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Defining the Chinese Biotechnology Market

A liberal regulatory environment and huge market demand has led to a thriving biotechnology industry

China's thriving economy and evolving political landscape are luring companies from around the world to explore the Chinese biotechnology market.

"How big is it? How fast is it growing?" companies ask. The answers vary by industry segment.

Our new, in-depth study, *Advances in Biopharmaceutical Technology in China*, copublished by the Society for Industrial Microbiology and BioPlan Associates, Inc., describes the vitality and breadth of China's biotechnological achievements.

This column is the first in a monthly series that is based on our study. Each installment will explore different aspects of China's biotechnology phenomenon.

HISTORICAL PERSPECTIVE

In 1989 China developed and marketed its first genetically engineered drug—recombinant human interferon alfa 1b. This was considered to be the official launch of China's modern biopharmaceutical industry. Since then, China's biopharmaceutical revenue has grown phenomenally—from \$33 million in 1986 [AU: first drug was in 1989; please clarify] to \$3.85 billion in 2005. Although these numbers are still small compared with the size of the biotech industry in the West (Amgen's 2005 revenue was \$12.4 billion, and is growing at 18%), this growth is greater than 100 fold. Venture capitalists are optimistic about the opportunity this represents, especially considering the country's 1.3 billion population.

China has developed and commercialized 30 biotech drugs and 150 more biopharmaceutical products are in the pipeline. [AU: later, you say more than 100 products are in pipeline. Please clarify] Over the next five years, 40 new "Class 1" innovative biopharmaceuticals are

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expected to complete clinical trials and enter the market. "Class 1" refers to innovative biological products, which have never been marketed in any country before, according to China's State Food and Drug Administration (SFDA).

The Chinese biopharmaceutical industry is beginning to establish itself as a research-driven, domestic, market-oriented industry. Meanwhile, China is also emerging as a global outsourcing hub for many overseas biopharmaceutical companies, especially those in the United States and Europe.

However, as companies continue to grow their business in China, a number of issues need to be resolved, including biogenerics versus innovative discoveries, intellectual property protection, quality and regulatory oversight, access to venture capital, and enterprise management.

BIOGENERIC MANUFACTURING PROVIDES THE FOUNDATION

Based on the enormous domestic need for biologics, public health policy in China established

biogeneric manufacturing as a cornerstone of China's biopharmaceutical industry. As the Western world argued about the definition and legality of biogenics, the Chinese industry quietly thrived, driven by a liberal regulatory environment and a huge domestic market demand.

China is the world's most populous country but it has an immature medical insurance system: two-thirds of Chinese citizens are not yet covered by any kind of medical insurance. The Chinese spent less than \$20 per capita on medications in 2003, compared with American per capita spending of \$700 in the same year. Therefore, inexpensive biogenics are deemed to play an indispensable role in the country's healthcare system. Affordable biogenics currently dominate 95% of the Chinese biopharmaceutical market. These include 30 recombinant products, 41 vaccines, 18 blood products, and more than 300 biodiagnostic products.

Today, China is home to more than 400 biogeneric manufacturers, which mainly develop and manufacture generic biopharmaceuticals for the domestic population. Chinese biogenics primarily include recombinant products, such as interferon series, colony-stimulating factor series, erythropoietin, insulin, growth hormone, interleukin-2, and various vaccines, blood products, antibodies, and diagnostic products. Table 1 lists major Chinese biogeneric products and their manufacturers. Notably, Tianjin Hualida Biotech Co., Ltd., one of the major Chinese biogeneric manufacturers, was acquired in early 2005 by Teva Pharmaceuticals, a generics giant based in Israel.

Chinese biogeneric pharmaceutical exports have also shown an upswing in recent years. In 2005, China exported \$478 million of

