

**Testimony before the U.S.-China Economic and Security Review Commission**

**Hearing On: “China’s Pursuit of Next Frontier Tech: Computing, Robotics, and Biotechnology”**

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“Biotechnology”

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The modern era of globalization was able to advance by putting forward several positive messages that are relevant to China’s pursuit of a domestic biotechnology sector in particular. First, what has been euphemistically referred to as “rising tides lift all boats,” or to say that in a more approachable way, that whatever short-term economic dislocations might be felt in developed economies, these would subside as new opportunities specifically related to globalization accrued to the benefit of consumers, workers and businesses in mature markets.

Second, that developed economies needed to divest themselves of low skilled industries, in particular manufacturing intensive sectors, and double down on higher technology manufacturing and disruptive service sector opportunities.

Third, that underdeveloped markets represented not only new opportunities to sell existing products and services into, but that in their own right these newly available markets held within themselves indigenous innovative capacity that, if properly directed, could lead to new technologies coming to market globally that would benefit everyone.

Each of these three positive messages has unique application to the biotechnology sector; however, to the extent today’s US-China relationship is marked by a renewed sense of imbalance and the need to recalibrate expectations by both public (government) and private (business) sector players, the biotechnology sector presents an opportunity to address these concerns in a way that is mutually beneficial and indicative of what may need to be incorporated in other high technology sectors going forward.

Should China prove to be able to successfully outcompete America in a high technology sector like biotechnology, it would represent another way in which assumptions about how the American economy and its workforce would be able to compete in today’s globalized world have been either overstated, or simply proven to be empty rhetoric. The mounting frustration as economic displacement felt by not only blue collar, vocationally trained workers, but also their white collar, college

educated colleagues, has the potential to create additional unhelpful political pressures that would greatly complicate US-China relations. Ensuring America can successfully compete in high technology sectors such as biotechnology is essential to ensure today's globalized world advances.

### **Critical Context**

Properly framing a response to the Commission's questions around China's pursuit of a domestic biotechnology industry requires four initial critical pieces of context that are specific to China's biotechnology sector. First, the very unique intersection between matters of China's healthcare economy with China's industrial policy. While China's pursuit of a biotechnology sector can be partially understood through the same lens as other high technology industries, there are peculiar matters specific to healthcare access, affordability and quality that will be equally, if not more, animating features in what drives China's policy makers as they craft policies specific to biotechnology. It is helpful to think of China's pursuit of a biotechnology sector as running along parallel tracks where one track is focused on the country's desire to develop domestic high technology champions in areas that employ skilled labor, while the other track is focused on the development of a domestic biotechnology sector that ensures cost effective access to basic medicines and therapies. As is often the case with China's policy making agencies, the stated intentions at the central government level are subject to wide interpretations at the sub-national level, which in the case of biotechnology makes for particularly diverse operating environments where these two tracks are communicated to industry in ways that are at best confusing, and at worst work at cross purposes with one another.

What should be said is that China's healthcare access, affordability and quality challenges are of paramount concern to China's policy makers, and that the bulk of China's policy making and regulatory power will continue to be directed towards endeavors that help address these concerns. These two tracks have the potential to cross in situations where China chooses to emphasize a particular therapy as essential to the country's healthcare system, and develop a domestic player capable of delivering the therapy at a cost the Chinese healthcare economy can afford to pay, at the disadvantage of a foreign company. To date, concerns over this type of intentional policy making apparatus have not been born out as China has been careful to ensure that it avoids crossing the sort of line that India did with compulsory licensing, which has had negative impact on multinational biotechnology companies willingness to invest in R&D capabilities in India. What can be said is that the trade of volume for aggressive price reductions has become a clear policy making tool by the Chinese government that has tempered MNC's unbridled enthusiasm about their respective upside potential in China.

The second piece of critical context is that the biotechnology sector requires a very unique ecosystem in order to incubate innovation and scale it commercially. There are reasons to believe China may struggle to build out the various elements that are

specific to biotechnology. There are at least six conditions required for a domestic biotechnology sector to take root: government incentives and funding for basic science, regulatory frameworks that address the long gestation periods for biotechnology to be developed and commercialized, talent in the form of both scientists and commercial specialists, a robust linkage between government, academia and the private sector, a vibrant venture capital space, and a national reimbursement system (whether public, private, or some combination of both) that rewards all of the stakeholders for innovation.<sup>1</sup> While China has made meaningful progress on each of these fronts, the country still suffers from very specific problems around regulatory systems that do not adequately facilitate innovation, a reimbursement environment that definitely does not reward risk taking, and a particularly poor linkage between academia and commercial sector players.<sup>2</sup> Much of what constitutes government biotechnology incentives in China remains focused on “digging holes and pouring concrete.” That is to say, Chinese policy making specific to biotechnology still elevates spending on new biotechnology industrial parks with the entire associated infrastructure, as opposed to levels of direct subsidization on core R&D activities – often referred to as “bench science” - that would compare to what the United States spends through the National Institute of Health (NIH). Biotechnology innovation is inherently reliant on early-stage, very high-risk R&D, which requires a mature ecosystem in order to scale and generate returns to both public and private sector stakeholders.

