



Opportunity and Influence for
Localized Development
Pharmaceutical R&D Trends in China



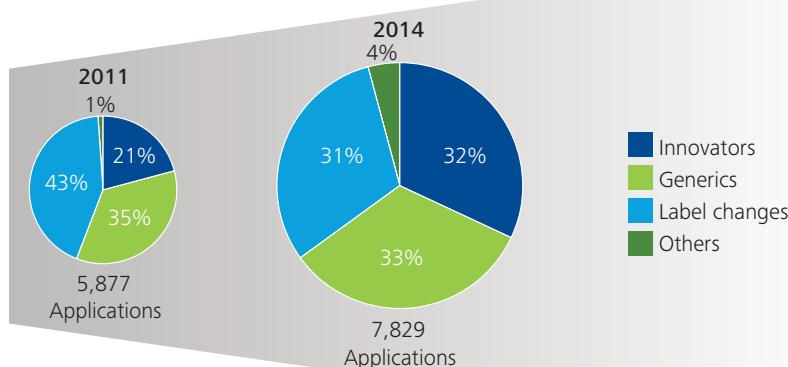
As China's government continues to face gaps in the quality of and access to healthcare—in addition to the growing burdens of population size, ageing and utilization on the existing system—one strategy will be continued support for the local R&D industry. The primary directives of this strategy are to develop innovative capabilities and upgrade applicable technologies as well as attract, develop and retain a strong talent base. This strategy will have strong implications for multinational pharmaceutical companies, who must adopt more localized R&D approaches to address new opportunities and challenges.

A shifting landscape — key implications

The Chinese government has made significant multi-pronged investments to grow the local R&D industry. The aggregate result is increased local R&D output, a more innovative R&D pipeline (Fig 1) and China's growing importance in support of global and regional study submissions.

Fig 1: R&D pipeline growth (2011-2014)

China Chemical Drugs Applications Structure



The growing local R&D industry is already challenging traditional, global-centric R&D models with increased R&D competition and regulatory complexities. Despite the long-term promise of accelerated time-to-market for more innovative products, large uncertainties still remain in timing and the extent of impacts. Opportunities do exist, however, for MNC pharma to adopt a more localized and integrated R&D strategy in China. This strategy would leverage increased local R&D capabilities in order to accelerate development of local, and in the longer-term, global products.

Great flux in R&D regulatory reform

Launching local clinical studies for overseas clinical programs have traditionally been challenged by two main barriers in China: the China Food and Drug Association's (CFDA) requirement that a drug be registered in a foreign country or in phase II or phase III clinical trials and a lengthier process for IND and NDA registration than in other markets. Altogether, these barriers can cause local product launches to take five to eight years, discouraging innovative programs from entering China by eroding larger revenues from patent protection.

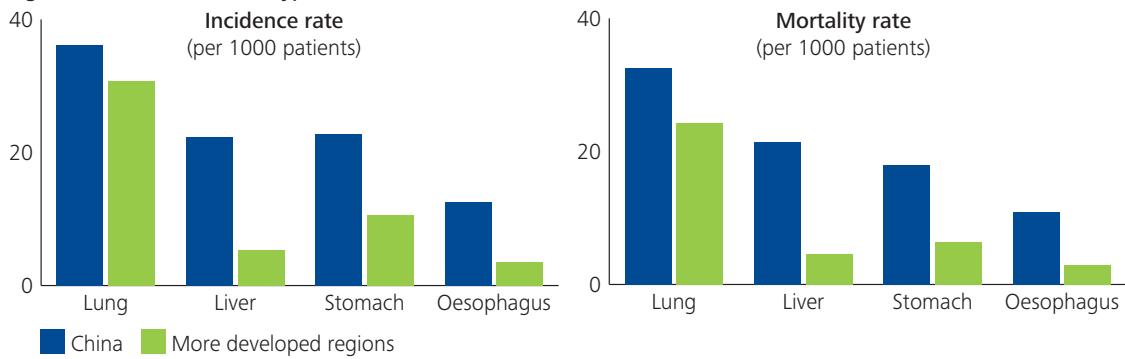
Though the government is accelerating R&D regulatory reform, large volatility has been seen and is expected to continue. For example, in 2014, the CFDA and R&D Based Pharmaceutical Association Committee (RDPAC) had several exchanges with seemingly opposite results. Despite a recent announcement from the CFDA about a pilot reform potentially cutting IND approval times for oncology drugs from one-two years down to 60 days, potential impacts on overseas development programs in China remain unknown, and more discussions are still required to define the specific reform agenda and timeline. Furthermore, identifying whether central or local regulatory agencies have the capacity to implement reform has always been a challenge, which could increase volatility in the near term.

