
China's pharmaceutical revolution and emerging contenders

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Abstract The past decade has seen tremendous changes in China's economic, political and regulatory aspects, and have led to an unprecedented consolidation in the industry. These changes have fostered competitiveness among the remaining Chinese manufacturers who increasingly recognise the need to upgrade to enter into the regulated markets and also to have some balance of sales on the domestic market. This paper will examine how seven companies are dealing with the current challenges and what strategies they are implementing to become contenders in the international arena. All have tremendous potential but have inherent problems that must be overcome to emerge as pharmaceutical 'powers'.

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INTRODUCTION

China is centre stage now with a 2005 GDP growth rate of 9.8 per cent with many sceptics now predicting that the economy will overheat. The optimists declare that China is 'at the early stages of one of the greatest industrial revolutions in world history'.¹ The economic reforms initiated by Deng Xiaoping in the early 1980s and renewed after the Tiananmen Incident in 1992 set the drivers again on unstoppable and rapid changes.

The impact on China's pharmaceutical industry has been phenomenal; growth rates of 20 per cent and over the past three years. China is now ranked as the ninth largest pharmaceutical market globally with domestic sales of US \$11.7bn, but still a fraction of the

US \$250bn market. Entrance into the World Trade Organization (WTO) and mandatory Good Manufacturing Practice (GMP) compliance has led to tremendous consolidation in China in the past five years. The heightened competitiveness within China has resulted in the development of new strategies to respond to these changes. In addition, increased investment into the industry by both foreign and domestic companies has given the recipients of capital a unique opportunity to execute the new strategies.

This paper will discuss how the economic and regulatory changes have impacted the Chinese pharmaceutical industry by examining how seven Chinese companies have positively responded to these changes and, consequently, how they have the potential to emerge as world-class contenders in the international arena. These companies were selected for growing revenues/profits, aggressive business strategies, strong leadership and above-average investment in R&D.

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Several of the companies have lucrative supply arrangements with foreign firms and additional ongoing discussions with foreign companies on partnerships/supply arrangements that could lead to major increases in profitability. But each also has weaknesses that could prevent them from becoming international contenders; the determining factors will manifest themselves in the next 3–5 years.

Certain potential 'greats' have been omitted; that is Shanghai Pharmaceutical Group due to ongoing reorganisation, Shandong Xinhua and Lukang due to recent retirement of their CEOs and Xinchang, due to their recent relocation of manufacturing facilities. Also excluded are North China Pharmaceutical and Northeast General Pharmaceutical that are former 'key' state enterprises within the top 20 pharma companies in terms of sales but that have very narrow profit margins (± 3 per cent) and that are still reliant on state support.

This is telling that these emerging companies do not have similar backgrounds/development, as the selected companies include both private and state-owned enterprises (SOEs). Private companies have many inherent advantages over SOEs but in the changing pharma environment, there is no single paradigm for success, but these promising emerging companies do share similar goals/strategies:

1. Develop strong managerial class via outside recruiting and enhancing/enriching skills of in-house staff.
Recruitment of overseas Chinese with pharmaceutical experience in the West.
2. Increased expenditure on R&D for new products and new formulations.
Investment in technological improvements to reduce cost of core products.
3. Strengthen regulatory departments and target USA/European markets.
4. Develop long-term supply arrangements/cooperation with USA/European companies.
5. Increase/enlarge marketing department and capabilities/skills.
6. Attract overseas Original Equipment Manufacturer manufacturing.
7. Seek private placement and venture capital/bank investment.
8. Invest in and seek regulatory approval for finished dosage forms (FDFs).

China, unlike Korea and Japan, began to encourage foreign investment in selected industries, including pharmaceuticals, in the early 1980s. The first pharma joint venture (JV) in China was formed in 1980 by Otsuka in Tianjin with China National Pharmaceutical Corporation. Initially, the Chinese government required pharma JVs to be majority owned by the Chinese, but the regulations were continuously changed and at present foreigners can establish wholly owned companies and can invest in SOEs as well.