The third contextual element is that China’s pursuit of a domestic biotechnology sector may well indicate the limits of its particular centralized economic planning capability. Biotechnology does not easily line up with those other high technology sectors such as clean-technology and semiconductors where China has been able to become a globally disruptive force. A helpful way to think of high technology areas where China has been most successful is in those areas that had already transitioned from bench science to application engineering, and in areas where process innovation (doing more manufacturing faster and at greater scale than in developed markets), has been most impactful.<sup>3</sup> The seminal study of whether Asia’s national economic development model in general works specifically in biotechnology is Joseph Wong’s book *Betting on Biotech: Innovation and the Limits of Asia’s Development State*. Here he writes, “... in science-based industries such as biotech, where technological, economic, and temporal uncertainties are still so pronounced, it is difficult, if not impossible, to strategically pick winners.”<sup>4</sup> Wong’s analysis of

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<sup>1</sup> Ajay Gautam, *Drugs, Politics and Innovation* (Singapore: Partridge Publishing, 2016), 2-3.

<sup>2</sup> Xiaoru Fei, Joseph Wong, “The Rise of Chinese Innovation in the Life Sciences,” The National Bureau of Asian Research, April 2016, 21.

<sup>3</sup> Dan Breznitz and Michael Murphree, *Run of the Red Queen: Government, Innovation, Globalization, and Economic Growth in China* (New Haven: Yale University Press, 2011), 162-163.

<sup>4</sup> Joseph Wong, *Betting on Biotech: Innovation and the Limits of Asia’s Development State* (Ithaca: Cornell University Press, 2011), 9.

attempts by other Asian nation states to emulate America's success in biotechnology is that Asia's economic development model does not map onto biotechnology particularly well: "... [the postwar developmental state in Asia] also benefited enormously from the advantages of late development. They were the beneficiaries of second-mover advantages, whereby the uncertainties of first-order technological innovations had been managed elsewhere. They were spared the uncertainty and the heavy lifting of creating, reaping at the other end the benefits of creatively copying."<sup>5</sup> Advancements in biotechnology, broadly speaking, are a constant series of pure R&D activities that are very high risk in nature – what Wong calls "first order technological innovations." While China is working to ensure it has similar biotechnology R&D infrastructure as its western peers, the ability to leverage pre-existing technology, manufacturing processes, and engineering principles is of more limited value in biotechnology as opposed to other high technology areas.

The fourth and final key contextual element is that where risks specific to China's efforts to develop a domestic biotechnology sector do exist for American business and consumers they are relatively easy to define, and as such, policy makers should be able to address proactively. Three risks are most notable: first, transparency as to where Active Pharmaceutical Ingredients (APIs) are manufactured in China, and robust regulatory mechanisms in place that ensure quality, safety and efficacy standards are upheld. Second, ensuring American multinational biotechnology companies (MNCs) have fair and timely access to the Chinese market under conditions that do not require them – either implicitly or explicitly – to transfer IP to Chinese partners or to wait unreasonable periods of time to sell into China because of incompatibilities between western and Chinese drug approval processes.<sup>6</sup> Third, working to ensure that those limited areas such as genomics and personalized medicine where China does have installed capacity that greatly desires to become world class, Chinese companies do not develop advantages over their American counterparts because of American regulatory bottlenecks, or lack of meaningful public and private sector sponsorship at a time of perceived fiscal austerity from within the US government.

### **China's Major Industrial Biotechnology Policies**

China's 13<sup>th</sup> Five Year Plan (5YP) calls for strategic investment in five industries, of which biotechnology is one. If successful, the 13<sup>th</sup> 5YP would result in a domestic biotechnology sector with revenue of RMB 4.5 trillion.<sup>7</sup> The primary areas the 13<sup>th</sup> 5YP emphasizes are vaccines (hepatitis A, malaria, TB, and AIDS specifically), oncology, central nervous system drugs (mental illness, Parkinson's and Alzheimer's specifically), monoclonal antibodies (mAbs), the most recent iteration of insulin (what is sometimes called "third generation insulin"), targeted efforts in CAR-T, and

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<sup>5</sup> Ibid, 168.

