The Top-60 Chinese Biopharma Companies

The Evolution of Modern Biotechnology in China Is Continuing at a Rapid Pace

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Eighteen years have passed since the first modern biotech firm, **Shenzhen Kexing Biotech**, was inaugurated in China. As China's biotech pioneer, Kexing brought the first Chinese-developed protein therapeutic (recombinant human interferon α1b) to the market in the early 1990s. Nearly 200 modern biotech drug firms have followed, and they have launched 35 biotech drugs to the domestic market in recent years.

According to a newly released study, "Top 60 Chinese-owned Biopharmaceutical Companies" published by BioPlan Associates (www.bioplanassociates.com), with the further expansion of the Chinese biotech sector, a growing number of innovation-focused biopharmaceutical companies are emerging.

To gauge this expansion, we first engaged in benchmarking and a reasonable ranking exercise of the existing companies in China. We believe this project, which required in-depth analysis of the performance indicators of the top-60 Chinese-owned biopharma firms, is the first study of its kind.

This project required thorough analysis of the companies involved in development and commercialization of recombinant proteins, monoclonal antibodies (mAbs) and vaccines. Detailed company profiles, including hard-to-get official financial and operational data, production capacities, pipeline products, were used to assess and rank firms. Because growth rates are important to track, we also used information from the China Biopharma Index™, a quarterly evaluation of trends and market growth in the Chinese biopharmaceutical industry.

Noticeably, while the majority of the Chinese biotechs are dedicated to the development and commercialization of follow-on biologics, several Chinese biotech innovators have launched biotech therapeutics, aimed at the global markets.

In 2004, **Shenzhen Sibiono GeneTech**, for example, reportedly commercialized the world's first gene therapy product, recombinant human adenovirus-p53 injection under the brand name of Gendicine. The company reports that Gendicine has been shown to be beneficial in the treatment of over 40 kinds of solid tumors and is safe and effective based on clinical results from thousands of cancer patients worldwide.

A further breakthrough in gene therapy was achieved in November 2005 when China's State Food and Drug Administration (SFDA) approved recombinant human adenovirus type 5 injection (Oncorine or H101) for the treatment of patients with late-stage refractory nasopharyngeal cancer in combination with chemotherapy.

Developed by **Shanghai Sunway Biotech**, Oncorine, the company claims, is the world's first oncolytic viral therapy approved by a regulatory agency. In 2006, **Shandong Simcere Medgenn Biopharmaceutical** launched another "world's first," a commercial recombinant human endostatin (Endu) for treatment of non-small-cell lung cancer, which is projected to have the potential to become a blockbuster in the Chinese market. These successful stories showcase Chinese biotechs' capabilities to perform and commercialize cutting-edge research.

In China, the biopharmaceutical industry has been recognized by the government as the most important and most promising industry for the 21st century. With a healthy 20–25% annual growth rate, and a diversified pipeline, the Chinese biopharmaceutical industry is moving toward globalization.

The industry is witnessing a surge of mergers, acquisitions, and partnerships between national big pharmas and small biopharmas, as big pharmas are actively looking to broaden their product portfolio with biotech therapeutics. Furthermore, big Chinese CMOs are lauching biopharma businesses by teaming up with international biotech giants such as the partnership between **Zhejiang Hisun Pharma** and **Amgen**.

Some startup CMOs, like **AutekBio**, based in both Beijing and Santa Clara, CA, have shown potential by receiving contracts for development of mAbs.

Although operation costs have increased with the value of the Chinese currency, the enthusiasm for Western biopharmas seeking outsourcing partners in China has not diminished.

Vaccine Producers

The first Chinese biotech companies were mostly vaccine providers. These

organizations have a relatively long history in China, and because of the domestic healthcare and vaccine needs of the world's largest population they tend to be much larger in size.

