China Partnering 2012: Driving Future Innovation

A four-year analysis of strategic partnership activity in China's pharmaceutical industry 2008-2011

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China Partnering 2012: Driving Future Innovation

ChinaBio® LLC provides consulting and advisory services to Western life science companies seeking to enter the China market directly or through strategic partnerships or acquisition. This paper presents an analysis of the trends and activity of strategic partnership transactions in the pharmaceutical industry in China using ChinaBio's proprietary data. For more information, please see www.chinabiollc.com or contact us at info@chinabiollc.com.

The 2012 London Olympics brought back vivid memories of China's impressive demonstration of its rising economic power four years earlier in Beijing. Since then, China has continued its rapid ascent while the rest of the industrialized world struggles with the aftermath of the great recession.

China's economic success also brings significant challenges: with increases in prosperity come the rapid rise in labor costs, making China less attractive to traditional labor-intensive manufacturing businesses. As the coastal cities have become too expensive for the low-margin labor-intensive industries, a large number of factories have moved inland or relocated to neighboring countries with more attractive cost structures.

To foster its continued growth, China has recognized the need to move up the value chain and invest in industries with higher growth potential and more lucrative margins. China's 12th Five Year Plan specifically identifies life science ("biotechnology") as one of its top industries to stimulate growth. Additionally, local governments, facing the exodus of tax-producing companies and seeking new sources of revenue, are also keen to offer incentives, grants, and to build specialized industrial parks to attract life science companies.

Healthcare spending in China is also increasing tremendously due to an aging population, rising incidences of chronic diseases, and the government's determination to provide healthcare to each of its citizens. As a result, China's pharmaceutical industry has seen an unprecedented level of growth: in just four years, China climbed from #9 in 2007 to become the #2 pharmaceutical market in the world in 2011, with an average annual growth rate of 22%. In contrast, the global pharmaceutical market has only seen 4-6% growth during the same period.

The boom of the pharmaceutical industry in China is fueled by a variety of internal and external factors, including the government's focus on innovation, the China domestic companies' need to transform themselves, and the Western pharmaceutical companies' desire to further expand their market share and profit margins in China.

The Chinese government, determined to build a world-class life science industry that rivals that of the West, is funneling huge sums of money to encourage innovation and R&D in the industry. In 2011, China released its 12th Five Year Plan that specifically committed more than $200 billion USD for new drug development and healthcare reform. In particular, there was a call to develop the domestic industry through consolidation of the over 7,500 companies and the creation of novel therapeutics and healthcare technologies in China.

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Pressure from the government to drive generic drug prices lower has also forced domestic pharmaceutical companies to shift from selling cheap generics and higher-priced branded generics to producing and selling premium priced innovative drugs. In order to fill their pipelines quickly with high-value products and reduce their development risks, China pharmaceutical companies are increasingly looking outward to in-license proven technology from the West. This also mitigates the risks associated with devoting significant resources to much lengthier and costly in-house development programs.

As the Western pharmaceutical industry slows down, multinational pharmaceutical companies (MNCs) are eager to jump into the high-growth Chinese market and find new consumers for their drugs. In the past four years, the China market has been rewarding to Western MNCs, as the growth rates for the top ten MNCs in China ranged from 15-32%, with an average annual growth greater than 27%.

To maintain the high growth rates and expand into new geographic and therapeutic markets, well-established Western MNCs are increasingly seeking out Chinese partners to provide regulatory expertise and market access. Development stage companies facing dwindling funding in the West are also looking to China partners to provide lower cost manufacturing and development support, as well as fund the clinical development expenses in China and potentially provide financing through either upfront and milestone payments or direct equity investment.