<sup>6</sup> "Understanding the Dynamics of China's Medicine Regulatory Environment," Centre for Innovation in Regulatory Science, June 2015, 2.

<sup>7</sup> [http://www.ndrc.gov.cn/zcfb/zcfbtz/201701/t20170112\\_834921.html](http://www.ndrc.gov.cn/zcfb/zcfbtz/201701/t20170112_834921.html)

personalized medicine.<sup>8</sup> These efforts largely follow the decisions made in the 12<sup>th</sup> 5YP, as well as the 2008 New Drug Creation and Development program. What is notable is the more specific emphasis on diseases the Chinese government recognizes will be major drivers of cost to the Chinese healthcare economy over the next several decades.

China's public and private sector players spend the bulk of all biotechnology R&D monies in Asia (\$160 billion in China out of \$243 billion from all of Asia).<sup>9</sup> In real dollars, China now spends more on biotechnology R&D than Japan and, at current trends, China's combined annual public and private sector R&D investment will be greater than all of the biotechnology R&D spending from Europe.<sup>10</sup> Much like what has been done in western markets where risk sharing between the public and private sector has proven to be an essential element to accelerating biotechnology innovation, China has established a "Fund of Funds," of which Cdb Kai Yuan Capital" and its \$10 billion allocation is the most well known. Efforts like this have been essential to Chinese companies' pursuit of various PD-1, IDO mAb, IL-2 IO, EGFR lung cancer and HBV drugs.

The most common types of incentives offered to both domestic and foreign biotechnology companies by the Chinese provincial governments is subsidized space, usually free office, laboratory and small scale production space within a biotech park for up to 6 months, and after that rental of manufacturing space, at scale, for free anywhere up to 5 years. In addition, tax incentives the Chinese government has developed for other high technology sectors such as semiconductors have benefit to biotechnology. These include up to a 15% reduction in corporate income taxes, and a 150% pretax "super deduction" on specific types of R&D activity in China.<sup>11</sup> Beyond these opportunities, China has rolled out what is called the "1,000 Talent Plan" that, if the person in question is selected, allows them to move to China from abroad and have the government make up the difference between what they were personally earning in a foreign market and what they would make in China at an equivalent job, as well as provide some start-up capital assuming the idea they want to pursue meets the government's objectives.<sup>12</sup> Biotechnology has been one of the government's specific points of emphasis for this program. McKinsey, who has developed a proprietary index that measures and monitors the public and private sector investment environment for biotechnology companies, rates China's government and VC funding for start-up at 6.3 versus the

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<sup>8</sup> James Shen, "China Issues 13<sup>th</sup> Five Year Plan for Biotech Sector Development," WiCON Pharma China, February 2017.

<sup>9</sup> Xuefei Mao, "Entering China's Emerging Life Sciences Markets," MaRS Market Insights, 2014, 5.

<sup>10</sup> Ibid., 12.

<sup>11</sup> "Worldwide R&D Incentives Reference Guide: 2014-15," EY, 42, [http://www.ey.com/Publication/vwLUAssets?EY-worldwide-randd-incentives-reference-guide/\\$FILE/EY-worldwide-randd-incentives-reference-guide.pdf](http://www.ey.com/Publication/vwLUAssets?EY-worldwide-randd-incentives-reference-guide/$FILE/EY-worldwide-randd-incentives-reference-guide.pdf).

<sup>12</sup> <http://www.1000plan.org/en/>

US 8 (out of 10), and 6.7 in China versus 8 (also out of 10) in the United States for developed biotechnology companies in 2016.<sup>13</sup>

In general, funding from central and local governments for specific programs to accelerate innovation in China's biotechnology sector should be understood as primarily emphasizing the creation of new infrastructure in the form of biotech industrial parks, expansion of the CFDA's presence at the sub-national level, and select funding to academic institutions. Additionally, the Chinese government has moved aggressively to incentivize Chinese companies and academics to file patents. Municipal governments such as Shenzhen currently subsidize patent filings in biotechnology less to secure meaningful IP, and more to build a culture that values IP and that thinks about IP in the ways western companies and investors do. The pace of these investments has increased since the 12<sup>th</sup> 5YP, but still widely lags that of the combined public and private sector investments into biotechnology in the United States.