INVESTMENT IN THE PHARMACEUTICAL INDUSTRY

Multinationals have been increasing their Chinese investments; 2006 announcements include Astra Zeneca's intention to invest US \$100m into an R&D centre. Novartis is breaking ground for a manufacturing and R&D centre in Jiangsu province, an US \$83m investment. This continuous investment has had a positive impact; foreign companies have introduced current GMP standards, regulatory knowledge and western managerial expertise. Foreign companies are also keenly looking for acquisition prospects. DSM acquired 7.6 per cent of NCPC in 2004, Bausch and Lomb acquired 55 per cent of Shandong Chia Tai Freda Pharma Group, and Teva acquired a 45 per cent stake in Tianjin Hualida Biotechnology Co Ltd through its Sicor acquisition and then subsequently increased its equity stake to 60 per cent in early 2006.²

The growth of the pharmaceutical industry as well as the government's opening up of SOEs to foreign investment has resulted in some new opportunities for not just pharmaceutical companies but also for

non-pharmaceutical-based companies, venture capitalists and equity banks to inject additional capital into this attractive industry. Examples include Warburg Pincus investing US \$100m along with CITIC Capital Markets into Harbin Pharma Group (Holding) Co Ltd. Goldman Sachs invested US \$40m into Shenzhen Neptunus, Morgan Stanley has shares in Huahai Pharma, and both Chinese venture capitalists and USA-based venture capitalists are also seeking investments. China Ding Hui Fund (a Chinese venture capital firm) is attempting to take a stake in Shanghai Pharma Group along with China Resources.

In addition, several non-pharma-based, cash-rich Chinese conglomerates are active; Zhejiang-based Holley Industrial Group (a privately held group with businesses in metres, controls and telecommunications) has begun investing in the pharma arena with majority shares in Kunming Pharma and Wuhan Jianmin.

Computer giant Lenovo Holdings' investment arm (Hong Yi Investment Management Company) took a 31 per cent stake in privately owned Simcere Pharmaceutical Company. The investment will enable Simcere to strengthen its R&D and marketing, and Hong Yi intends to have Simcere listed on foreign stock markets within the next three years. Beijing-based Founder Group (an IT company) began investing in pharma in 2001 through the acquisition of Southwest Synthetic Pharma and then acquired Chongqing Daxin and Yantai Zhongzhou.³

Certainly by the mid-1990s, China's pharmaceutical industry had already been positively impacted by mandatory GMP enforcement, changes in the State Drug Administration and entrance into the WTO, but this growing trend of outside capital has enabled the recipients to make unprecedented investment in improving facilities, hiring pharmaceutical experts and increasing R&D capabilities.

Still a note of caution of the longevity of some of this investment is exemplified by Shanghai Worldbest. Worldbest had been one

of the most active in pharma investments over the course of the past four years making large investments into Beijing Pharma Group and Shanghai Pharma Group. In February 2006 after announcements on corporate governance issues and financial problems, the State-owned Assets Supervision Administration Commission of China (SASAC) appointed China Resources Group to take over some of Worldbest's pharma stakes. Given the weaknesses of Chinese companies with respect to corporate governance issues, it is too early to predict the viability of the above-mentioned investments.

RETURN OF OVERSEAS CHINESE

The return of Chinese nationals to the country is another contributing factor for many of the strong pharmaceutical companies in China. The USA and China have long had a number of academic associations that have communicated on pharma developments for some years. The Sino American Pharmaceutical Association (SAPA) boasts a membership of over three thousand Chinese American scientists working at USA-based pharma firms. The SAPA newsletter and frequent seminars disseminate knowledge between the Chinese and USA pharma communities. But it is the growing 'reverse brain drain' that is fuelling the development of China's pharma industry.

One model success story that has attracted quite a bit of publicity is the success of Wuxi Pharmatech, an outsourcing firm started in 2001 by Dr Ge Li with revenues of US \$21.5m in 2005. Dr Ge, who received his PhD from the USA and subsequently worked in the USA for years, has combined his Western expertise with the lower cost of Chinese scientists, who receive 'rigorous training to bring them up to speed', to spearhead a company that already has established relations with leading USA firms such as Merck. Other Chinese expats have founded StarVax and South Gene Technology in China.⁴

Returning Chinese expatriates are also being lured by Chinese companies who cannot afford the salaries of the West but can offer them an opportunity to assist in transforming companies to world-class competitors and, in many cases, offering equity shares in the company. Hisun has several overseas Chinese on its staff and Fosun Pharma has recently hired several former Ivax employees in its formulation department.

