MARKET STRATEGIES FOR PHARMACEUTICAL DEVELOPMENT IN CHINA ... AND THE U.S.

THE GLOBAL 505(B)(2) EXPERTS
Camargo
PHARMACEUTICAL SERVICES

China is having a dramatic impact on the world pharmaceutical market.

Its massive $64 billion government initiative to modernize the pharmaceutical industry and improve health care in rural regions has spurred significant interest and investment from big pharma as well as from many small and midsized drug, device and biotech development companies.

Basically, there are three ways for pharmaceutical companies to enter the Chinese market: apply to the China Food and Drug Administration (CFDA) to market their product as a foreign drug; partner in China with local firms; or build their own research and development and manufacturing facilities. In the past decade, a number of international companies including AstraZeneca, GlaxoSmithKline, Medtronic and others have chosen this last path, making huge investments in facilities, administration and distribution in hopes of profiting long-term from China's vast population.

In a different way, Chinese pharmaceutical manufacturers have a lucrative opportunity to turn the process around and develop products for marketing in the United States. The U.S. is, after all, the world's largest free-pricing market for pharmaceuticals and has a favorable patent and regulatory environment. If properly approached, the rewards of success can be substantial.

In both China and the U.S., companies have the opportunity to gain approval for generic drugs as well as for new molecular entities. However, both countries also offer a regulatory pathway for the approval of drugs that are based on new formulations of existing drugs that offer a demonstrable benefit to patients.

In the paragraphs that follow, we will explore regulatory requirements governing repositioned drug development in both China and the U.S. and look at ways companies may benefit from a better understanding of this approval process and from better guidance in its execution.

China Today

According to IMS Health Inc., China is currently the third largest pharmaceutical market in the world, posting $67 billion in revenue in 2011.

With an anticipated compound growth rate of 24 percent between 2010 and 2020, China is expected to be the second largest market by 2015 and become the number one drug market globally by 2020; it was number seven in 2009.

The Chinese government is determined to transform the industry into an innovation-driven, drug-development powerhouse. The government program has targeted several areas to address, including securing pharmaceutical supply lines, funding research, eliminating bottlenecks in distribution and ensuring that drug quality is compatible with global standards.

Despite what appears to be a rosy economic outlook, there are concerns that need to be addressed, including slowing economic growth in China and intense local competition as the government seeks to bolster homegrown firms. Prudent manufacturers will seek to establish partnerships with firms that are well-connected and well-versed in the regulatory requirements of the country.

Using 505(b)(2) for Foreign Drugs

Meanwhile, for Chinese and other foreign companies seeking to enter the U.S. market, 505(b)(2) offers an efficient pathway. As the slate of blockbuster drugs coming off patent declines, the 505(b)(2) pathway offers a faster and less costly drug development route as well as potential marketing advantages for new products.

> The 505(b)(2) process may also help relieve the pressure on what will become an even more competitive generics landscape.

Although this discussion will concentrate on explaining how this pathway can lead to U.S. approval of foreign drugs and the resulting benefits, it is important to reiterate that China and other countries have a similar process and significant profits are possible. However, it is essential to be guided through the process by a partner that understands the particular nuances of each country's regulations. Companies that specialize in 505(b)(2) will be experienced with current regulatory agency guidelines and relevant precedents and will often have established relationships with regulatory staff.

An early understanding of the regulatory landscape and relevant precedents can build a framework for the overall development plan and help determine the fastest route and the pathway to market with the greatest value. Strategic regulatory planning helps develop the scope of nonclinical, technical and clinical testing that will be required for registration.

Whether a device or a drug, the U. S. Food and Drug Administration requires evidence that the investigational product under consideration can be produced consistent with current good manufacturing practice (cGMP) standards. This will require submission of well-defined written procedures for production and testing; verification of an adequately controlled production environment and equipment; and accurately and consistently recorded data. The level of detail required will vary depending upon the investigational phase.

To enhance the probability of having your application accepted by the FDA, it is advisable to consult with FDA staff at a pre-IND meeting. Pre-submission meetings allow sponsors to validate proposed clinical endpoints and trial design characteristics and negotiate approvability criteria to avoid unnecessary studies. FDA regulators see all INDs that are under development and have an overall understanding of the development arena and will provide fair and balanced advice.

Two Aspects of Success

Chinese generic companies may also be handicapped because they lack expertise in evaluating either the scientific or the commercial feasibility of proposed products — and both are vital to market success and return on investment.

The 505(b)(2) process is ideal for reformulations of existing products that address different indications, populations or routes of administration, but merely being able to demonstrate a new formula based on an existing drug is not enough on which to base a go/no-go decision to pursue a 505(b)(2) development program.

It's important to make certain your candidate has sound scientific footing to meet the requirements of a 505(b)(2). In addition, a plan must be developed for testing, formulation and manufacturing as well as for conducting any needed preclinical and clinical studies. Finally, it is essential to assess whether a product can be effectively marketed at a profit and verify potential before development begins in order to help investors recognize the value and reduce the risk.