### **Comparison Between US and Chinese Biotechnology Capabilities**

In the last decade, China's efforts to develop an indigenous biotechnology sector have gone from being purely aspirational, with resources directed primarily to capacity building in the form of biotech parks, to much more intentional and focused, with the results to match. Last year saw three domestic Chinese biotechnology companies file for their IPOs (two of which – BeiGene and Chi-Med – were listed on the NASDAQ, and one of which – BETTA – was listed in Shenzhen). As would be expected if the public sector's initial incentives were going to bear commercial fruit, private capital in China has followed, with VC biotechnology funds more than quadrupling since 2011 (from \$600 million to \$2.7 billion).<sup>14</sup>

While the growth in private sector activity in China's biotechnology sector has accelerated, much of it remains focused on molecules that were passed over by foreign MNCs, either because the market was deemed too small to justify the investment, or because the molecule was viewed as a "me-too" by established industry players. Various MNC and VC experts have voiced caution over the flurry of public and private sector activity and investment that has flowed into China's biotechnology sector: the relative immaturity of China's R&D infrastructure, its uneven enforcement of clinical trial standards, and its patchy regulatory scheme all combine to create a situation where academics and entrepreneurs can rush both less than desired "innovations" or what are essentially de-risked assets to the market and cloud the picture as to the effectiveness of China's various incentive schemes. This has all been captured with the phrase used in China's biotechnology community, that much of what is happening thus far is "not yet efficient or effective, but may some day become the latter, even if it never becomes the former." In

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<sup>13</sup> Franck Le Deu, "Building Bridges to Innovation," McKinsey and Company, October 2016, 31.

<sup>14</sup> Ibid., 32.

addition, 2016 saw reports that up to 80% of clinical trial data that had been submitted to the CFDA in support of domestic pharmaceutical companies' various filings was withdrawn.<sup>15</sup> Stories like this speak to the relative immaturity of China's biotechnology space, and equally reinforce the need for caution when thinking about the efficacy and scalability of China's capabilities.

Where Chinese firms have demonstrated technological advantages over American businesses is primarily in gene sequencing. Led by BGI in Shenzhen, China's gene sequencing industry has been successful for two primary reasons, neither of which are purely the result of direct investment or subsidization by the Chinese government. First, BGI's gene sequencing relies on a chip array whose manufacturing techniques are analogs to much of what constitutes semiconductor chip manufacturing. Modifications to semiconductor chip manufacturing processes were necessary for gene sequencing chip manufacturing, and companies like BGI showed great process engineering competency in their ability to make these changes and drive down costs. While this chip manufacturing capability can be directly associated to semiconductor chip manufacturing, there were significant deviations BGI had to design and develop that led its capabilities to ultimately diverge from those of traditional semiconductor chip manufacturing. Second, while gene sequencing as a technology platform has become more automated, which is partially responsible for driving the price down for genetic testing, there is still a significant part of the underlying diagnostic processes that require human interaction. The ability of a company such as BGI to access a cost-effective highly skilled labor force in China has been an important feature that has allowed the field of gene sequencing to explode in China and around the world.<sup>16</sup>

It should be said that gene sequencing's ultimate impact to global health will be the insights it creates around personalized medicine (tailoring molecules and treatment therapies to meet the unique genetic make-up of each individual person). Many of the previously mentioned challenges that face domestic innovation for the biotechnology sector across China suggest the country's potential to become a leader in gene sequencing might never reach its full potential. This disconnect is because personalized medicine requires the unique ecosystem that China lacks, and in particular because China's reimbursement for innovation is no where near close enough to be a trigger for the type of spending on personalized medicine interventions genomics has the potential to reveal. This remains a challenge even in developed markets, where the costs related to personalized medicine stand as one

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<sup>15</sup> Phil Taylor, "CFDA disputes claim that 80% of Chinese trials faked data but admits serious problems," Fierce Pharma, October 24, 2016, <http://www.fiercepharma.com/pharma-asia/cfda-disputes-claim-80-chinese-clinical-trials-were-faked>.

<sup>16</sup> Benjamin Shobert, "Meet The Chinese Company That Wants To Be The Intel of Personalized Medicine," Forbes, January 18, 2017, <https://www.forbes.com/sites/benjaminshobert/2017/01/18/meet-the-chinese-company-that-wants-to-be-the-intel-of-personalized-medicine/#314b86247555>.

of the looming obstacles that could govern the speed with which personalized medicine expands.