This flux can have a large impact on MNC pharma wanting to import innovative programs to China. The companies must change their current global R&D models to mitigate the efficiency risk introduced by China's local policy environment.

Growing need for "Made for China" drugs

Addressing unmet needs specific to Chinese patients is a key lever for expediting the CFDA approval process. For many under-represented but rapidly growing Therapeutic Areas (TAs), such as liver and gastric cancer (Fig 2), there is a strong rationale for fast-track qualification—if superior clinical results from mainland China, backed up by data from Asian populations in global trials, can be demonstrated.

Fig 2: Prevalence of cancer types in China (2013)



Source: World Health Organization

Aside from fast-track approval for these TAs, the CFDA has also introduced pilot programs to delegate workloads to provinces. Companies are able to work with local regulators to conduct smaller trials leading to commercialization in a local jurisdiction before potentially addressing nation-wide trials.

These adjustments have seen a number of recent successes. Several cancer or hepatitis therapies were launched in China less than two years after their global launch, rather than the typical five to eight years of "drug lag." Recently, Xalkori, the

first personalized medicine for lung cancer, received speedy approval when the minimum cohort size requirement was waived (Fig 3).

As healthcare reform deepens to increase access and quality, it is expected that TAs with urgent unmet needs will continue to benefit from favorable consideration and first-mover advantages. This means companies need to think about how they can develop R&D models to best capitalize on the need for "Made for China" products.

Fig 3: Case study on Xalkori



3 Inclusion of China Since Global Phase II and CFDA Accepting a Smaller Patient Cohort



Source: clinicaltrials.gov, press releases, Monitor Deloitte analysis

Alternative R&D models — local integration

In light of shifting R&D needs and regulatory reform, significant evolution is required from traditional, global-centric R&D models to accelerate time to market while managing risks in China. This is a strong impetus for building alternate R&D models through partnerships.

Increasing competition from local players

The Chinese government's investments into R&D, though questionable in efficiency, have cultivated local leaders that are now more competitive with Westernized R&D capabilities. This would put high-cost, global-centric R&D models at a disadvantage.

More local leaders are leveraging R&D capabilities to advance innovative assets in ways that provide them with competitive advantages. Zhejiang Beta Pharma's NSCLC drug, Conmana, was heralded for both applying a cheap R&D approach as well as for reaching RMB100 million in sales within seven months of its launch. Kanghong's novel monoclonal antibody, Conbercept, was the first innovative MAb approved by the CFDA in 2013 for the treatment of Macular Degeneration.

These R&D models are certainly not new, but their development, combined with strong familiarity with the local regulatory environment, may grant local players unique competitive advantages. This only intensifies the impetus for MNC pharmas to change how they operate in China.

Local R&D integration through partnerships

To respond, MNC pharmas are investing more in localizing R&D, such as new R&D centers, clinical CoEs and *de novo* programs. However, these all require large investments and long lengths of time to generate desired impacts. As such, MNC pharmas should look at building alternate R&D models through partnerships, which not only mitigate traditional development risk but can also leverage local efficiencies to add value. A partnership approach presents unique benefits as local companies tend to be more efficient operationally due to familiarity with the local R&D and regulatory environment. They also capitalize on policy incentives that lead to shortened approval times and reduced development costs.

