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The Human Genome: Investment Proposal

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Section 1: Executive Summary

The idea for this investment proposal originated in an evolutionary genomics laboratory at Indiana University one afternoon while I observed the day to day practices of a post-doctorate fellow I know. The lab was full of people and instruments whose jobs I could never guess and whose research results appear in a language far more difficult than Chinese. My friend took me on an informal tour of the lab, all the while introducing me to their bizarre apparatuses, researchers who were as curious about my department as I about theirs, and concepts that I still struggle to grasp. Translating to layman's terms did little to clarify my obvious incomprehension. I was told, "the central goal of our research is to examine the nature of nucleotide substitution within various genomes in the *Daphnia* microcrustacean. We do that by isolating the genomes which make up the DNA strands in order to..." Suddenly recalling my own field of study he interjected, "you might be interested to know that we are sending the DNA to an institute in China called BGI to be sequenced." He had no idea how interested I would be.

Isn't it strange, I thought, that the DNA from an organism in a lab in Bloomington is being shipped to China to be sequenced. I decided to look into the mysterious BGI to find out what obscure industry existed around DNA sequencing. The more I looked into BGI; however, the more I became aware that it belonged to anything but an obscure industry. BGI, until 2007 officially known as the Beijing Genomics Institute, is not only a leader of China's growing bio-service and bioinformatics industries, but also ranks highly in the expanding field of genomics and genome sequencing.¹ It has gained notoriety in recent years with published papers on genomic sequencing in top-tier scientific journals and has made a substantial effort to get involved with every major international genome

sequencing project during the past decade.² To display their Chinese identity, BGI sequenced the first genome of a person of Asian descent, the Giant Panda genome, the silkworm genome, and the rice genome, all of which were published in the journal Nature.³ Substantial financial support from the government allowed BGI to purchase 128 of the world's latest genome sequencers, engineered in California by Illumina.⁴ All of these discoveries suggest that BGI alone represents several industries ripe for investment. This is especially true in China where ambition is high, the educational foundation for sciences is strong, and the government is eager to support scientific and technological innovation. Investors often fear the Chinese government's eagerness to develop industries, citing intellectual property theft and corruption as their primary concerns. However, careful assessment of policy risks surrounding intellectual property rights, such as China's government procurement and indigenous innovation policies, reveals that investors have little to fear for investing in genome related industries. Furthermore, with careful investment these industries can impact the future of biology, medicine, and agriculture in ways beneficial not only to China but also to the rest of the world.

Section 2: Economic Opportunities & Risks

Having completed some informal research in BGI, I went back to the evolutionary genomics laboratory to ask about why, out of all the possible genome sequencing operations in the United States, they had chosen BGI way off in Shenzhen. The answer was straightforward, "they are fast, reliable, and cheap." Analysis of this statement with regards to economic opportunities and risk, as well as comparisons with other industries will clarify the investment atmosphere surrounding genome specific bio-service & biotech

industries in China. First I would like to broadly summarize China's economy today in order to place the specific industries in context.

In the years since China began its economic reforms in 1978 it has undergone transition from, as Naughton puts it, "one of the world's most isolated socialist states to a powerhouse of the global economy."⁵ A constant theme in the introductions to readings throughout the semester has been that as late as fifteen years ago, few people if any could have predicted China's remarkable trajectory into a prosperous market economy. While I won't go into the details about how this transition occurred, I want to point out that it happened despite pessimistic predictions and contrary to the models set by other developing nations. Even this year, for example, when China surpassed Japan as the world's second largest economy, Eswar Prasad from the Brookings Institution responded by saying the ranking "is a marker of its increasingly dominant role in the global economy."⁶ On one hand, this understatement represents the pessimism China confronts with regards to its role as a global economic powerhouse, pessimism largely based off of fear from competition. At the same time, understatements like these allude to legitimate concerns over the endless range of difficulties facing China's emergence as a global powerhouse. When investigating China's investment potentials it is crucial to judge risks and opportunities with these thoughts in mind.