Where personalized medicine's advance could prove problematic to US-China relations are in artificial intelligence, computing and data storage. In each of these three areas, China's currently stated policies on cloud computing run counter to the sort of bilateral, scientifically transparent and globally portable arrangements that would ensure a level playing field between domestic and foreign companies. These are particularly of note because the next field of research in personalized medicine will require the aggregation, synthesis and analysis of large bodies of genomic data. Individual gene sequences can create between 100 GB and 1 TB of raw data, which must be stored and then analyzed on its own, and in comparison to other data sets, in order for basic scientific insights to emerge. To say this differently: the first obstacle to personalized medicine was the cost of gene sequencing itself, and the second obstacle will be the ability to analyze the resulting data at scale. It remains to be seen as to whether these data sets will readily reveal meaningful scientific insights, or if additional core science needs to be done in order for personalized therapies to be developed and commercialized.

If the insights from personalized medicine do not reveal themselves through the brute force of AI, then human endeavor will be required. Should that prove to require significant expenditure of time and money, it is realistic to assume that China could develop a meaningful lead over American business in this field. In addition, should China's early efforts to develop a National Gene Bank move at a velocity and scale beyond that of America's own endeavors, it is equally possible that the most vibrant and scalable set of data would be domiciled in China, and not the United States. According to current policies on data storage and data privacy, the computational work supporting this all would need to take place in China, leaving American businesses with many of the same questions as other American cloud computing and software as service companies currently see as not only unresolved, but benefiting Chinese companies.

### **Assessment of US and Foreign Firms Operations in China**

In the aftermath of GSK's 2014 corruption scandal and subsequent \$492 million fine from the Chinese government, there was wide consternation within the MNC pharmaceutical industry as to the government's intentions.<sup>17</sup> At the time, much of what constituted GSK's non-FCPA compliant business practices were the direct result of long-standing funding shortfalls within China's public hospitals. Because of these, GSK's behavior was understood as being more or less the same type, if at a different scale, that many other domestic and foreign companies were also guilty

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<sup>17</sup> Keith Bradsher and Chris Buckley, "China Fines GlaxoSmithKline Nearly \$500 Million in Bribery Case," New York Times, September 19, 2014, <https://www.nytimes.com/2014/09/20/business/international/gsk-china-fines.html? r=0>.

of.<sup>18</sup> Many MNCs feared the Chinese government was getting ready to blame foreign pharmaceutical and medical device companies for the problems Chinese families face around access to affordable healthcare. Since the summer of 2014, these fears have more or less subsided, with the exception of a December 2016 expose on CCTV where six Chinese physicians were shown on video taking bribes from pharmaceutical companies.<sup>19</sup> Any time the government allows a story like this to be elevated by the national media, it re-introduces fear to domestic and foreign pharmaceutical companies that the government again has designs on them as a proxy for pervasive problems specific to China's publicly managed healthcare system.

Beyond FCPA related concerns, American companies continue to struggle with the trade between volume and price that characterizes the China market. In late February 2017, the National Reimbursed Drug List (NRDL) was finally updated after over seven years without revision. Inclusion to the NRDL allows Chinese patients to get reimbursed through China's Basic Medical Insurance (BMI) for specific medicines that previously would have been paid for entirely out of pocket. The actual price reductions pharmaceutical companies put forward in order to be included by the NRDL varies, but can be substantial (GSK's Viread offered a 67% price reduction for inclusion to the NRDL).<sup>20</sup> The backdrop to much of what animates American biotechnology companies' market access discussions in China today is at what price their products can be either paid for out of pocket by the consumer, or ultimately be reimbursed for (at any level) through the BMI. Absent additional expansion of the BMI in general, and in particular available funding for provincial level expansion of reimbursement policies, many western innovative biotechnology platforms may never come to the Chinese market. This partially explains the wide disparities in revenue performance specific to the Chinese market over the last two years that exist between various western pharmaceutical companies.

China's CFDA has made incredible progress over the last three years as it has addressed many of the problems around drug lag that have plagued American pharmaceutical companies. The CFDA is a fairly new regulatory agency in China, and as such has been characterized by inadequate funding, too little in the way of skilled technocrats with experience in drug and device approvals, and an approval process that was neither transparent nor particularly scientific. The net of these

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<sup>18</sup> Natasha Khan, "Novartis to Settle SEC's China Bribe Case for \$25 Million," Bloomberg, March 23, 2016, <https://www.bloomberg.com/news/articles/2016-03-24/novartis-agrees-to-settle-sec-china-bribe-case-for-25-million>.

<sup>19</sup> Liu Jiaying, Ge Mingning, Wu Jing and Li Rongde, "Doctors and Red Envelopes: How Corruption has Blighted China's Public Health System," Caixin, June 20, 2017, <http://www.caixinglobal.com/2017-01-20/101047316.html>.