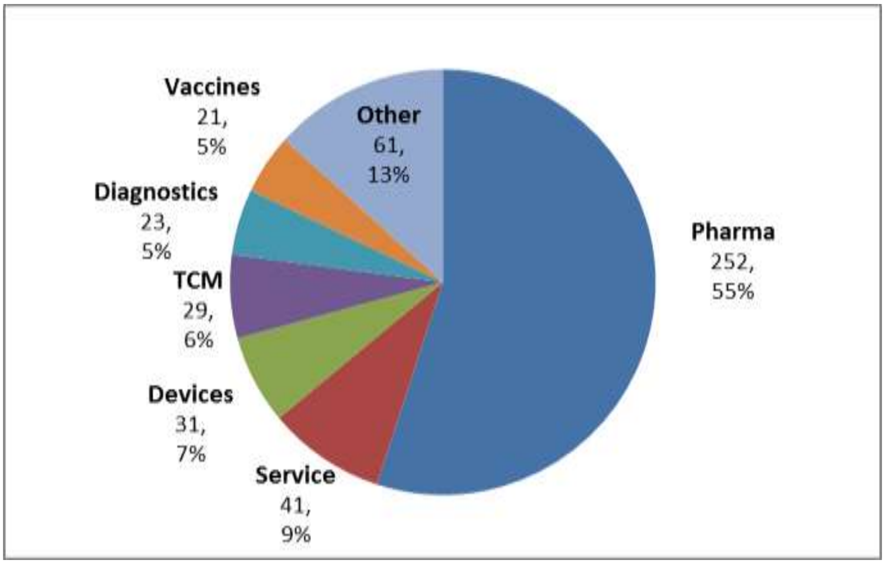

Figure 1. Major life science deals in China, 2008-2011 (Source: ChinaBio)

As a result, the China pharmaceutical industry has been very busy doing deals. As shown in Figure 1, analysis of the 458 major life science M&A, strategic alliance and partnership transactions in China between 2008 and 2011, indicates that more than half of these deals were in the pharmaceutical sector. Other active sectors included contract services (CROs and CMOs), medical devices, diagnostics, traditional Chinese medicine and vaccines.

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Increasing Cross-Border Strategic Alliance Activity

In the past few years, there has been a rapid growth in the number of cross-border partnership deals and joint ventures in the Chinese pharmaceutical industry. As shown in Figure 2, analysis of major partnership deals, mostly involving innovative drugs (drugs that have not been marketed in China, including novel drugs and improved generics), and major joint ventures from 2008-2011 show a predominance of cross-border deals. This trend is a reflection of the Chinese companies' appetite to enter into the higher-margin innovative drug market through acquiring Western technologies, drug candidates, and products.