China's economy now ranks the second largest in the world behind the United States. Last year China overtook the United States as the world's largest automobile market and surpassed Germany as the world's number one exporter.⁷ As these examples illustrate, China has successfully made the transition from a socialist command economy into a market economy, and the significance is enormous. China has become a major driver

of global growth and has “reshaped the way the global economy functions by virtue of its growing dominance of trade, its huge hoard of foreign exchange reserves and United States government debt, and its voracious appetite for oil, coal, iron ore and other natural resources.”⁸ Furthermore, its expanded role in the global economy has linked it with a global network of countries that China must now rely for its own economy to function. In his recent book, Edward Steinfeld explains that China welcomed and took advantage of this network by essentially outsourcing to foreigners the power to structure Chinese domestic industry while simultaneously becoming a part of the global economy.⁹ At the same time, countries such as the USA must rely more than ever before on China, especially since China controls a huge chunk of our nation’s debt. Finally, this year China’s economy is expected to expand about 10 percent, continuing on a trajectory of remarkable growth.¹⁰ This summary of the Chinese economy will hopefully serve as a foundation for understanding the relative health and investment opportunities for a few industries that represent a spectrum of investment potential.

“No one sector in China is “typical” of all of Chinese industry,” Kennedy wrote, “hence the need for and utility of comparison.”¹¹ The telecommunication industry, as portrayed in Tong and Kenninger’s October analysis of the industry, while seemingly ripe for investment, is upon closer inspection not. Their telecommunication industry analysis makes a few implications regarding the government’s role in industry. To begin, Tong and Kenninger summarize the industry to show that it is healthy and growing, much like I have done in my summary of the Chinese economy. What their paper shows us is that healthy and growing doesn’t necessarily mean ripe for investment.

The Chinese telecommunication industry grew simultaneously with the economy for two reasons. The first is that historically the telecom industry's "end users," (military and government organizations) demanded the industry conform to their needs. As they modernized and expanded, the telecommunications industry was expected to follow and support them. Secondly, the government as a whole accepted the role of the telecommunications industry as an essential tool in support of economic development.¹² The link with the government in the initial stages is obvious, and it continues, although to a lesser degree to this day. Tong & Kenninger trace the regulatory body controlling the industry from the Ministry of Posts and Telecommunication, to the Ministry of Industry and Information Technology. When the telecom industry reform began with the introduction of China Telecom's first competitor, they note the changes in the industry signified by increased competition and growth. Despite China's entrance into the WTO, the authors argue that the continued dominance of the industry by state controlled entities, and "massive amounts of regulation" from China's government "make it difficult for foreign firms to gain a foothold."¹³

The biotech and bio-service industries are relatively new and do not have a historic attachment to government regulatory bodies. Not to say they don't fall under the any regulatory body but unlike China's major telecom providers, China Telecom and China Unicom to name a couple, China's biotech and bio-service companies are not remnants of pre-WTO SOE's, subject to stringent government control. While they may have strong support from the government, and even heavy monetary investment, companies from the bio-service and biotech industries are seeking investment in bids to open up shop in the United States and Europe.¹⁴ Still, at any moment the Chinese government has the potential

to regulate the growth of the biotech industry, just as it suddenly did with the airline industry in 2007.¹⁵

That brings me to my second industry comparison. A look at the airline industries 2003 initiative is helpful for understanding the ways in which the Chinese government might decide to regulate an industry in a way designed to foster its growth. Yap and Wampler are especially critical of the fourth initiative from the 2003, “to encourage market entry.” What they prove is that the Chinese government actually created their own “back-door incentives for its airlines to create barriers to entry.”¹⁶ In this case it seems that the government would like to create competition for the three national airlines, Air China, China Southern, and China Eastern, but would also like to ensure that they maintain dominance in the industry. When flight routes are in question and there is no other option, independent airlines don’t even share the potential for government support like their national competitors. The authors acknowledge that the industry’s potential for growth is high but concede the harsh reality of barriers and difficulties posed by the strong arm of the government.