<sup>20</sup> Angus Liu, "China updates national drug list, adding some blockbuster western meds," February 23, 2017, <http://www.fiercepharma.com/pharma-asia/china-updates-basic-medical-insurance-drug-list-adds-133-western-style-meds>.

problems had been that MNC pharma and device companies could not predict how the CFDA would respond to a new filing, which meant most companies tabled their China market entry strategy until they had moved forward in more developed markets. The exceptions to this were few and far between, and tended to be only those molecules that had specific relevance to a peculiar problem in China's public health.<sup>21</sup> A number of pilot projects going back to late 2014 have accelerated the approval of innovative products through the CFDA, and have also dramatically reduced the number of invalid submittals the CFDA was working through.

American biotechnology companies have also embarked on an aggressive series of co-investments, joint ventures and licensing deals with domestic Chinese players. Notable examples of this include Bayer's additional EUR 100 million investment in its Beijing facility, Sanofi's JV with China Resources Sanjiu Medical and Pharma, and Pfizer's R&D collaboration with PegBio.<sup>22</sup> Of note are several outbound deals on the part of Chinese companies, such as WuXi Apptec's investment in a new gene therapy manufacturing facility in the Philadelphia Navy Yard, Humanwell's acquisition of the American company Epic Pharma (with a follow-on investment in a US R&D facility by Humanwell) and Athenex Pharmaceutical and Beijing Scieure Pharma's FDA approval of five injectables for the North American market. Overall, cross border R&D deals that involve Chinese biotechnology companies have increased by 70% from 2012 to today.<sup>23</sup>

### **Foreign Firms Market Access**

To date, the Chinese government has avoided triggering any of the problems specific to the biotechnology sector that have developed in India around compulsory licensing or other localization requirements. In addition, where the Chinese government greatly desires to see MNCs invest in local manufacturing and R&D capabilities, it has not explicitly linked these objectives to market access. If anything, ongoing problems in China's public healthcare finances prevent any such linkage from having teeth, simply because the Chinese government's reimbursement system does not have the ability to deliver on their side of the deal. As has been previously discussed, where market access problems do persist in China is around the timely updating of hospital, provincial and national drug reimbursement lists and a CFDA regulatory review process that is predictable and runs at a schedule that ensures American innovation can access the China market under adequate patent protections.

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<sup>21</sup> Benjamin Shobert, "A Decade Old Drug Launch in China With Important Insights Today," *Forbes*, March 18, 2015, <https://www.forbes.com/sites/benjaminshobert/2015/03/18/a-decade-old-drug-launch-in-china-with-important-insights-today/#75f3ee1d644a>.

<sup>22</sup> James Shen, "A New Storm is Breeding for China Healthcare in New Year," *WiCON Pharma China*, January 2, 2017.

<sup>23</sup> Le Deu, 40.

Where problems continue that are relevant to the biotechnology sector are around specific IP issues. First, China's State Intellectual Property Office (SIPO) has been badly remiss in addressing MNCs concerns that when they file for marketing approval in China through the CFDA, the submission requires that they disclose what is ambiguously defined as a "new chemical entity" as part of the application. Upon approval, the submission is supposed to create six years of proprietary coverage of the product in question. Industry has brought forward several examples where domestic Chinese manufacturers have produced generic versions of the newly submitted products within the six-year period of protection the CFDA's filing stipulates a foreign company should enjoy. This type of IP slippage will need to be monitored as the CFDA's reforms continue to accelerate. Hopefully, these cases are artifacts of a previous era when the CFDA was an unreliable partner and that this type of slippage will not continue given commitments the central government has made during recent SE&Ds to maintain the integrity and focus of the CFDA's reforms.

Second, problems specific to the SIPO examination process continue where SIPO rejects applications that in form and function are equivalent to those filed and approved in western markets. This problem goes back to concerns in the language of Article 26.3 of China's SIPO that requires a level of disclosure beyond what is required in other developed markets.

Third, the CFDA continues to inconsistently solicit industry feedback when developing new policies. The most recent example of this, beyond the already referenced NRDL and its nearly 8-year gap in being updated, is the April 2016 "Announcement Concerning the Undertaking on the Sales Price of Newly Marketed Drug."<sup>24</sup> This aspirational document required an up-front commitment to cascading price concessions in order to obtain CFDA approval for the launch of new drugs in China. While this was rescinded later in the year as part of the ongoing JCCT meetings, it reflects both the clumsy inner workings of the CFDA as a government agency, as well as the ongoing willingness to associate market access to aggressive price concessions.