The earliest traditional vaccine producer, National Serum and Vaccine Institute (NVSI), was founded in 1919. NVSI is currently one of the nine subsidiaries directly controlled by China National Biotec Group (CNBG). With more than 9,000 employees and worldwide revenues of $421 million in 2006, CNBG is the largest producer of vaccines and blood derivatives in China, enjoying more than 80% and 30% domestic market share, respectively.

CNBG produced over one billion doses of vaccines in 2006 and claims to be among the top-10 vaccine manufacturers in the world.

As a state-owned company, CNBG plays a critical role in China's National Immunization Program and has been providing 90% of the country's "planned immunization vaccines" under the program with limited profit margin. To date, CNBG has marketed 34 vaccines (mostly traditional vaccines), 17 hematologic products, and over 30 diagnostic agents, primarily in the domestic market but has recently entered international markets through its trading subsidiaries and business partners.

Two of CNBG's subsidiaries are preparing to obtain WHO prequalification for a Japanese encephalitis vaccine and polyvalent rotavirus vaccine through collaborations with PATH. Meanwhile, NVSI, in partnership with **Beijing Tiantin Biologica Products** and the Virology Institute at China Disease Control Center, is working on establishing a National Engineering Center for Novel Vaccines, aimed at providing a research and commercialization base for novel vaccine candidates.

Another important state-owned vaccine manufacturer is the Institute of Medical Biology affiliated with the Chinese Academy of Medical Sciences. It is the largest poliomyelitis vaccine producer in China and has provided more than five billion doses of polio vaccines to Chinese children since the 1960s. The institute is also one of the major providers of hepatitis A vaccines in China.

By comparison, privately owned vaccine manufacturers tend to be small and principally engaged in the production of non-government-planned vaccines with higher profit margins. Major privately owned producers include **Sinovac Biotech**, **Changsheng Life Science**, **Shenzhen Kangtai**, **Zhejiang Tianyuan**, **Jiangshu Yanshen**, **Liaoning Yisheng**, **Liaoning Chengda**, **Dalian Hassen**, and **Forwell Biopharma**.

According to the SFDA, Chinese vaccine producers have marketed 49 vaccines to fight 26 infectious diseases, with over one billion doses annual output, including 500 million doses of vaccines against major infectious diseases such as hepatitis B, poliomyelitis, measles, pertussis, and diphtheria. As a result of the work of these traditional biotech companies, China claims to be the world's largest vaccine manufacturing country in terms of production scale.

Foreign Biotech Competition

Since the 1990s, a number of multinational biotech players have established their presence in China lured by a wealth of advantages. The most successful foreign biotech player in the Chinese market today is **Novo Nordisk**, which entered the Chinese market in 1993 and opened its first production facility in Tianjin in 1996. Novo Nordisk has grown rapidly in China, and the company has dominated the human insulin market there for many years, with 1.9 billion RMB ($261 million) sales in 2006.

Another aggressive foreign player is **Sanofi-Pasteur**, which set up an influenza vaccine facility in Shenzhen in 1996. In November 2007, the company announced that it will invest 700 million RMB ($94 million) to expand facilities in Shenzhen, with the goal of producing seasonal influenza vaccines for the Chinese market by 2012. This will undoubtedly create powerful competition for Chinese influenza vaccine manufacturers. **GlaxoSmithKline** also set up an influenza vaccine production facility in Shanghai Zhangjiang High-tech Park in 2004.

Changing Biotech Environment

The Chinese biotech industry has established critical mass and is now aggressively working to catch up with its foreign competitors from developed countries. The government has realized the importance of biotechnology and has prioritized the biotech industry on its agenda.

China has enticed an abundance of high-caliber China-born biotech employees with many years of education, research, and work experience in the West to return to their motherland to set up or take senior positions in Chinese biotech companies. Many Chinese firms are spending extensively for faciltiy expansaion and upgrades to meet Western GMP standards. Some are beginning to import production lines from the West. This trend is likely to continue.