This industry shares characteristics with the telecommunications industry in that both have tremendous growth potential yet are virtually off limits to profitable investment because in both cases it would mean taking business from the Chinese government. In the biotech and bio-service industries, there are no flight routes to be allocated, there are no companies grandfathered in to the government’s protection, and the pace of change in the industry is too rapid for any one country to control. Therefore, for now, the Chinese government must encourage foreign investment and accept its role as a player in the

network of innovation that currently defines the biotech and bio-service industries much as it did with the Internet Content Provider (ICP) industry.”¹⁷

In their analysis of the ICP industry, Wei and Albertson show how significant government political and financial support of the industry contributed to rapid development and impressive growth. The government would like to appear as the controlling body, but in this case that is not the reality. Instead, non-state-owned domestic firms dominate the industry, and have likely received significant investment from foreign competitors like Yahoo and Google.¹⁸ This is an example of an industry in China that the government supports, yet wasn't born from a Chinese ministry. Still, Wei and Albertson highlight a couple of cases of Chinese attempts to gain a stronger foothold in the industry. The first example describes the battle between Google and Baidu, from which Baidu emerged as the victor. Wei and Albertson suggest that Baidu benefited when the government redirected Google traffic to Baidu's site resulting in Google's loss of 10 to 15% of the market share.¹⁹ This is an interesting new twist on China's efforts to control an industry. In this case, it seems, China helped a domestic company just because it was domestic and that meant money in China's pocket instead of a foreigner's pocket. It also suggests that China is more comfortable with a domestic company controlling the lion's share of its ICP industry rather than a foreign company. Not to mention, China has historic beef with Google.

The other example Albertson and Wei present is perhaps nothing more than a suggestion but one that demonstrates a method by which the Chinese government is seeking to gain control of an industry where it has no roots. They suggest that a joint venture between SOE's China Mobile (telecom industry) and Xinhua (state-run media) is an

effort by the clever Chinese government to increase control over data and information while simultaneously penetrating the lucrative online market.²⁰ Despite this forecast, Albertson and Wei conclude that the ICP industry will maintain its phenomenal growth for years, so long as Chinese netizens are content with government control of information.

With regards to the biotech and bio-service industries, almost the opposite is true. China has fewer restrictions on stem cell research and applications of genomic research than the US and Europe, making it an attractive place for scientists to conduct research that they otherwise would not be able to. Furthermore, Chinese have fewer restrictions on genetically modified organisms, and were the first to allow a gene-therapy drug to enter the market.²¹ If Chinese companies like BGI want to expand into the US than they will have to follow our rules, but it seems that they could easily transfer any questionable research and projects to their base in China. I will address all of these latter issues in the following sections on policy and political risks surrounding investment in the biotech and bio-service industries.

Section 3: Policy Risks

When questioning how certain policy risks can affect an investment, it is useful to gauge the likelihood of the risk and whether its impact would be high or low. By doing so, investors can save a lot of time and prevent unnecessary worrying by understanding that not every policy risk is a risk to their specific investment interests. In this section I want to address some of the policy risks likely to affect investors in biotech and bio-services, and also some that are unlikely but would have high impact on investors. Those that are unlikely and low-impact I will not mention.

Of all the potential policy risks, the most likely to affect an investment in the high-end biotech or bio-service industries in China is the risk surrounding intellectual property rights (IPR). Stevenson-Yang and DeWoskin claim that high-tech companies don't fear the technological competition "but a copy center which tears down the value of innovation across the entire world."²² High-tech companies like Illumina who make quarter million dollar genome sequencing machines must be careful in identifying vulnerabilities in IPR when dealing with China. For the time being there is not much concern of IP risks because Illumina sells directly to an institute that is a member of the Illumina Genome Network, "a global partnership designed to link researchers interested in conducting large-scale whole human genome sequencing projects with leading institutions that can perform such projects using Illumina sequencing."²³ Becoming part of this network makes Illumina's customers part of a global effort, not only a local or national effort. Illumina's effort to build a network reminds me of Edward Steinfeld's observation of R&D networks depleting the cases of IP theft by linking local R&D centers with an international network.²⁴ Doing so eliminates the advantages of IP theft and creates incentives for institutes like BGI to focus on building a team of highly skilled technologists and scientists who can use the machines to their fullest potential.²⁵ The technology is also evolving too quickly for Chinese companies to hope to imitate it, let alone innovate and improve upon it. These points are not necessarily true for low-end biotech equipment like test tubes, and reagents, that can be manufactured in China for comparatively little and don't represent nearly the IP value as high-tech genome sequencers.²⁶ It is unlikely that Chinese high-tech firms alone will be able to "leap-frog" stages in the development of competing technology. Their only hope is

