foreign Investment Risk Review Modernization Act
FTAPO	Foreign Trade and Payments Ordinance
FTC	Federal Trade Commission
FYP	Five Year Plan

GDP	Gross Domestic Product
GINA	Genetic Information Nondiscrimination Act
GM	Genetically Modified
GMP	Good Manufacturing Practices
GDPR	General Data Protection Regulation
GSK	GlaxoSmithKline
HHS	United States Department of Health and Human Services
HIPAA	Health Insurance Portability and Accountability Act
HITECH	Health Information Technology for Economic and Clinical Health Act
HIV	Human Immunodeficiency Virus
IBM	International Business Machines Corporation
ICH	International Council for Harmonisation
ICT	Information and Communications Technology
IND	Investigational New Drug
IP	Intellectual Property
IPO	Initial Public Offering
IPR	Intellectual Property Rights
ISAAA	International Service for the Acquisition of Agri-biotech Applications
IT	Information Technology
ITAR	International Traffic in Arms Regulations
JITRI	Jiangsu Industrial Technology Research Institute
JRI	UCLA-PKU Joint Research Institute in Science and Engineering
MAH	Marketing Authorization Holder
MD	Doctor of Medicine
MII	Ministry of Information Industries (China)
MIIT	Ministry of Industry and Information Technology (China)
MIT	Massachusetts Institute of Technology
MOA	Ministry of Agriculture (China)
MOE	Ministry of Education (China)
MOFCOM	Ministry of Commerce (China)
MOST	Ministry of Science and Technology (China)
NGS	Next-Generation Sequencing
NIH	National Institutes of Health
NSDD	National Security Decision Directive
NSF	National Science Foundation
OECD	Organisation for Economic Co-operation and Development
OPM	Office of Personnel Management
PCR	Polymerase Chain Reaction

PHI	Protected Health Information
PRC	People's Republic of China
PYC	Peking-Yale Joint Research Center for Plant Molecular Genetics and Agrobiotechnology
QBIC	Qilu Boston Innovation Center
QDII	Qualified Domestic Institutional Investor
QFII	Qualified Foreign Institutional Investor
RHG	Rhodium Group
RNA	Ribonucleic Acid
S&T	Science and Technology
SEI	Strategic Emerging Industry
SBIR	Small Business Innovation Research
STEM	Science, Technology, Engineering, and Mathematics
TBSI	Tsinghua-Berkeley Shenzhen Institute
UC	University of California
UCLA	University of California at Los Angeles
UK	United Kingdom
US	United States
USD	United States Dollar
USDA	United States Department of Agriculture
VC	Venture Capital