STATE-OWNED ENTERPRISES

One of the most interesting aspects of the transformation of the pharmaceutical industry is that it is not just the private companies that are emerging as world contenders but even several SOEs are taking advantage of new opportunities to revitalise and revamp.

Harbin Pharmaceutical Group exemplifies the potential of a SOE to modernise despite the burdens that are typically associated with SOEs, that is bureaucratic, financially burdened and unmotivated. The Group has focused on the domestic rather than export market, and its 'Hayao' brand was voted the most valuable pharmaceutical brand in 2005. Sales were over US \$1bn in 2005 and a mere 15 per cent of its products were exported. The Group has established a state-of-the-art finished dosage facility (Sanjing) that has not only engaged in production of its own brand products, but also entered into contract manufacturing for several multinational brands. Its domestic salesforce is one of China's largest, and as is the case of Yangtze River Pharma and Shanghai Fosun Pharma, the Harbin Group has offices in all provinces, its own distribution company and retail outlets.

The Group's general Manager, Mr Jiang Linkui, has also stated the Group's future intention to invest in the regulatory arena and to have some of its core Active Pharmaceutical Ingredients (APIs) approved by Food and Drug Administration (FDA). They have expanded their regulatory department and are filing a number of European Certifications of Suitability (CoS)

in 2006. Located in the northeastern city of Harbin, the company's profile was enhanced by the 2004 announcement of Warburg Pincus and CITIC Capital Markets of a US \$200m investment for a 22.5 per cent stake in Harbin Group. Mr Jiang announced at that time that the funding would provide 'the necessary capital to leverage both domestic and international opportunities'.⁵

OTHER COMPANIES

SJZ Pharma Group

SJZ Pharma Group is a good example of the increasing importance on team building and cultivation of a Westernised managerial team. The Group was formed in the mid-1990s via the merger of five SOE API/FDF facilities, all of whom were struggling due to declining profits. The Group has implemented a two-pronged strategy of expanding its domestic market share and increasing its exports. It has spun off some of its non-core business (its infusion manufacturer, SJZ No. 4 was sold to management and employees in 2004), increased its R&D spending from 3 to 6 per cent and enlarged its regulatory department. The Group also made a large investment by building a new 10,000 metric tonne capacity penicillin G factory in Inner Mongolia. The Group's CEO, Mr Cai Dongchen, stated that this move would ensure the Group's continued ability to have a low cost base for one of its core products. Mr Cai has also offered educational subsidies to his management team and initiated a rotational system whereby top managers spend time at each of the production sites. One of the Group's subsidiaries, China Pharmaceutical Corporation, is listed on the Hong Kong stock exchange and this has enabled the Group to increase their profit margins on commodity API sales by lowering production costs through technological improvements. All of the sites are being renovated with new equipment, and the company is expanding its product portfolio outside its traditional anti-infective core.⁶

Hisun Pharma

Hisun Pharma is the showcase of how a SOE can become an international player. With 12 FDA-approved APIs, Hisun was one of the earliest Chinese companies to make substantial investments in the regulatory arena. Although 40 per cent is still owned by the Zhejiang government, Hisun is also one of the few domestic factories that are primarily producing for export (80 per cent). Hisun strategy is to pursue more contract manufacturing particularly in the low-volume/high-value APIs, as well as to seek regulatory approval on FDFs and has also invested in a new FDF facility to do both solid orals and injectible products. In June 2006, Alpharma announced a joint production agreement for vancomycin with Hisun, which involves building a plant at Hisun (to be owned and operated by Alpharma).⁷ Hisun is also the manufacturing partner for Eli Lilly's capreomycin.

Hisun is currently restructuring with the goal of further reducing state ownership. The restructuring has diverted its management from full focus on its core business and first quarter 2006 revenue was up 17 per cent but earnings declined. Still, with its new dosage facility coming up and expansion into the domestic market (via the acquisition of a distribution company), Hisun will continue to be China's leading supplier to the regulated market.

