

# biotech focus

## China commits itself to biotech in healthcare

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China has started to impress the world with its advances in healthcare biotechnology, such as the commercialisation of the world's first gene therapy product. At the same time, traditional Chinese medicines (TCM) still play an important role in its healthcare system. The best demonstration of the benefits associated with increased activities of the healthcare industry is the significant increase in life expectancy, which rose from 35 years in 1949 to 72 years in 2005. In several big cities such as Beijing and Shanghai, average life expectancy has exceeded 80 years, a figure that is very close to that of developed countries.

In 2006, the annual output of China's biotech industry reached 60 billion Yuan (US\$ 7.8 billion) [1]. In terms of industry size, China is now the world's manufacturing leader in the annual production of antibiotics, vaccines and vitamins [1]. By April 2006, China had launched more than 35 biotech drugs onto its domestic market [2]. The country's biopharmaceutical industry has been expanding at about 25% annually for the past few years and is poised for further expansion. Independent assessments in 2006 such as the joint publication by the Society for Industrial Microbiology and BioPlan Associates and the biotech scoping mission by UK Trade and Investment (UKTI), a government department, have confirmed that China's biotech industry is maturing [3,4] (Table 1).

### Transforming China's biotech environment

Historically, China's biotech industry was completely based on developing and producing

generic biological products. This changed only in 1989, when the first biotech drug with Chinese-owned intellectual property rights, recombinant interferon alpha 1b, was successfully developed and commercialised in China.

China is a large producer of pharmaceuticals, but this is only in terms of crude chemical drugs, rather than of innovative products. The export of these products generates valuable revenue for many manufacturers, who, however, do not tend to invest sufficiently in research and development, and thereby hampering the prospects for innovation. As a consequence, China is faced with difficulties in developing a productive biotech industry, where innovation is a necessity to compete internationally. Currently, R&D to sales investment ratio is only 2.7% in Chinese companies, which is far below the double-digit R&D to sales ratios of their US counterparts, lying in the range of 15–20%. The difficulties in boosting innovation in the biotech sector are further complicated by a lack of capital and venture capital (VC) support [4].

To change this situation, the Chinese government has introduced a number of policies to kick-start its biotech sector, one of them being the promotion of biotech and biopharmaceutical parks. The focus of these parks is to capitalise on regional skills such as biomanufacturing, TCM, and marine and agricultural biotechnology. China's Five-Year Plans are some of the better known government policy measures, which include promises of official funding for key biotech-related technologies. China's 11th Five-

Year Plan (2006–2010) has the stated objective of achieving 'independent innovation' to transform China from being viewed simply as a cheap source of labour into a nation at the cutting edge of technology. Although this funding has been welcomed, the investment may not be channelled as effectively as it should be because besides the lack of venture capital support, many companies also lack the experience in managing innovative R&D projects.

### Establishing a starting point for innovation

On a global scale, China's biotech sector remains very small and 95% of the Chinese domestic biopharmaceutical market is made up of biogenerics (copies of biotherapeutics developed outside China) [5].

The area where China has an undoubted global lead is in the development of gene therapy, which has benefitted immensely from Chinese scientists who have returned from working in the biotech field abroad. Although at present this leadership is almost exclusively based on the activity of a few companies, such as SiBiono Gene Technology and Shanghai Sunway Biotech, it is a clear sign of China's ability to carry out and commercialise groundbreaking research. Previously, the United States and France were considered to be the pioneers in gene therapy, but serious setbacks, including the death of a trial participant, halted further clinical development projects in these countries.