### **Opportunities for Collaboration**

Relationships between US and Chinese academic and commercial entities have thus far been sporadic. China has managed to cultivate three advantages relative to these collaborations. First, China does enjoy a cost advantage related specific to lab scientists that has resulted in nearly 250 Contract Research Organizations (CROs) taking root in China. Estimates are that conducting R&D in China as opposed to

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<sup>24</sup> "NAM Priorities for 2016 U.S.-China Joint Commission on Commerce and Trade," National Association of Manufacturers, April 2016, [http://documents.nam.org/IEA/NAM\\_2016\\_U.S.-China\\_JCCT\\_Submission.pdf](http://documents.nam.org/IEA/NAM_2016_U.S.-China_JCCT_Submission.pdf).

western markets can result in up to an 80% cost savings.<sup>25</sup> This cost savings has to be understood within the previous comment about China's biotechnology capability as "not being efficient, but effective." As biotechnology MNCs and start-ups seek to drive R&D costs down, CROs have become a more important part of the path to market, and China's CROs enjoy meaningful cost advantages that create collaborative opportunities. The learning that is being gathered by Chinese CROs will serve to help China's biotechnology companies improve themselves in much the same way as has happened in other high technology sectors where China's initial foray was limited to low value-added functions.

Second, a pattern has emerged around the ability to scale manufacturing pilots more cost effectively in China than in developed markets. This capability does reflect similar structural advantages that began to present to clean-technology start-ups who viewed China as a more amenable location to make the transition from concept to reality.

Third, much of what is driving Chinese biotechnology innovation – outside of personalized medicine – is the desire to identify cost effective therapies. As Yanzhong Huang noted in his 2016 testimony before the Commission, "It is estimated that diabetes alone may consume more than half of China's annual budget if routine, state-funded care is extended to all the diabetes sufferers."<sup>26</sup> Cost pressures of this nature will require that China's domestic biotechnology sector dual path its efforts and not purely focus on opportunities in developed markets, with their lucrative price points, margin and ROI, but also address pressing public health and chronic disease management issues for countries like China with under-developed healthcare systems and a vulnerable consumer.

These opportunities to collaborate are taking place at a time of significant capital outflows from China into western markets, in particular towards sectors such as biotechnology that align with the central governments 5YP. Thus far, foreign companies have been able to invest in domestic Chinese biotechnology companies with relative ease. The limiting factor of inbound investment is not unfair or artificially constructed market access issues, but rather that most of the domestic biotechnology investment opportunities in China remain de-risked "me-too" platforms that do not rise to meet the investment criteria of western MNC biotechnology companies. As China's domestic capabilities in the biotechnology sector increase, it will be critical to watch and ensure today's market access standards do not revert to norms seen in other high technology spaces where foreign investment has been either entirely prohibited, or limited.

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<sup>25</sup> Ivy Teh, "China's Biotech Long March," Asia Biotech, Volume 11, Number 14, 2007, 3.

<sup>26</sup> Yanzhong Huang, "China's Healthcare Sector and U.S.-China Health Cooperation," Council on Foreign Relations, April 27, 2016.

American policy makers will need to remain vigilant as to how the Chinese government responds in pursuit of its biotechnology aspirations. Should the Chinese government come up short of its economic objectives, it is possible Beijing could become more assertive around market access, IP transfer, or compulsory licensing. To date, China deserves credit for not relying on these heavy-handed tools in pursuit of its economic goals. In addition, should the Chinese government's ongoing problems specific to the nation's healthcare system continue to mount, MNCs could well again face uneven application of AML or other corruption standards that are designed to extract concessions from foreign businesses. Finally, the ability of foreign MNCs to invest in, manage, and extract knowledge from targets in China's biotechnology sector must not encounter the same type of limitations as has been the case in other high technology sectors.

### **Maintaining the United States' Strategic Advantages**

In order for the American biotechnology sector to maintain its advantage over China and other global players, the American government needs to pursue five policies. First, the government must continue to emphasize its investments in pure R&D. Amidst the current administration's stated goals of revitalizing the nation's infrastructure and seeing additional capital be directed towards traditional manufacturing, parallel efforts must be made to ensure funding to the NIH in particular is expanded. According to the Federation of American Societies For Experimental Biology (FASEB), "From FY 2003 to 2015, the National Institutes of Health (NIH) lost 22% of its capacity to fund research due to budget cuts, sequestration, and inflationary losses."<sup>27</sup> While the 2016 NIH budget reversed this trend with a 5.9% increase, current inflation adjusted spending on the NIH is still well below its 2003 level. The biotechnology community employs over 800,000 people directly, and supports 3.4 million jobs in the United States.<sup>28</sup> These jobs are the direct result of decades of investment, partnerships and shared risk between the American government, academia, venture capital and biotechnology companies. The net of these investments has been the ecosystem that China very much wants to re-create in order to compete with American biotechnology companies. American policy makers should not assume this ecosystem is self-sustaining; it will also require similar tending to as its counterpart is receiving in China, at the hands of the Chinese government.