How the Product Selection Process Works

The first step to choosing a product to develop is to narrow the focus to highly specific definitions of unique products and the discrete market segments they will address. Once a market segment has been defined, the next stage is to identify, assess and rank unmet medical needs within the segment in terms of product viability. Considerations to establish product viability cover a lot of ground and include the need for a broad range of potential research and reporting activities, including:

Market segmentation

- Disease overview
- Epidemiology
- Current standards of care
- Needs assessment

Product analysis

- SWOT analysis
- Critical success factors
- Strategic objectives
- HEOR
- Drug development programs
- Positioning and Target Product Profile (TPP) development
- Nonclinical programs

Production analysis

- Regulatory considerations
- CMC considerations
- 505(b)(2) candidate assessment

Marketing analysis

- Market and competitor assessment
- Detailed commercialization plan
- Distribution assessment and plan
- Key messaging

Investor analysis

- Financial analysis
- Partner targets
- Pipeline analysis
- Compendium assessment and plan

Profit potential

- Payer reimbursement plan
- Pricing development

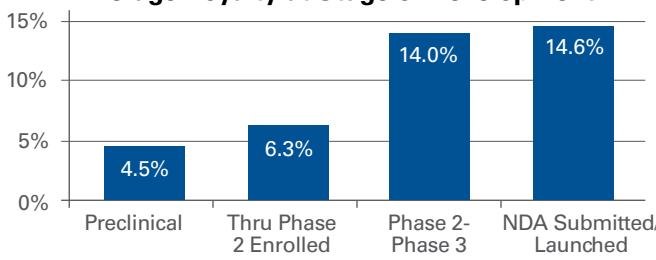
With the results of this research in hand, the viability of a product can be ascertained and a comprehensive development plan created.

Inviting Investors In

Investors in traditional generic drugs — regardless of whether that drug is developed in the U.S., in China or some other country — make a relatively simple calculation of what a product's potential might be. The same cannot be said for the differentiated products developed under 505(b)(2) in the U.S. Basically, there are four distinct "inflection points" that impact the value of a 505(b)(2) drug candidate during clinical development:

- Completion of a pre-IND meeting with FDA
- Proof of concept (PoC) achieved in humans
- Filing of NDA
- FDA approval of new drug application

Average Royalty at Stage of Development



Adapted from 2009 Global BioPharmaceutical Royalty Rates & Deal Terms Survey

As indicated in this chart, the largest increase in the value of a product under development occurs when proof of concept (PoC) trials establish a therapeutic effect. Investors in pharmaceutical development, like all investors, are eager to minimize their risk and are therefore more comfortable in funding projects where it is obvious that due diligence has been performed. Before approaching investors, it's vital for companies to nail down a defense of the value of their product in each of several areas:

Clinical development

- Project management by established experts in:
  - Technical assessment and product formulation
  - Clinical trial management
  - Regulatory strategy and interaction with FDA

Intellectual property

- Types and sufficiency of product patents
- U.S. marketing exclusivity
- Life cycle management strategy

Product revenue forecasts

- Product differentiation and market positioning
- Pricing and discounting strategies by payer class
  - Managed care
  - CMS programs
- Compendia positioning
- Distribution strategies
  - Third-party logistics, wholesalers and retail chains
- Sales and marketing strategies
  - Targeted physician audience (breadth and depth)
  - Direct to consumer promotion
  - Social media, other nontraditional promotion

Product and promotional cost forecasts

- Manufacturing strategy
  - Product unit cost expectations
  - Licensed technology royalties
  - Redundancy
- Product liability/insurance strategy
  - Assessment of insurance industry capacity
  - Insurance costs and structures
- Sales and marketing infrastructure
  - Size and cost of sales force
  - Cost of A&P programs
  - Effective tax rate optimization

505(b)(2) in a Global Development Strategy

As the global pharmaceutical market becomes more intertwined, companies are freed to look for profit opportunities anywhere in the world. China, the European Union and many other countries have adopted pharmaceutical development pathways that are similar to 505(b)(2); many, in fact, are based on the U.S. model.

Camargo's proficiency in this regulatory area as well as its expertise in evaluating market opportunities and development plans make it an ideal partner for foreign companies seeking to enter the U.S. market as well as for U.S. companies looking for marketing opportunities abroad. Companies that choose to market drugs not manufactured in-country may have additional hurdles to approval but, with proper regulatory guidance, excellent opportunities exist especially for differentiated products of approved drugs.

About Camargo Pharmaceutical Services

Camargo Pharmaceutical Services is the most experienced global strategist providing comprehensive drug development services specialized for the 505(b)(2) approval pathway and global equivalent processes. By assessing the scientific, medical, regulatory and commercial viability of product development opportunities, Camargo systematically builds and executes robust development plans that align with business strategies and ensure FDA buy-in every step of the way. Routinely holding three to six pre-IND meetings a month, Camargo works with product developers across more than 25 countries.

Worldwide Reach

In more than 25 countries across North America and Europe, to India, Israel and China, Camargo's regulatory know-how and customized clinical solutions are as varied as our clients' global drug development needs.

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