Huahai

Huahai Pharma illustrates the power of the Chinese entrepreneur and how investment in the correct segments leads to rapid growth. Founded by Mr Chen Baohua and Mr Zhou Minghua in 1989, the company listed on the Shanghai Stock exchange in 2005 and achieved sales of US \$70m (from US \$43m in 2003). The two co-founders own about 50 per cent of the stock, while the other ten shareholders are primarily mutual funds and institutions (including Morgan Stanley International Fund). Huahai has invested more than US \$50m in expanding its R&D

capability, expanding API capacity, establishing a new finished dosage facility and also in its sales and marketing. The new API site will consist of 40 manufacturing bays, to be completed by the end of 2007. Six per cent of its revenue is reinvested in R&D (vs the typical 2–3 per cent of other Chinese factories).

As China's leading manufacturer of ACE-inhibitors (used to treat high blood pressure), Huahai is expanding into antihypertensive, antidepressant, diabetes and also Alzheimer's and Parkinson's. Similar to Hisun, Huahai has targeted the international market that accounts for 90 per cent of its sales. The company is also planning to have some of its finished dosages approved by USA/EU authorities. Huahai attributes its success and growth to its 'open minded' management, in-house R&D, regulatory department and an ability to make quick decisions. The company employs about a dozen overseas Chinese personnel in quality assurance, business development and sales, which has enabled the company to 'bridge the gap in regulatory knowledge and provide product development experience'.⁸

Yangtze river pharmaceutical company

Yangtze River Pharmaceutical Company is a very interesting pharmaceutical case. It is privately held and has a 'rags to riches' history. It was started by the current CEO in 1971 and has ranked in the top five in pharma sales and profits in the past five years where sales have grown from US \$17m in 1994 to over US \$1bn in 2005. It is a fully integrated company producing APIs, finished dosages, and has its own distribution companies concentrating on the domestic market with sales of almost 90 per cent in China. Having made investments in the past few years in new facilities (both API and FDF) in Shanghai, Jiangsu and Sichuan, Yangtze River has no foreign regulatory approvals and a very small export business. With seven manufacturing sites and its healthy profits, the

company has only just begun to focus its attention on the international market, and the future potential is immense.

Zhejiang Hengdian Group

Zhejiang Hengdian Group has a similar early history. It was founded in 1975 by a young man in the village of Dongyang and the company was originally engaged in silk manufacturing. The company expanded into pharmaceuticals by acquiring several old, financially distressed SOEs and, by 2005, the total turnover of the Group was US \$1.7bn. The company has continued to reinvest into its three core API facilities, but has also established an R&D centre in Chengdu and is building an R&D facility for formulation R&D in Shanghai. Hengdian pharmaceutical companies have several toll manufacturing arrangements with multinational firms. The company attributes its success to its managerial team, its emphasis on service and its follow-up with its foreign customers.

Shanghai Fosun group

Shanghai Fosun Group was founded in 1992 by four friends with an initial investment of US \$4,500 starting with clinical diagnostics on a hepatitis A drug. The Group has diversified into retail, securities underwriting, real estate and steel in addition to pharmaceuticals. It is in the Top 500 companies in China and the second largest privately owned company after Lenova. The Group has invested in pharma via an aggressive acquisition strategy, owning five manufacturers, majority stakes in an additional six and minority holding in a further five manufacturers. This is an extremely dynamic, well-run company with motivated management and cash for investment. They have a strong distribution company, 1500 retail pharma outlets and over-the-counter (OTC) shops in over 3000 supermarkets.

Fosun signed an agreement in March 2005 with China Europe International Business School (CEIBS), whose MBA programme is rated number 1 in Asia, to have CEIBS

provide training and support with tailor-made programmes for Fosun's middle and senior managers. CEIBS will also provide marketing/strategic consulting services to assist Fosun to achieve its goal of becoming one of China's top three pharmaceutical enterprises. The company is also seeking overseas investments and is focused on developing their own branded Fosun line internationally.⁹

Neptunus Group

Neptunus Group was founded in 1989 and, while initially best known for its OTC products and extensive retail chain (NepStar) has been heavily investing in new API facilities and looking to increase its exports to the regulated markets. Neptunus is concentrating on four core segments: functional foods, traditional Chinese medicines, pharma APIs and biotech products. In the biotech arena, they have two new plants under construction, a vaccine manufacturing unit and a blood products factory. They are continuing to invest in the upgrade of logistics for their wholesaling companies and are the major franchisee for Medicine Shoppe.