Major Pharmaceutical Deals in China

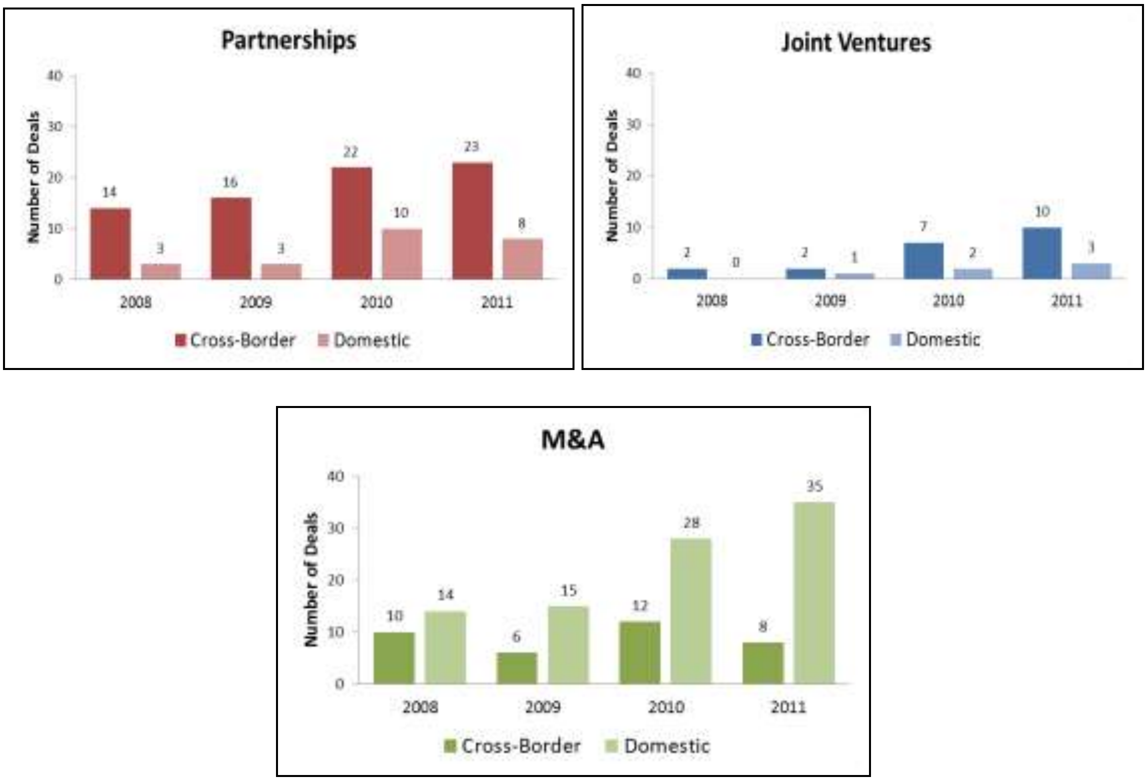

Figure 2. Cross-border and domestic transactions, 2008-2011 (Source: ChinaBio)

Cross-border partnerships and joint ventures also provide the Western companies a cost-effective and efficient way to enter the China pharmaceutical market. The increased activity in cross-border joint ventures reflects the trend that foreign companies are increasingly willing to directly work alongside their domestic partner and share development risks and financial rewards. It also reflects the increasing confidence Western firms have with China domestic companies and jurisdictions as well as China's IP protection.

Since 2008, M&A activity is also increasing significantly among China domestic companies (see Figure 2). As the profit margins of China domestic companies have narrowed due to pricing pressure and competition, consolidation has become a necessity for traditional generic companies to stay competitive. It is also increasingly common for Chinese companies to expand into new therapeutic areas, acquire new sales channels and distribution networks, and/or manufacturing capabilities through M&A activities. This clearly reflects the trend in the Chinese pharmaceutical industry for consolidation and the relative ease of striking M&A deals between two domestic companies, as opposed to the more complex nature of cross-border deals.

Even though cross-border M&A has not kept pace with domestic activity, the recent acquisition of Nanjing C&O Pharmaceuticals by Japan's Shionogi may signify the beginning of the increasing trend for cross-border M&A deals in China. Comparing to other MNCs, Shionogi is a relatively late-comer to the China market. The acquisition of a Chinese company with highly profitable products, established regulatory expertise and distribution network enables a newcomer such as Shionogi to rapidly establish a presence in the highly competitive China market.

Academic Partnerships for Innovation on the Rise

Contrary to the West where pharmaceutical companies are constantly scouting for academic assets to bring into commercial development, in China, the values of academic-industry alliances have just started to become recognized.

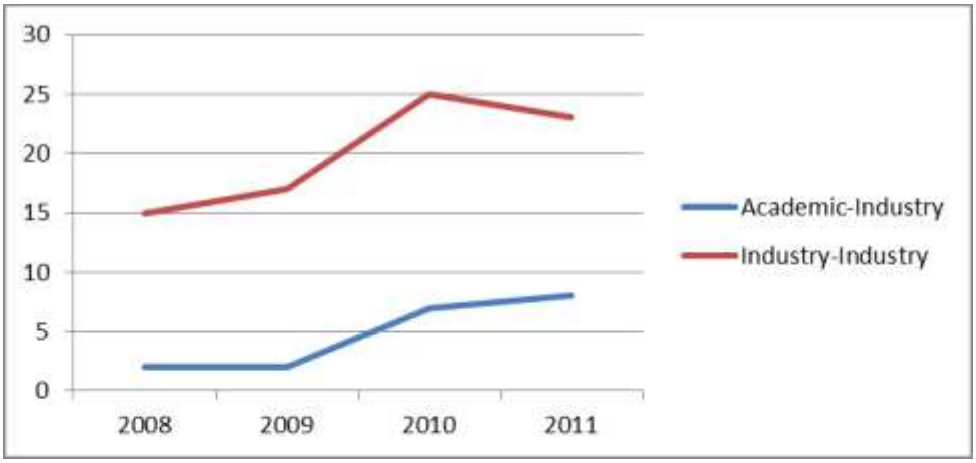

Figure 3. Academic and industry partnership deals, 2008-2011 (Source: ChinaBio)

As shown in Figure 3, prior to 2010, there were only a few notable academic-industry deals relating to drug development established each year. Coinciding with the boom of industry partnership activities in 2010, academic-industry partnership deals have also increased significantly, accounting for more than 20% of total deals in 2010 and 2011.