Table 1. Major biogeneric Chinese manufacturers

Company Name	Biogeneric Drugs
Shanghai Institute of Biological Products	Blood products, vaccines, recombinant products, diagnostic products
National Serum & Vaccine Institute	Vaccines
Beijing Tiantan Biological Products Co., Ltd.	Human albumin, Human immunoglobulin, Human immunoglobulin (PH4) for venous injection
Chengdu Rongsheng Pharmaceuticals Co., Ltd.	Human albumin, Human immunoglobulin, Human immunoglobulin (PH4) for intravenous injection
Changchun Institute of Biological Products	Vaccines, rh IL-2, rh IFN α -2a, rh IFN α -1b, rh IFN α -2b, rh GM-CSF
Wuhan Institute of Biological Products	Vaccines, Murine anti-CD3 monoclonal antibody
Shenyang Sunshine Pharma	rh-IFN α -2a, rh-IL-2, rh-EPO
Anhui Anke Biotechnology Co., Ltd	rh Growth Hormone, rh IFN α -2b
Tonghua Dongbao	rh Insulin
Changchun ChangSheng Gene Pharma Co., Ltd.	rh IFN α -2a; rh IFN α -1b, rhIL-2; b FGF
Changchun GeneScience Pharmaceutical Co., Ltd.	rh Growth Hormone, rh G-CSF, rh GM-CSF
Guangxi Beisheng Pharmaceutical Co., Ltd.	rh IFN α -2b, Human albumin, Human immunoglobulin,
Shenzhen Kexing Biotech Co., Ltd.	rh IFN α -1b , Insulin, IL-2, Growth Hormone
Shenzhen Neptunus Interlong Biotech Co., Ltd.	rh IFN α 2b, IL-2 (125 Ser), Subunit Influenza Vaccine
Sinovac Biotech Ltd.	Vaccines (Hepatitis A, Hepatitis A+B, influenza and SARS)
Tianjin Hualida Biotechnology Co., Ltd.	rh IFN α -2b Injection and Spray
Xiamen Amoytop Biotech Co., Ltd.	rh G-CSF, rh IL-11
Beijing SL Pharmaceutical Co., Ltd.	rh G-CSF, Als IL-2, rhIL-11, rh-bFGF
Beijing Four-rings Biopharmaceutical Co., Ltd.	rh IL-2, rh RPO, rh G-CSF, Hepatitis B diagnostic kits
Beijing Tri-Prime Genetic Engineering Co., Ltd.	rh IFN α -1b
Hualan Biological Engineering Inc.	Human albumin, immunoglobulin, Tetanus Immunoglobulin, Hepatitis B Immunoglobulin
NCPC GeneTech Biotech Development Co., Ltd.	rh-GM-CSF, rhG-CSF, rh EPO

Table 2. Novel biopharmaceuticals with Chinese-owned independent IPR

Approval	Products	Developer	Manufacturer
2005	Recombinant Human Adenovirus Type 5 Injection	Shanghai Sunway Biotech	Shanghai Sunway Biotech
2005	Recombinant Human Tumor Necrosis Factor- α ReceptorII:IgG Fc Fusion Protein for Injection	Shanghai CP Guojian Pharma	Shanghai CP Guojian Pharma
2005	Iodine 131 Tositumomab Monoclonal Antibody Injection	Fourth Military Medical Univ.	Chengdu Hoist Group
2005	Recombinant Humanized Anti-epidermal Growth Factor Receptor Monoclonal Antibody Injection (hR3)	Beijing Biotech Pharma	Beijing Biotech Pharma
2005	Recombinant Endostatin Injection	Tsinghua Univ. & Yantai Medgenn	Yantai Medgenn
2005	Recombinant Human Brain Natriuretic Peptide	Chengdu Nodikang Biopharma	Chengdu Nodikang Biopharma
2005	Recombinant Thrombopoietin Injection	Shenyang Sunshine	Shenyang Sunshine
2004	Recombinant Human Ad-p53 Injection	Shenzhen SiBiono GeneTech	Shenzhen SiBiono GeneTech
2004	Recombinant Staphylokinase for Injection	Shanghai Institute of Biological Sciences	Tonghua Yujin Pharma
2003	Recombinant Tumor Necrosis Factor	Fourth Military Medical Univ. Biotech Center	Shanghai Celstar Biopharmaceutical Center
2003	Oral Cholera rBS-WC Vaccine	Institute of Bioengineering, Chinese Academy of Military Medical Sciences	Shanghai United Cell Biotech
2001	Mouse Nerve Growth Factor for Injection	Lanzhou Institute of Biological Products	Xiamen PKU Bioway Biotech
2001	Recombinant Human Epidermal Growth Factor (rh EGF)	Shenzhen Watsin GeneTech Ltd.	Shenzhen Watsin GeneTech Ltd.
2000	Recombinant Human Basic Fibroblast Growth Factor [®] for External Use (rh bFGF)	Beijing SL Pharma	Beijing SL Pharma
1999	Recombinant Streptokinase for Injection	Shanghai Univ. of Medical Sciences	Shanghai Shiye Medical Univ. Biotech Co.
1989	Recombinant Interferon α - 1b	Institute of Virology, Chinese Academy of Preventive Medicine	Shangzhen Kexing Biotech Co.

biopharmaceuticals to foreign countries, a 54% growth over the previous year. Tonghua Dongbao Group, the domestic recombinant human insulin manufacturer in China, has been exporting insulin to Germany, Italy, Egypt, Mexico, Russia, and other countries, which has generated \$30 million in foreign income since 2001. Not a significant figure by Western standards, but it shows proof-of-concept that Chinese biotherapeutics can be sold internationally.