Second, America's regulatory infrastructure, in particular that embodied through the FDA, needs to be updated. Drug and medical device approvals remain a critical component that ensure patient safety; however, like any regulatory scheme, they also can take on a life of their own and become a bottleneck that stifles innovation.

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<sup>27</sup> "NIH Research Funding Trends," Federation of American Societies For Experimental Biology, <http://faseb.org/Science-Policy-and-Advocacy/Federal-Funding-Data/NIH-Research-Funding-Trends.aspx>.

<sup>28</sup> Alden F. Abbot, "FDA Reform: A Prescription for More and Better Drugs and Medical Devices," The Heritage Foundation, June 20, 2016.

Various reforms have been put forward specific to the FDA. The most interesting is a reform proposal that would allow other foreign regulatory agencies who conform to global standards, and who have approved a particular drug or device, to use this foreign approval for sale and marketing in the United States.<sup>29</sup> Such an approach would require additional emphasis around global standards in order to ensure competition does not lead to cutting corners around approvals. The framework that would allow competition between the FDA and foreign regulatory agencies could also be deployed to allow for private laboratories to compete with the FDA. This has been successful in the United States, in particular with companies such as UL and MET. A more immediately accessible reform would require the FDA to take its approach to clinical trials, which has understandably evolved and become more complex over many decades, to streamline itself specifically in response to biomarkers and new statistical methods that today's computational systems can illustrate are clinically accurate.<sup>30</sup> These reforms are particularly important given personalized medicine's ability to target specific patients and the un-necessary need to structure a double-blind clinical trial whose entire methodology assumes biological similarity, versus the ability to personalize therapies as the science behind genomics and personalized medicine makes possible today.<sup>31</sup>

Third, ongoing efforts to reform America's patent system need to address the challenges unique to biotechnology, in particular the time that can be lost when claims are challenged or additional data is required in order to support the claim. While improvements in these areas have been made over the last several years, the combined challenges of an unwieldy regulatory scheme, coupled to a patent law system that is not uniquely tailored to the needs of biotechnology, could act as a disincentive to conduct cutting edge research in the United States versus more responsive foreign markets.

### **Recommendations for Congress**

- Protect, and where possible increase, NIH spending with particular emphasis on additional funding for those diseases that are likely to contribute the greatest cost to the American healthcare system (oncology and Alzheimer's in particular). The goal should be to match, in inflation-adjusted dollars, the NIH's 2003 budget.

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<sup>29</sup> Adam Thierer and Michael Wilt, "The Need for FDA Reform: Four Models," The Mercatus Center, George Mason Center.

<sup>30</sup> "Policy Solutions: Delivering Innovative Treatments to Patients," PhRMA, March 2016, 3.

<sup>31</sup> James P. Evans and Michael S. Watson, "Genetic Testing and FDA Regulation Overregulation Threatens the Emergence of Genomic Medicine," January 5, 2015, <http://www.law.uh.edu/assignments/spring2015/19040/jvp140181-jpevansmwatson.pdf>.

- Continue to bring the market access issues within planned Strategic and Economic Dialogues (SE&D) that American biotechnology companies face, specific to the CFDA's regulatory model, lack of reimbursement, and concerns around the uneven application of Anti-Monopoly Law (AML) standards between domestic and foreign companies.
- Complete a comprehensive review of the FDA's ability to monitor the production of APIs and generic pharmaceutical products in China. This is likely going to require additional funding for the FDA to expand its presence in China. Such efforts may also encounter resistance from within China as to the ability of FDA inspectors to audit suppliers in China without notice; however, this type of transparency is critical especially if China is going to continue to consolidate the global production of generic pharmaceuticals.
- Ensure American biotechnology companies in the personalized medicine and genomics field do not run into market access issues around the ability to conduct business and engage in scientific research in China. This should include specific attention to outstanding matters around data privacy issues that cloud-computing companies are currently experiencing in other industrial sectors beyond healthcare.
- Pursue targeted reforms within the FDA that allow competition within global regulatory bodies, accelerated drug and device approvals, and that reflect insights from personalized medicine and new statistical methods that no longer require traditional double-blind placebo clinical trial protocols.