SiBiono GeneTech Co. Ltd., based in Shenzhen, is responsible for the launch of the world's first commercial gene therapy product in 2003, the recombinant adenovirus encoding human p53, marketed as Gendicine [3]. The product is used for the treatment of head and neck cancers and is widely reported as safe and effective. The development of Gendicine reportedly cost RMB

TABLE 1

**Major Chinese biopharmaceutical companies**

Company	Location	Major products	Website
China National Biotec Group (CNBG)	Beijing, Shanghai, and so on	Vaccines, blood products, diagnostics	<a href="http://www.cnbpc.com.cn">http://www.cnbpc.com.cn</a>
GeneScience Pharmaceutical Co., Ltd.	Changchun	rh growth hormone (GH), G-CSF, GM-CSF	<a href="http://www.genescience.cn">http://www.genescience.cn</a>
3S Bio Inc. (Shenyang Sunshine Pharma)	Shenyang	rh EPO, TPO, G-CSF, IFN a-2a	<a href="http://www.3sbio.com">http://www.3sbio.com</a>
Shenzhen Kexing Biotech Co., Ltd.	Shenzhen	rh IFN a-1b, GH, Insulin, IL-2	<a href="http://www.kexing.com.cn">http://www.kexing.com.cn</a>
Sinovac Biotech Ltd.	Beijing	Novel vaccines	<a href="http://www.sinovac.com">http://www.sinovac.com</a>
Tonghua Dongbao Pharmaceutical Group	Tonghua	rh insulin	<a href="http://www.dongbao.com.cn">http://www.dongbao.com.cn</a>
Hualan Biological Engineering Co., Ltd.	Xinxiang	Blood products	<a href="http://www.hualanbio.com">http://www.hualanbio.com</a>
Anhui Anke Biotechnology Co., Ltd	Hefei	rh IFN, GH	<a href="http://www.ankebio.com">http://www.ankebio.com</a>
Beijing SL Pharmaceutical Co., Ltd.	Beijing	rh G-CSF, IL-11, IL-2	<a href="http://www.slpharm.com.cn">http://www.slpharm.com.cn</a>
Changchun Changsheng Life Sciences Limited	Changchun	Vaccines	<a href="http://www.cs-vaccin.com">http://www.cs-vaccin.com</a>
Hangzhou Jiuyuan Gene Co., Ltd.	Hangzhou	rh G-CSF, heparin sodium	<a href="http://www.china-gene.com">http://www.china-gene.com</a>
Shanghai CP Guojian Pharmaceutical Co., Ltd.	Shanghai	rh TNFR: Fc, IL-11	<a href="http://www.cpgj-pharm.com">http://www.cpgj-pharm.com</a>
Xiamen Amoytop Biotech Co., Ltd	Xiamen	rh GM-CSF, CSF, IL-11	<a href="http://www.amoytop.com">http://www.amoytop.com</a>
Dalian Hissen Bio-Pharm Inc.	Dalian	Vaccines	<a href="http://www.hissen.com">http://www.hissen.com</a>
Shanghai Kehua Bio-engineering Co., Ltd.	Shanghai	Bio-diagnostic kits	<a href="http://www.skhb.com">http://www.skhb.com</a>



Numbers of bio-industry parks in each province in China

Source: *Advances in Biopharmaceutical Technology in China*, BioPlan Associates Inc. and Society for Industrial Microbiology

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80 million (US\$ 9.6 million) in addition to research grants from the government. The clinical development of the product took around 5 years and since its launch, 800 patients, 100 of them foreign patients, have been treated [3].

The approval of a gene therapy product in China caused surprise elsewhere in the world, as the State Food and Drug Administration, P.R. China (SFDA) has a reputation of being cautious in approving novel therapies that do not already exist on foreign markets. Indeed, Gendicine was

only licensed after thorough review and considerable persuasion [3]. At present, Gendicine is only available in China, but SiBiono is keen to market the product abroad. To do so, it is currently undertaking additional clinical trials to satisfy foreign regulatory authorities.

A further boost for gene therapy in China came when SFDA approved Shanghai Sunway Biotech's genetically modified adenovirus H101, the world's first oncolytic viral therapy for cancer [6]. Interestingly, the development of H101 in China was similar to a research approach that was carried out but then abandoned by Onyx Pharmaceuticals, a US biotechnology company. Onyx Pharmaceuticals had been working on Onyx-15, an almost identical virus, but discontinued Phase III trials when its marketing partner decided to leave the project [6]. Shanghai Sunway Biotech is now reported to have bought the rights to Onyx-15, which it will be comparing with H101 in a Chinese trial [6].