While academic-industry partnerships between Chinese pharmaceutical companies and academic institutions remain sparse, collaborations between Western pharmaceutical companies and prominent Chinese academic institutions and hospitals are on the rise. In the past few years, a number of Western MNCs have established broad academic-industry

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collaborations, where the MNC funds the academic research, often with an option to in-license the technology at a later stage.

Notable examples include the Pfizer-Peking University partnership on a broad range of disease indications, the partnership between Sanofi-Aventis and Shanghai Institutes for Biological Sciences (SIBS) for cancer drugs, and the joint R&D center established by J&J and Tianjin Medical University. Several other Western MNCs including Roche, Bayer and Genzyme have also established collaborations with academic institutions in China.

Innovation through Acquisition of Western Technologies

As China's pharmaceutical companies transform from traditional generic manufacturers to the more lucrative innovative drug category, a large number of them are developing a two-prong approach for their product development strategy: acquiring drug candidates or technologies with potential to reach the market within a short timeframe (generally 3-5 years), as well as establishing in-house development programs to meet longer-term growth goals.

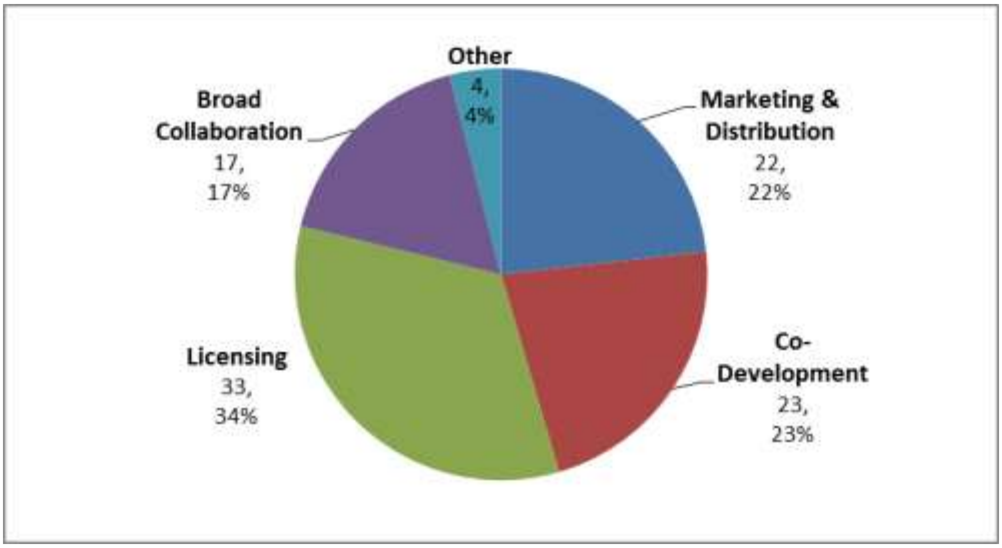

Figure 4. Pharmaceutical partnerships by deal type, 2008-2011 (Source: ChinaBio)

This trend is reflected by the analysis of 99 major pharmaceutical partnership deals from 2008-2011 (see Figure 4) showing partnership deals being predominantly licensing (34%) and co-development (23%), as opposed to the more traditional marketing and distribution deals (22%) that dominated the landscape just a few short years ago.

The widespread occurrence of licensing and co-development deals also reflects an increasing trend of bi-directional traffic with Western companies partnering with Chinese companies, and Chinese companies acquiring innovative Western technologies. Through partnership with a China domestic company, Western companies are taking advantage of the experience and

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resources of their China partner to expedite and de-risk their entry into a market than can be both rewarding and challenging.

