How emerging biotechs can enter the Chinese market and prosper

Alberto Grignolo, Ph.D., Corporate Vice President, Parexel
John Zhang, Ph.D., Vice President -Technical, Regulatory Consulting, Parexel

Small and emerging biotechs in the United States and Europe have long been wary of trying to enter the Chinese market, despite its vast potential. They've shied away due to changing regulatory and reimbursement policies, unreliable intellectual property protections, and fear that the Chinese government may favor domestic firms. But things have changed, and companies don't need to be hesitant anymore.

Since 2015, a slew of economic and regulatory reforms have improved the Chinese market dynamics for foreign companies. In 2018, the Chinese State Council eliminated tariffs (of 6% to 10%) on all imported cancer drugs and slashed the value-added tax on them from 17% to 3%. In 2020, 28 new drugs from non-domestic companies were approved by the National Medical Products Administration (NMPA), faster and more dependably than before. In May 2021, China was reelected for a three-year term to the management committee of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use, further aligning it with international regulatory standards.

Large international pharma companies often include China because of its market size, and many put it near the top of the list when sequencing global marketing submissions. But how can small and emerging foreign companies with limited resources gain a foothold in the Chinese market? Here are five approaches that help.

1 Deliver value for money

China's population is aging at relatively lower income levels than in the West, driving demand for low-priced cancer and chronic disease drugs. China implemented centralized volume-based procurement (VBP), also known as the "4+7" program, to control the cost of generic drugs in 11 major cities that purchase the greatest volumes of medicines. But newer drugs with patent protection still command premium prices, albeit lower ones than in the West.

As generic drug prices decrease due to VBP, a more substantial budget will likely be available in China's national and provincial reimbursement systems for novel drugs. Companies can price innovative

parexel BIOTECH

products for a sustainable return on investment (as they have in Europe) and offset lower prices in China with volume. To be included in China's National Drug Reimbursement List (NRDL) in 2021, companies cut prices by an average of 51%, but they've reaped the rewards. For example, Novartis's immunosuppressant Cosentyx reportedly accelerated sales in China in the second quarter of 2021 after winning a spot on the NRDL at the end of March.

No oncology drug developer can overlook unmet need in China: In 2020, the country suffered 30% of worldwide cancer-related deaths and accounted for 24% of newly diagnosed cases. But new cancer drugs must differentiate on efficacy, safety, route of administration, or treatment stage. To enter China successfully, biotech companies should focus on products that deliver value for money and consider moving China further up their sequence of global marketing filings.

2 Study the landscape

China is as diverse ethnically, economically, and culturally as the expanded European Union, yet it has a strong centralized government. It's more akin to a continent than a country. Beijing and Shanghai are comparable in socioeconomic terms to big cities in developed countries, such as London or New York. But in provincial capitals and smaller towns, average income and other economic metrics are closer to eastern Europe and developing countries.

Disease prevalence and incidence vary significantly by province and ethnicity. Diabetes afflicts 11% of the Chinese population, but in a recent study, total diabetes and prediabetes prevalence ranged from 6.2% in Guizhou to 19.9% in Inner Mongolia. The report showed disparities in awareness, treatment, and disease control between young and older diabetics and urban and rural environments. Companies looking to deliver products to Chinese patients should parse such data in detail and tailor their product development and market launches from an early stage.

Once a company has secured a coveted spot on the NRDL, it must negotiate pricing and reimbursement province by province, so it must understand each area.

3 Leverage strengths; compensate for shortfalls

China's local biotech market is booming, creating an increasingly competitive landscape for foreign companies. More than a third of 2020 global biotech IPOs were Chinese companies, and foreign venture capital investment in Chinese start-ups shot up 34% year-over-year (to $91 billion) in the first half of 2021. However, foreign firms may still have an advantage over local ones. While Chinese companies may benefit from lower labor and manufacturing costs, western biotechs have the advantage of coming from environments with a track record of developing complex biologics and commercializing drugs with novel mechanisms of action.