to accept foreign investment as a means to gain access to the technology their growing bio-service industry needs.

As the sequencing technology advances; however, it is becoming cheaper to sequence genomes and it can be done faster than ever. In 2006, Illumina bought Solexa, the developer of a genomic-scale sequencing technology, and by combining their technologies became the leader in genome sequencer manufacturing.²⁷ That same year, BGI struck a deal with Illumina and is at the forefront of genome sequencing because it has the biggest collection of the latest and best sequencers in Asia²⁸. What happens when BGI's sequencers are no longer the fastest and best? Right now, bio-service companies worldwide are completely reliant on advances in technology from a handful high-end biotech companies.

Few developed countries and MNC's will accept China's reputation for IP theft as China transitions from the world's factory and becomes a competitor in technology innovation. Even as they shift away from outright IP theft, technology policies such as government procurement and technology sharing mandates leave people wondering if IP theft has just been given an official name in an effort by the government to cover up its sinister intentions. In Steinfeld's chapter, "Playing to Win," he labels these thinkers as, "believers." He defines them as those who think China is strategically, through legitimate and illegitimate means, facilitating foreign investment in order to gain access to technologies that it can't develop on its own.²⁹ This point of view has some backing in criticism of China's controversial indigenous innovation policies.

Currently, indigenous innovation policies are designed to boost the innovative potential of Chinese companies. The policy's opponents object to the means through which the policy is implemented. They claim indigenous innovation favors Chinese products,

services, and standards over foreign-invested firms through tax incentives that foreign high-tech firms don't receive, government procurement (GP) regulations, standards (as in the case of the gene-therapy medicine approved in China), subsidies, and national security requirements. An example of these policies made headlines in today's New York Times. A hefty article on wind energy in China told how the Chinese government began to slip new provisions into the bidding requirements for state-run wind farms, "requiring more and more of the content of turbines to be equipment produced within China – not imported."³⁰ Similar to what happened to Google's market-share when it was redirected to Baidu for a few weeks, by violating W.T.O. rules on local-content policy, China gained dominant market-share before anybody had even complained. By the time the US applied pressure on China, some of the foreign wind turbines in China exceeded 95 percent local content, and those Chinese parts have begun to undercut prices in US made parts formerly used by wind turbine manufacturers in the US.³¹ This example represents an extreme, and also barely touches on the fact that foreign companies are too eager to gain access to the Chinese market to worry about trade regulations. They are equally guilty for participating in the Chinese plot.

I agree with Steinfeld when he recommends being careful about ascribing motives and intentions to China or the Chinese government. As he puts it, "it is by no means clear that China is collectively bent on becoming an S&T superpower and on doing it at the West's expense (...) What exactly indigenous innovation means, though – whether zero-sum competition with outsiders, cooperative efforts to solve common global problems, contributions of proprietary domestic knowledge to globally developed products, or something else entirely – is as unknown to us as it probably is to them."³² From the

information I have provided on the bio-service industry in China, I think it falls under China's willingness to engage in "cooperative efforts to solve common global problems." In a way, an institute like BGI can be viewed as a Chinese branch of an international R&D network (genome sequencing), whose specialized skills and talents (cheap, reliable, fast) contribute to a truly global workflow.

Overall, I don't think that the current policy risks are likely to affect the bio-service industry in the near future. In addition, high-end biotech is too advanced and the technology too fluid to acknowledge low-tech IP concerns.