Similarly, Chinese companies have recognized the benefit of leveraging the research and development investment made by their Western partners to short-cut the lengthy development time and reduce the costs normally associated with Innovative drug development and approval in China. Armed with large sums of investor money and management teams with significant Western experience, pre-commercial stage innovative companies such as Ascletis, Hua Medicine, and BeiGene have all brought Western assets into their product development pipeline as a key component of their business strategies.

Partnering Activities Shift toward Development Stage Assets

The traditional China pharmaceutical industry has been based on the manufacturing of chemical APIs (active pharmaceutical ingredients) and generic drugs. These usually have been previously approved in the West and/or in China, so there is little regulatory risk involved.

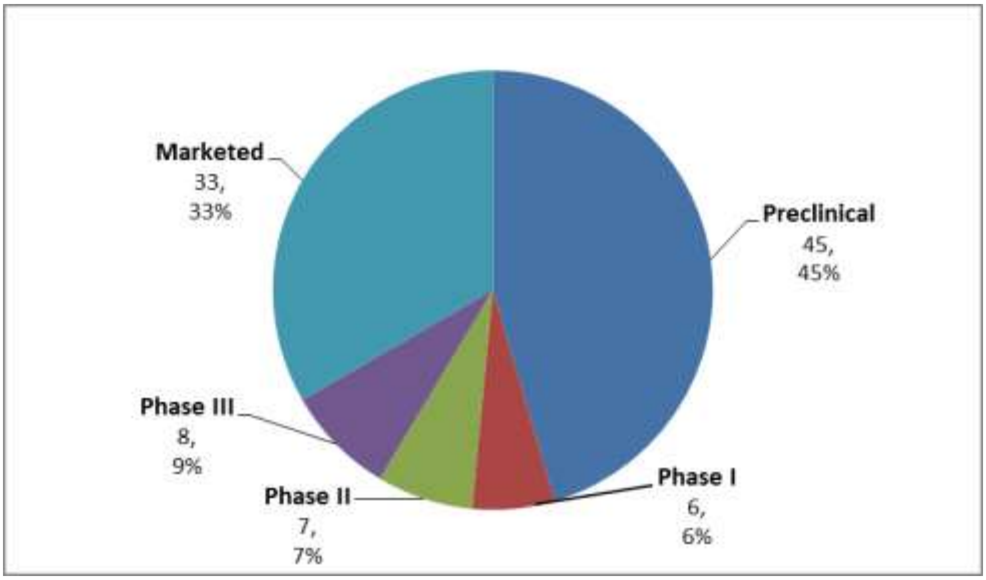

Figure 5. Major partnerships by development stage, 2008-2011 (Source: ChinaBio)

While approved products have previously been the most attractive assets to partner in China, in the past few years, partnership activities in China have shifted toward earlier stage assets that are still in preclinical and clinical development and may not have yet been approved anywhere in the world. As shown in Figure 5, 67% of the partnering activity is in preclinical/clinical-stage assets, clearly signifying a paradigm shift in the attitude of China pharmaceutical companies toward risk-taking, moving toward a more Western-style R&D model, often through partnership with a Western company.

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This trend is evidenced by the fact that more than 75% of the major partnership deals between 2008 and 2011 in the China pharmaceutical industry are cross-border, and that three quarters of these deals involve drug candidates that are still in preclinical or clinical stage of development (see Table 1). This trend indicates that China companies are becoming more comfortable with the development risks, and the recognition of the cost-benefit of acquiring a promising asset at an earlier development stage. It also indicates the increasing confidence of Western companies in their Chinese partners' ability to conduct and execute the preclinical and clinical studies necessary for SFDA approval or even to be included as one of their global development partners.

Table 1. Cross-border vs. domestic partnerships by development stage, 2008-2011

	Preclinical	Phase I	Phase II	Phase III	Marketed	Subtotal
Cross-Border	39	4	6	8	19	76
Domestic	6	2	1	0	14	23
Total	45	6	7	8	33	99

(Source: ChinaBio)

As the large MNCs have routinely included China as a part of their global clinical development programs, Chinese domestic companies have also become increasingly interested in establishing partnerships with Western companies for clinical-stage assets. In exchange for the China rights, the China partners are often willing to cover the costs of conducting additional preclinical and clinical studies to fulfill the SFDA regulatory requirement. These partnerships offer Western companies the benefit of leveraging the China partner's resources and experience for expedited entry into the China market.