The growing number of international biotechs partnering with Chinese compa-

nies in R&D and production has provided opportunities for Chinese biotechs to gain management know-how from their Western partners. As an emerging biopharmaceutical outsourcing hub, China is rapidly becoming an important cog in multinationals' global strategies.

In the early 2000s, Western companies tended to look to China for cheap labor and raw materials. Today, what makes China attractive to foreign biotechs is the country's more open economic and political landscape coupled with a large biotech talent pool.

2007 has been a critical transformative year for China's pharmaceutical and biotech industries. The SFDA vowed to streamline regulatory processes and strengthen surveillance on pharmaceutical companies, with the purpose of ensuring drug safety and efficacy, and encouraging innovations and IP protection. Many new regulations associated with drug registration, labeling, and recalling have been promulgated by the SFDA in this year.

New GMP standards, which are believed to be close to European GMP standards, have also been issued. Meanwhile, the government has taken serious measures to eliminate corruption and abuse of power within the agency. These initiatives are creating a more healthy regulatory environment.

Threats and Weaknesses

Today, the largest threat to Chinese biotechs comes from competition from foreign biotech companies and imported biopharmaceuticals on the Chinese market as a result of China's entry to the WTO in 2001. With the world's largest population, if China fails to develop its own proprietary products, the country will become the world's largest destination for imported products. These products are becoming increasingly more affordable to Chinese consumers.

Some Chinese biosimilar manufacturers with limited knowledge of international IP law may be faced with potential IP conflicts or lawsuits from foreign companies; this may impact global market plans. Other challenges facing Chinese biotechs include higher tax rate (compared to traditional industries), the increase of raw material costs, and potential government-imposed drug price cuts. In addition, the lack of a strong, mature capital market, and the use of government investments to fund biotech research also hinder the development of Chinese commercial biotechs.

Chinese biotech firms need to overcome many weaknesses before they are able to become competitive in the global market:

- Size: In general, Chinese biotech firms remain small, with the exception of CNBG.
- Financing: Most companies don't have sufficient funds to foster intensive R&D and facility upgrading.
- R&D: The majority of Chinese biotechs do not invest enough in R&D and as a result do not possess innovative research personnel. Consequently, 90% of these firms focus on the development and production of follow-on biologics.
- Production: So far, no Chinese biopharma has managed to obtain Western GMP certifications or WHO prequalification.
- Management and Marketing: Many companies do not have managers with international managerial or marketing experience.

Innovation and Outsourcing

Based on our study of the Top-60 Chinese biopharma companies, we predict that innovation and outsourcing will become major drivers for China's biotech industry over the next 5–10 years. At present, the potential for Chinese biotechs to become competitive in the global market has not yet been realized.

Chinese biotech companies still remain as diamonds in the rough. It is, however, only a matter of time before Chinese biotech firms become influential players in the global market. We believe that the key to China's future success will be the commitment and persistence of Chinese biotech professionals to polish the diamond. We will not be surprised if ten years from now, some of the Chinese companies on our Top-60 directory will have become well-known names in the international biotech community. GEN

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The Top-60 Chinese-Owned Biopharmaceutical Companies