### Developing future talent for the biotech sector

At present, gene therapy is the only area where China's biotech sector has been a leader in commercialising an innovative product. However, China hopes to expand its biotech expertise beyond current specialisations through using the skills acquired overseas by its students and industry professionals [4]. Official figures suggest that since 1978, more than 580 000 Chinese students have gone abroad to pursue advanced studies and that 150 000 of them have returned to China [7]. Students who have been educated overseas are sought after by Chinese companies and educational institutes, because recruitment of these people provides their employees with the means of transferring Western practices and knowledge [3].

A number of these returning industry professionals have started their own companies that have been at the forefront of the domestic biotech industry. The success of these companies has been due to these personnel using the industry experience they have gained abroad together with their knowledge of how to operate in the Chinese market. Many are working with academic centers and attempting to commercialise the most promising projects.

China is also preparing a future generation of home-grown talent for the emerging biotech sector. This has been facilitated by the 1981 reorganisation of the higher education system to enable students to pursue bachelors, masters and doctoral degrees [4]. Between 1997 and 2003 the number of undergraduates enrolling in biosciences, biotechnology and biology has more than tripled, with those graduating during this period nearly doubling [4]. In 2002, the Ministry of Education and the National Development and Planning Commission approved the

establishment of the 'National Life Sciences and Biotechnology Professional Talents Training Bases' at 36 universities, designed to encourage students to seek further education in life sciences and biotechnology [4].

### Challenges for China's biotech ambitions

While there is no doubt that China has improved its industrial biotech outlook, it still faces considerable challenges on the way to maturing its biotech sector. Generally, although there have been numerous attempts to introduce official policies to encourage the biotech sector, there remains a general lack of coordination of these initiatives at local and institutional level. This means that although a variety of programmes are in place that are designed to create incentives for those interested in biotech research, it is unclear how these policies are implemented to support companies.

One ambition of China's biotech sector is to commercialise innovative technologies, but as has been noted earlier, only a few organisations have managed this. The continuing major obstacles include the lack of capital markets (such as venture capital) financing growth and heavy tax burdens on new and emerging companies [4].

Even if a company can overcome such immediate obstacles to commercialise a product, in the longer term, it can find the route to the market complicated by ambiguous bidding procedures, illegal copying, poor distribution channels and anti-competitive behavior [4]. Interestingly, there is a growing trend of Chinese companies to use China's intellectual property legislation to fend off domestic competitors [3]. Although this suggests that the intellectual property environment is improving, it highlights further obstacles for those companies examining whether or not to take the biotech research 'plunge'.

An ongoing issue for many companies is that although they may be capable of scientific innovation, they lack the business management skills to build on promising projects. Aside from indecision over committing to long-term investment, there is also a poor coordination of projects. For example, units of the same company can be involved in overlapping research efforts without knowing it. Not surprisingly, many Chinese biotech companies lack appropriate business plans to deliver reasonable profits even if they were to advance a product to market. All too often, companies are stuck at the 'cash-burning' stage with poor prospects for survival. Unfortunately, one-third of China's

biotech companies are presently operating at a loss.

### Outlook

The Chinese government has high hopes of creating a viable biotech sector with the capabilities of taking on foreign industries. At present, many Chinese organisations have their basis in manufacturing and are not in a position to rival the highly experienced leading US and European biotech companies. Whether government policies alone can help transform these Chinese companies into realistic competitors is unclear as they lack management expertise in innovative R&D.

The outlook is better for the newer biotech companies that have been set up, particularly by those who have returned from working abroad. As has been seen in the field of gene therapy, China does have some biotech success stories and it is hoped that these will act as an example to others. In the longer term, China's higher education system has been redesigned to promote the study of biotech-related subjects at universities. This should create a steady stream of graduates to work in the growing number of biotech companies that are being set up.

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