Challenges

At present, China's pharmaceutical industry is far stronger than it was a decade ago. The first wave of plant consolidations and reorganisations resulted when the government transitioned from a planned to a market economy and withdrew its subsidies for failing plants. The second wave of consolidation/acquisition began in 1998 with the SFDA issuance of compulsory GMP guidelines. Thousands of factories were unable to make the estimated US \$3–4m investments to meet the new guidelines and were forced to close or were acquired by stronger companies. In 2003, China entered WTO and China's already competitive domestic market was now faced with the additional threat of foreign imports when import tariffs were reduced from 14 to 3 per cent. This was additional impetus for factories to upgrade equipment

and product portfolios to withstand the heightened competition. Beginning in 2000, China opened even SOEs to foreign investment, and there has been continuous capital flow into the pharma industry from both domestic non-pharma-based Group Companies, as well as foreign investment banks, and both domestic and foreign venture capitalists. Clearly, there is no one single model for the emerging giants of China's pharmaceutical industry nor is it clear which of the companies will be able to sustain present growth and remain competitive in the international arena.

Chinese companies still have a number of challenges that must be met.

Many of the 'success' stories at present depend on a few core individuals in the firm, and a corporate culture with a well-established management system will need to be implemented to ensure sustained future success. Many Chinese companies tend to hire employees from their local area and this limits severely the recruitment pool. Lastly, to date, no Chinese company has hired a Western non-Chinese person with extensive pharmaceutical experience to serve on their management, business development, production or marketing teams. 'Outside hires' in China still mean overseas Chinese. There are also external problems that are emerging with the rapid economic developments that the industry will have to contend with.

Narrow product portfolios can also become a liability in an increasingly competitive field against Indian companies as well as the more established European firms. China remains a 98 per cent generic market with little new product development investment.

For companies such as Harbin, Neptunus and Yangtze River who have concentrated on the domestic Chinese market, it may well be that ultimately domestic sales and not international will remain their focus. Fosun has a strategic plan but its implementation will require a significant cash investment and a very strong regulatory department as well as sales and marketing that they do not yet have.

Consolidation in the industry has been ongoing for more than a decade. But consolidation inevitably leads to unemployment and the potential for social unrest. The Ministry of Public Security officially announced in 2005 that social unrest incidents were up 6 per cent. In the pharma arena, early retirement is encouraged and the traditional basket of benefits, healthcare, schooling and housing for employees has been reduced and/or eliminated.

The Chinese government has been enhancing its environmental laws and stepping up enforcement. Still the recent benzene incident in Harbin coupled with the demonstrations in Taizhou regarding pollution from a pharma factory clearly indicates that severe problems still exist. As factories are forced to invest to comply with the new regulations, their costs also rise.¹⁰

Over the course of the past several years, China has continued to strengthen its intellectual property (IP) legal framework. Milestones include extending patent protection to 20 years from the date of filing to patent linkage and data protection. The State Food and Drug Administration (SFDA) now also requires that Chinese applicants for clinical studies on new drugs submit a letter of guarantee that their process is non-infringing.

The recent ruling by China's State IP office, which overturned the 2004 revocation of the Pfizer Viagra patent, has been regarded positively as demonstrating 'China's commitment to creating an effective patent-protection environment. IP concerns are still a paramount issue for multinational pharmaceutical firms.¹¹

With respect to patent issues, Chinese firms do not have legal departments specialising in patents. Typically, a firm will do an internet patent search but this does not give access to submarine or polymer patents and, hence, limits the Chinese's ability to develop and/or challenge existing patents and an inability to issue non-infringing statements to potential API customers.

Chinese factories have, with few exceptions (ie Hisun), belatedly recognised the importance of entering into the regulated markets through drug master file (DMF) filing. Regulatory departments only recently sprung up as extensions of Chinese GMP offices mandated to be established by the SFDA. Still China has not invested in the training of their regulatory departments in terms of participation in Western GMP/FDA/EDQM seminars. The greatest challenge for the Chinese is whether they will be willing to make the investments needed for strong regulatory departments as well as for ongoing cGMP training.

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