Section 4: Political Risks

In Jerome Cohen's article "China's Reform Era Legal Odyssey," he outlines China's path from essentially an archaic legal system with no contemporary legislation thirty years ago to a formal legal system that incorporates concepts taken from legal systems around the world. China has revived and strengthened its courts, Ministry of Justice, commercial arbitration organizations and other relevant institutions but companies investing in China still have doubts, and rightfully so.³³ The main question is, does the rule of law mean anything in China now that they have a functioning, modern legal system? Stories of trouble with locally appointed judges abound, as in Clissold's book, "Mr. China," and locally appointed judges are still targets of extrajudicial pressure from local government officials. But those stories are increasingly out of date as the demands of modernization and globalization infiltrate China's judicial system and the minds of China's public who are increasingly asserting their rights and dissatisfactions.³⁴ Nobody can deny that the legal system is improving, even if at tortoise speed.

The second important political risk to consider is how to cope with the corruption so pervasive in Chinese politics and business. And when is corruption distinguishable from guanxi? In another article, Cohen states, “the guanxi net can be very wide” when recommending necessary reforms to the China International Economic and Trade Arbitration Commission (CIETAC).³⁵ A closer look at his suggestions reveals that there exists a fine line between what he refers to as guanxi and corruption. In his example, he tells a tale of the advocate for the respondent in an arbitration hearing who turned out to be vice chairman of CIETAC and the superior of the presiding arbitrator. In this instance it is very difficult to distinguish whether this was an attempt to get by with a blatant act of corruption, or merely a gross misunderstanding of acceptable application of guanxi in an international arbitration hearing. No matter the case, when it comes to doing business and investing in China, companies must renew precautionary efforts and make sure to adhere to Chinese laws and more importantly, the US Foreign Corrupt Practices Act (FCPA).³⁶ Tread carefully is the name of the game because there is no telling when the government might initiate a crackdown. Even so, “Chinese-style anticorruption campaigns are unlikely to deter corruption.”³⁷

Labor rights are unlikely to affect investments in the high-end biotech or bio-service industries because the workers in the industries come exclusively from biology related university programs or are returnees from foreign biotech operations. Yasheng Huang wrote that “the vast majority of the knowledge production takes place in research institutes and academic institutions, rather than in firms...(and) requires an elite but and extraordinarily small number of workers.”³⁸ Even in a place like BGI that is part institute

part business, the trained bioinformaticians and scientists are unlikely to cause labor unrest.

Mass movements are always a risk in China because of the instability resulting from a massive population undergoing a political and social transition that approaches upheaval at any given second. Today, unrest large enough to create turmoil for businesses in China is only likely in the disputed regions of Xinjiang or Tibet, or in some parts of the countryside. Elsewhere in China, including the crowded cities on the Eastern seaboard flooded with migrant laborers by the tens of thousands and factory workers by the millions, the people seem to be happy with the progress and improvements in their lives. Since the high-tech industries are concentrated in these areas, they maintain ideal access to the type of workers they seek, and to the foreign investment that they need.

Section 5: Action Plan

The high-end biotech and bio-service industries are growing throughout the world, but no place more rapidly and with more enthusiasm than in China. The industry was nothing until the Beijing Genomics Institute ambitiously joined the Human Genome Project in 1999, and in doing so gave China tremendous face by making it the world's only developing nation to contribute.³⁹ They started high on the ladder with a combination of ambition and government funding, and the ambition has not ceased as BGI grows and seeks involvement in every major genome sequence project it can find. BGI has turned itself into a genomics factory striving to make a name for itself on a world scale. But, as Edison Liu, head of the Human Genome Organizations put it, "if they are just a sequence-for-money operation, they will not be remembered."⁴⁰ Historically, there is no greater insult in China

than to say somebody will not be remembered, and for more reasons than that, BGI is torn between scientific and financial goals. Presciently, the founder of BGI prepared for this type of criticism when he announced the establishment of BGI on September 9, 1999, at nine seconds past the ninth minute of the ninth hour, a number signifying longevity in Chinese numerology.⁴¹ What is it then that BGI is interested in doing? Their mission, according to BGI staff, is to prove that genomics matters to ordinary people.⁴²