Once a company has defined the market opportunity for its product, it can choose from the following approaches:

- Go direct, opening a small office as a foothold, and gain Chinese experience and contacts throughout the development

parexel BIOTECH

- Initiate drug development in China, such as early Phase I/II or bridging studies, but partner with a Chinese company to handle late-phase studies, marketing, and distribution
- Partner from the start with a multinational company that knows the Chinese market well and has the infrastructure to be successful

Modeled after the FDA and EMA, China's Center for Drug Evaluation (CDE) has streamlined the quality and timing of its reviews, increasingly displaying a certain degree of "predictability." CDE reviewers will recognize the characteristics of a safe and efficacious product supported by sound data. They are open to negotiating the proportion of China-based patients required for a successful global clinical development program.

4 Use every tool available

Emerging companies can benefit from Chinese government programs to streamline development. For example, since late 2018, China's Bo Ao Lecheng International Medical Tourism Pilot Zone has provided an alternative pathway for foreign medical devices and drugs to enter the country by leveraging real-world data (RWD) and real-world evidence (RWE). The pilot zone is a collaboration between the CDE and the government of Hainan, an island province at China's southernmost point.

For example, in March 2020, the NMPA approved Allergan plc's XEN Gel Stent for glaucoma, making it the first imported medical device utilizing RWE for registration in China. Allergan obtained permission to collect RWD through the Hainan pilot zone's program. The number of overseas companies applying to collect RWD in the pilot zone to supplement foreign clinical trial data increased sharply after the Allergan approval.

In December 2020, Hainan province established the Hainan Real-World Data Research Institute to develop standards for using RWE and RWD to replace bridging studies and as key evidence. Early entry to this fast-evolving field will have challenges, but companies that engage now can foster relationships with Chinese investigators and institutions to speed up RWE research studies.

Emerging companies can also leverage streamlined regulatory processes in China to accelerate development if their treatment is deemed "urgently needed." Although rare disease drug development in China lags the West by years, since 2018, the

parexel BIOTECH

NMPA has approved 37 drugs for rare diseases on an accelerated basis. All were deemed "urgently needed" orphan drugs, eliminating the requirement for clinical trials in China and reducing review times to three months. On October 11, 2021, the CDE issued a draft guideline on rare disease drugs that reinforced the use of biomarkers and model-informed drug development (MIDD). Although data are scarce, China probably has the largest population of rare disease patients globally —16 million people by one recent estimate. Companies that help improve awareness, diagnosis, and treatment of Chinese rare disease patients may secure faster access to the market.

5 Be patient and creative

Overoptimism about the Chinese market and hasty entry won't help companies make good development decisions or realize a return on investment. Fast-learning companies that are patient in navigating the Chinese system have the best chance of success.

China is modernizing quickly, but it retains its traditional culture. A typical product market launch may go slower in China, with a wavering uptake trajectory from NMPA approval through provincial tendering, hospital formulary review, and, ideally, NRDL authorization. It's a journey that companies with patience and perseverance can successfully navigate to deliver products to Chinese patients who need them. Progress may be gradual. Unexpected setbacks, such as the now 2-year-old global coronavirus pandemic, or political flare-ups, may intrude. Companies should expect stop-start progress.

Although there are limitations on foreign ownership of healthcare facilities and clinics in China, there are strategic workarounds. For example, Parexel has partners in China to conduct Phase 1 studies and deliver ethnobridging studies at Phase I clinics in the United States and the UK. By including Chinese subjects in early-stage ethnobridging trials, companies can detect ethnic variations in drug metabolism, absorption, distribution, elimination, safety, tolerability, and pharmacodynamic profiles), Collecting this information early in development greatly facilitates the inclusion of Chinese patients in a global development plan.

Forge ahead, but manage risks

A company with a cost-effective product that addresses an unmet need in China—one that can be geographically stratified and targeted—should seriously consider the opportunity afforded by this large and evolving market.

Never stop bioteching.

Let Parexel Biotech connect every step of development with you. Get the flexibility and adaptability it takes to #NeverStopBioteching. Connect with one of our experts for further insights for accessing the China market with your next breakthrough.

parexel BIOTECH