Company Name	Employees	Bio-Revenue 2006) Mln RMB	Marketed Biologics	Primary Business**
Part 1: Modern Biotech Firms				
3S Bio	370	100-150	5	R
Changchun GeneScience Pharmaceutical	500	150-200	5	R
Shenzhen Kexing Biotech	150	100-150	6	R
Tonghua Dongbao Pharmaceutical Group	1,910	100-150	4	R,S
Anhui Anke Biotechnology	350	100-150	7	R
Jiangsu Wanbang Biopharma	355	100-150	3	R&S
Hangzhou Jiuyuan Gene Engineering	205	50-100	2	R,S
Tianjin Hualida Biotechnology	150	50-100	3	R
Beijing SL Pharmaceutical	270	50-100	4	R,S
Zhongshan Hygene Biopharm	80	150-200	1	R,C
Beijing Tri-Prime Genetic Engineering	190	40-50	2	R
Xiamen Amoytop Biotech	190	40-50	3	R
Beijing Four Rings Biopharmaceutical	125	40-50	5	R
Zhuhai Essex Bio-Pharmaceutical	130	40-50	5	R,S
Shanghai CP Guojian Pharmaceutical	190	30-40	2	mAb&R
Baiao Pharmaceutical	215	50-60	1	E
Guangdong Techpool BioPharma	390	40-50	1	S,E
Shandong Simcere Medgenn Biopharmaceutical	80	20-30	1	R
Shenzhen Wastin Genetech	80	30-40	2	R
Harbin Pharmaceutical Group Bioengineering	245	20-30	6	R,S
Shanghai Sunway Biotech	100	20-30	2	R
Shandong Kexing Bioproducts	115	20-30	3	R
Shenzhen Neptunus Interlong BioTechnique	315	20-30	3	R,V
Shanghai Wanxing Biopharmaceutical	130	10-20	3	R,V
Shenzhen Xinpeng Biotechnology	80	10-20	2	R
Beijing Yuance Pharmaceutical	45	10-20	2	R
Part 2. Biopharmas with High Growth Potential				
Shenzhen SiBiono GeneTech	60	5-10	1	R
Biotech Pharmaceutical	90	0	1	mAb
Yunnan Waston Biotech	170	0	1	V
Chengdu Hoist Biotechnology	30	0	1	mAb
Changchun BCHT Pharmaceutical	110	0	1	V,S
Part 3. Vaccine and Blood Products Manufacturers				
China National Biotec Group (CNBG)*	9,000-10,000	3,200	>100	V,H,R,mAb
*CNBG Shanghai Institute of Biological Products	1,300	550-600	30	V, H,R
*CNBG Lanzhou Institute of Biological Products	1,500	400-450	45	V
*CNBG Beijing Tiantan Biological Products	1,300	400-450	25	V,H
*CNBG Chengdu Rongsheng Pharmaceutical	515	350-400	9	H
*CNBG Wuhan Institute of Biological Products	1215	250-300	30	V,H,mAb
*CNBG Chengdu Institute of Biological Products	920	150-200	20	V
*CNBG Changchun Institute of Biological Products	1650	150-200	40	V,R,H
*CNBG National Vaccine & Serum Institute	300	N/A	5	V
Hualan Biological Engineering Inc.	455	350-400	9	H,V
Sichuan Yuanda Shuyang Pharmaceutical	445	250-300	7	H
Liaoning Yisheng Biopharmaceutical	210	250-300	4	V
Liaoning Cheng Da Biotechnology	100	200-250	1	V
Shandong Taibang Biologic Products	200	150-200	7	H
Changchun Changsheng Life Sciences	525	100-150	7	V
Shenzhen Weiwu Guangming Biological Products	300	100-150	9	H
Sinovac Biotech	250	115	3	V
Jiangsu Yanshen Biological Technology Holding	440	150-200	6	V
Chinese Academy of Medical Sciences	420	100-150	8	V,R
Shenzhen Kangtai Biological Products	215	50-100	1	V
Shanghai Xinxing Medicine	260	100-150	8	H
Jiangxi Boya Biopharmaceutical	320	50-100	6	H
Zhejiang Tianyuan Biopharmaceutical	220	50-100	4	V
Dalian Hissen BioPharm	320	50-100	4	V
Dalian Jingang-Andi Bioproducts	100	50-100	4	V
NCPC GeneTech Biotechnology Development	300	50-100	3	V,R
Forwell Biopharm	270	50-100	1	V
Zhejiang Pukang Biotech	125	50-100	2	V
Dalian Aleph Biomedical	200	<50	1	V

Source: Top 60 Biopharmaceutical Organizations in China, 2008, BioPlan Associates

** V-vaccine, R-recombinant product, H-hematologic product, mAb-monoclonal antibodies, E-therapeutic enzyme, S-small molecular pharmaceuticals, C-cosmetic