GOVERNMENT ENCOURAGES INNOVATOR PRODUCTS

China's economy is growing at an

China has a promising biopharmaceutical pipeline, with more than 100 products under development.

annual rate of 8%. China's middle class is also expanding and is now about the size of the population of the UK or France. Chinese consumers' ability to afford more expensive biopharmaceuticals, especially novel biopharmaceuticals, is also increasing.

China recognizes that intellectual property (IP) rights protection is critical to the development of its domestic industry and biopharmaceutical products. China entered the World Trade Organization in December 2001 as part of its focus on independent innovation. IP rights protection has been strengthened as one of the fundamental

China is the first country in the world to complete clinical trials for a vaccine for severe acute respiratory syndrome (SARS).

national strategies of China.

The government also encourages private enterprises, rather than government-subsidized, public research institutions. Meanwhile, the government is increasing investment in the biotechnology sector by building biotechnology parks and funding research projects. China's "863 Program" [can you briefly define what this is?] has been successful in funding promising R&D projects. These efforts have provided a supportive environment for biopharmaceutical innovation.

After 2003, a growing number of innovative biopharmaceuticals with Chinese-owned independent IP rights were launched into the Chinese market through the efforts of biopharmaceutical companies and research institutes. Many research-based Chinese companies, such as Shenzhen SiBiono GeneTech Co., Ltd., Shanghai Sunway Biotech, Ltd., and Beijing Biotech Pharmaceutical Co., Ltd., have gained international recognition for their products. The most productive year for innovative biopharmaceuticals in China was 2005. Seven new Class I biologics were approved for production by the SFDA that year (Table 2).

Table 3. A sample of innovative products in the pipeline

Company Name	Pipeline products
Tianjin Fusogen Pharma	Sifuvirtide, Fusolin (HBV inhibitor), Fusopin, (HCV inhibitor)
Sinovac Biotech, Ltd.	SARS Vaccine, Pandemic Influenza Vaccine (Human-used Avian Flu Vaccine)
Shanghai Sunway Biotech	H102, H103
Beijing Biotech Pharma	rEGF-p64K/Mont vaccine, Humanized Anti-CD6 Monoclonal Antibody
Beijing SL Pharma	rh Parathyroid Hormone for Injection
Wuhan Institute of Biological Products	Monoclonal antibody against hemorrhagic fever for injection
Xiamen PKU Bioway Biotech	HWAP-I, Dx-Hemoglobin
Guangzhou Double Bioproduct, Inc.	Recombinant human endostatin adenovirus injection
Changchun BCHT Pharma	AIDS vaccine
Anhui Golden Sun Biochem	Tumor vaccine
Suzhou Landing Biopharma	Recombinant human pro-urokinase for injection

PROMISING PIPELINE

China now has a promising biopharmaceutical pipeline of more than 100 products. This includes 35 innovative products at clinical trial stages and another 30 to 40 novel products in R&D. China is the first country in the world to complete clinical trials for a vaccine for severe acute respiratory syndrome (SARS) and to develop and conduct clinical trials for an avian flu vaccine. In November 2004, the first vaccine for acquired immune deficiency syndrome (AIDS) was approved for Phase 1 clinical trial, which was completed in 2006. Table 3 lists some of the innovative products currently in the pipeline.

Tianjin Fusogen Pharmaceuticals, Inc., founded by Dr. Genfa Zhou, a US-trained Chinese scientist, has three promising anti-HIV products in the pipeline. Sifuvirtide, Tianjin's HIV fusion inhibitor, entered phase 2 clinical trials in July 2006. The company's R&D was subsidized by

funds from the national 863 Program.

Shanghai Sunway Biotech Co., Ltd., a research-based biopharmaceutical company, launched its first novel product, Recombinant Human Adenovirus Type 5 Injection (H101), in 2005. Now the company is developing H102 and H103.

LOOKING AHEAD

Compared with developed countries, China has a short history of developing novel biopharmaceuticals with established IP rights. An integrated environment that favors enterprise innovation has not completely formed in terms of new drug approval, drug price management, taxation policies, and biopharmaceutical contract manufacturing. Lack of financial support still remains a big obstacle for many Chinese biopharmaceutical companies. Excess production capacity and a shortage of pipeline products are driving them to seek foreign partnerships or contract manufacturing

opportunities.

Future columns will explore how these obstacles balance against China's assets, such as its extremely talented pool of scientists, low production costs, rapid growth rate, and immense domestic market potential. ♦