For example, Western companies are increasingly targeting late Phase II to strike a deal in order to include their China partner in the global Phase III trial. This can provide the China partner with a faster, less costly path to approval in China, as the SFDA allows the China data from the global Phase III trial to be used for the approval of an imported product. This also provides the additional advantage to the Western partner that the China partner should cover a portion of the global Phase III trial costs.

Key Therapeutic Areas for Partnership Activities

As one of the most populous countries in the world, China is facing the significant challenge of providing healthcare to its rapidly aging population. Chronic conditions such as cancer, cardiovascular disease, diabetes, and aging-related neurological diseases are on the rise. A recent report by the China Ministry of Health indicated that 85 out of every 100 deaths are caused by chronic disease, making this a major healthcare concern in China.

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Not surprisingly, one of the most active areas for partnership in China is oncology, with approximately a quarter of the pharmaceutical partnerships focusing on the treatment of a variety of different cancers (see Figure 6). Oncology is also a therapeutic area rich with innovation, with a relatively straightforward regulatory path, and the potential to be highly profitable. As cancer is considered a terminal disease, Chinese families often devote significant financial resources to save the lives of their loved ones, and are willing to pay out-of-pocket for better treatment options utilizing innovative drugs.

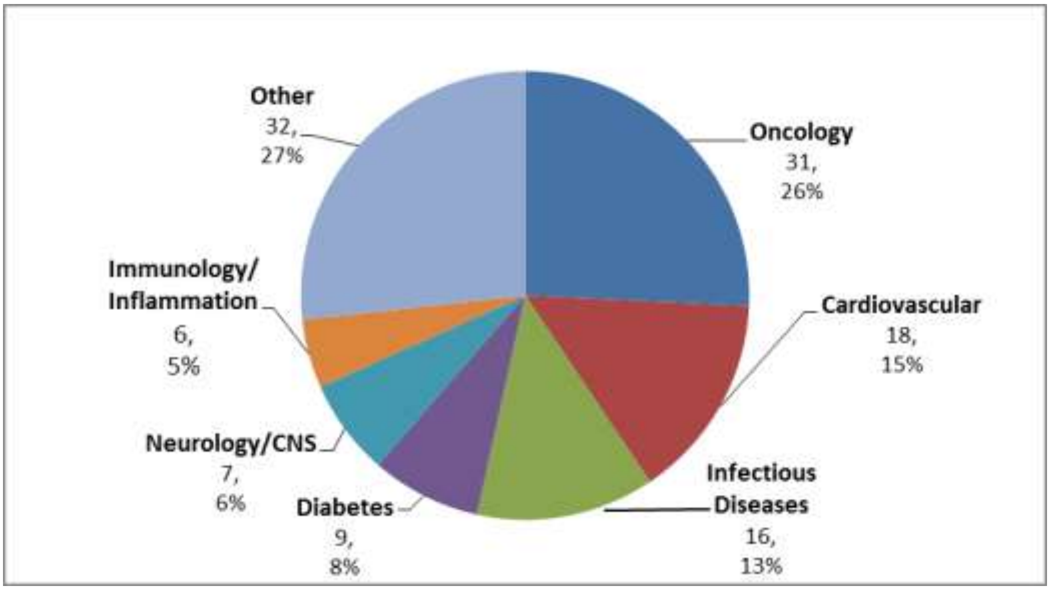

Figure 6. Partnerships by therapeutic area, 2008-2011 (Source: ChinaBio)

Several recent partnership deals in the oncology space reflect the interest of China pharmaceutical companies in acquiring oncology drug candidates that have the potential of treating a large patient population in China. The partnerships between Simcere and BMS on a preclinical MET/VEGFR-2 inhibitor, and between BeiGene and Janssen on several clinical stage oncology drugs reflect this trend.