Was their mission mistranslated? What on earth do they mean they want to prove that genomics matters to ordinary people? As far as I know, most people on the Indiana University campus don't know what a genome is, let alone China's laobaixing. Their mission statement belies their expectations for the future of not just the bio-service industry, but the future of the genome in applications ranging from biopharmaceuticals to agri-biotech applications and green energy. BGI and its sponsors in the government aspire to become the world leaders in the sprouting industries that are now barely visible to anybody but scientists. Someday their work in genomics will mean that genome sequencing is not just cheap, it is also standard procedure for people, necessary in fact, to keep pace with advances in medicine and personalized health care, both linked in a virtuous cycle.

The next question is, how and where to invest the money? One option is to begin by investing in a high-end bio-tech R&D center in China, providing them with enough money to acquire an up and coming technology that would give them the potential to join a network with the likes of Illumina. Right now, Illumina's competitors are sprouting up all over California, the center of bio-technology research and development.⁴³ The model set by Illumina in 2006 illustrates the advantage of investing in technology. Illumina

purchased its fellow biotech company Solexa in an all-stock deal worth \$600 million in 2006.⁴⁴ The two company's combined technologies launched it to the forefront of genome sequencer development.

BGI chairman Yang Huanming expresses the concept on the institute's Americas website. "Science can never be done alone. We all recognize that genomics is in its beginning. International collaboration is more important than ever before."⁴⁵ BGI needs to follow the model in the United States where three national centers test a broad range of technology, constantly challenging one another to improve and also cooperating on large international sequencing projects, all the while constructively critiquing one another to improve production and analytical methods.⁴⁶

Now that the Chinese have proven that they can master the use of the technology, faster and better than most genome sequence operations to boot, it is a given that they will want to invest in the supporting technology.

Another way to invest in the future industries would be to build a competitor to BGI from scratch. It would mean selecting the latest technology that surpasses what BGI uses, recruiting and training the best talent, and engaging in an international project like BGI did on the Human Genome Project in 1999. This investment strategy would essentially kill two birds with one stone. On one hand it would create an in-country competitor, driving down the cost of genome sequencing and by doing so increase demand for it. Though BGI would initially see the company solely as a competitor, before long they could work hand in hand by building a Chinese network. Just as participants in the global network of genome institutes develop specialties and critique each other in order to grow, so too could the two Chinese sequencing institutes.

The best chances for making the investments would be to find a place like the science and technology park in Suzhou.⁴⁷ Incentives from the city could include start-up grants and other annual grants worth millions of RMB like the type that lured BGI from Beijing to Shanghai.⁴⁸ BGI already covers the Shenzhen/Hong Kong technology corridor, so moving toward the Shanghai region while staying out of Beijing's regulatory reach is a logical step. Like Shenzhen, this location is full of foreign enterprises that would facilitate international projects and cooperation. High-tech R&D is strong in the region, and bioinformaticians from Shanghai's Fudan University and Zhejiang University are near at hand for convenient recruitment.

Investing in the biotech & bio-services industries now is to invest in the future. Biofuels, biopharmaceuticals, the future of agriculture, aquaculture, and environmental products are growing industries that rely on a foundation of biotech and bio-service to grow. China has structured itself to emerge as a green energy giant, and is structuring itself to become a world leader in these emerging industries. When President Obama's bioethics commission issued a recent report giving the green light to synthetic biology in the U.S. (all based on genome research), they essentially eliminated self-imposed blockades that allowed countries like China to surge to the forefront of the field while leaving the U.S. in the dust.⁴⁹ This suggests the key for successful investment is to act now while the industries and technologies are in their infancy. BGI is a model for the future of the industries it incorporates and a model for investment. While you are wiring your billion, I'm going over to the genomics laboratory to see if any of those fellows are interested in investing!

Notes:

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