With the aging population and adoption of Western lifestyle and diet, cardiovascular diseases and diabetes have also become a large and growing concern in China. It is estimated that more than 150 million people in the country have hypertension, and stroke is being diagnosed at a rate of almost 220 patients per 100,000 people per year. As the main cause of long-term disability in adults and the second highest cause of deaths, stroke and cardiovascular diseases have created a large void to be filled by pharmaceutical companies. Similarly, over 90 million adults in China are carrying the burden of diabetes, and an even larger number of Chinese are pre-diabetic. China now has the largest population of diabetes patients in the world, making it an extremely attractive market for MNCs and China domestic companies.

Some of the more notable cross-border deals in the cardiovascular disease space involve the NYSE-listed Simcere Pharmaceuticals, which has entered a co-development partnership with BMS to develop cardiovascular drugs in China. Luye pharmaceuticals, another innovative

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company, also entered into a partnership with one of South Korea's largest pharmaceutical companies, Dong-A, to develop an oral DPP-IV inhibitor for treating type II diabetes for the China market. This deal continued the path of Luye's entrance into the diabetes market after its acquisition of Sichuan Baoguang Pharmaceutical and its diabetes medicines.

China's rapid transformation from a poor developing country into an economic superpower means that it is still in the process of building the infrastructure enjoyed by the wealthy developed countries, especially in the areas of public health. Less than ideal healthcare conditions in the rural areas of China, and the lack of public health awareness of some of its 1.3 billion citizens, coupled with the dense population, make China a hotbed for infectious diseases including hepatitis and multiple-drug resistant tuberculosis (MDR-TB). The Chinese government has made controlling and eradicating infectious diseases one of China's top national priorities. Partnership activities closely mirror this trend.

The partnership of Pfizer and US/China-based MicuRx Pharmaceuticals and Shanghai-based Cumencor Pharmaceuticals to discover new drugs that treat MDR-TB signifies the recognition of large MNCs on the importance of targeting infectious diseases unique to the Chinese population through partnership with domestic companies.

Even though the current CNS market is quite small in China, there is an increasing interest among Chinese companies to bring innovative drugs into the China market, including treatments for epilepsy, insomnia, and pain. Partnership activities in neurodegenerative diseases and aging-related neurological conditions such as Alzheimer's disease and Parkinson's disease have also been on the rise in China. As the awareness of mental health issues has increased dramatically in recent years, Chinese companies are showing interest in bringing in new treatments for mental conditions such as schizophrenia and bipolar disorders, and conditions that are widely treated in the West, but currently under-diagnosed and under-treated such as depression and ADHD.

Tianjin Tasly Pharmaceutical, a company well-known for its TCM (traditional Chinese medicine) products, has established a partnership with ProteoTech to develop Alzheimer's drugs for the China market. This is indicative of the transformation of Chinese companies from their traditional generics- or TCM-based business models into the more challenging realm of innovative products, and the increasing willingness to take risks.

The recent establishment of GSK's global CNS R&D Center in Shanghai will also likely spark an increase in interest for Chinese companies to expand their partnership as well as in-house development activities to bring innovative products into the potentially lucrative but largely untapped CNS market.

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Conclusions

Since the implementation of the 11^{th} Five Year Plan in 2006 and the 12^{th} Five-Year Plan in 2011, China has committed more than $200 billion USD for its Healthcare Reform Program, addressing the need for better healthcare services for its expanding population. In addition, the China government has committed billions more to the development of novel drugs in China, with the ambition of building China into a world-class innovative center for the biotech and pharmaceutical industry. These factors, coupled with its rapidly growing economy, have enabled China to surpass Japan in 2011 to become the #2 pharmaceutical market in the world, just behind the United States.

China's large, robust market along with its lower development costs, large R&D talent pool and availability of funding, is attracting a large number of Western companies to bring their novel drugs and technologies to China. In parallel, the China government's increased pricing pressure on generics, combined with the availability of government grants and incentives to stimulate novel drug development, are increasing the desire and the ability of China companies to commercialize more complex Western technologies.

This has created a perfect storm of high demand for Western innovative pharmaceutical products and technologies by China pharmaceutical companies and ready availability of novel drug candidates from Western companies that will drive increasing cross-border strategic partnership activity for the foreseeable future.

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Acknowledgements

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