These partnerships can take many forms. They should have their own associated uses and should be pursued based on the capabilities and risk appetites of involved parties.

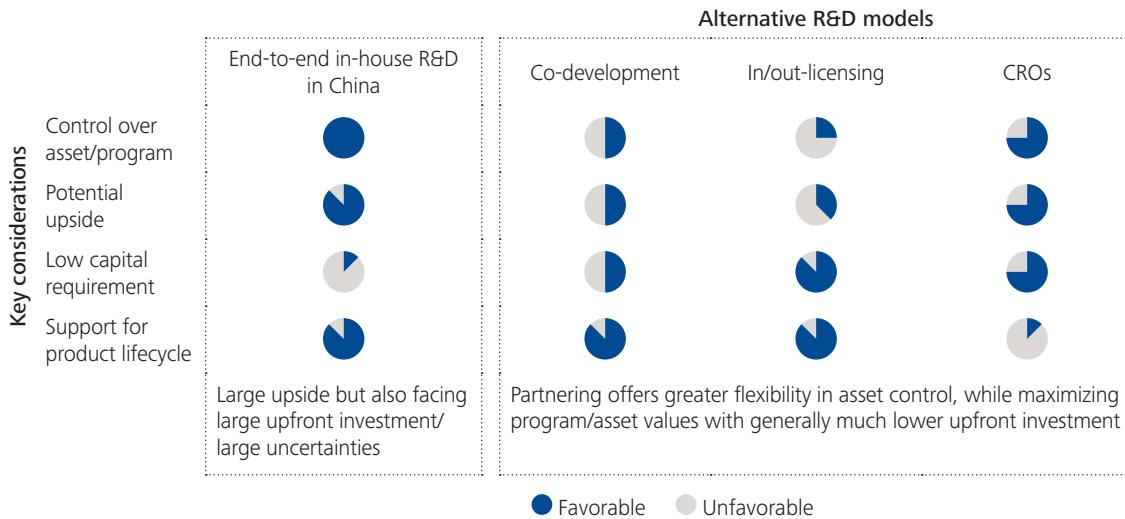
A local-MNC development partnership is a major venue to realize benefits. It is frequently associated with the development of a particular TA-specific portfolio that addresses a significant need in China. It also can be strategically developed to capitalize on local sales and other operational efficiencies. Despite the large upside, these partnerships tends to last the entire duration of the product lifecycle and require substantial commitment from both parties in the face of considerable uncertainties.

Out-licensing strategies (to a local company) is another way to provide benefits similar to the local-MNC partnership but are more suited to MNC pharmas with less presence in China or a smaller appetite for commitment to the market, such as Ambrix's developmental cancer drug out-licensed to Hisun Pharma. Because MNC pharmas have less control after the license agreement takes effect, this strategy is usually more suited for those with lower expected value from a go-it-alone R&D and commercialization strategy.

There is also the emergence of local Contract Research Organizations (CROs), which can create new opportunities for MNC pharmas. CROs provide the benefits of a local R&D partnership but generally lack the ability to support commercialization. They are best suited for MNC pharmas who see the benefits of a localized R&D process yet want to maintain control over their assets throughout the product lifecycle. While many partnerships with CROs are short term and project based, Wuxi Pharmatech built a dedicated facility for its partnership with BMS to support development of small molecule entities more long term.

These partnership-based R&D models collectively demonstrate much greater flexibility and risk tolerance when compared to in-house R&D. Some local pharmaceutical companies are more interested in exercising their R&D capability than building a portfolio, while some CROs are more willing to engage in risk-sharing agreements. There are limitless variations on and combinations of partnership models, but the tradeoffs of each must be carefully weighed against the strategic rationale behind them.

Fig 4: Local R&D partnership comparison



Source: Monitor Deloitte analysis

Challenges and mitigation

While perceived benefits for partnership-based alternate R&D models are strong, they all face traditional, systemic R&D challenges in China that can take years to overcome and therefore need to be mitigated through careful design.

A major challenge in the Chinese market for MNC pharma that still remains is the large perceived gaps in IP regulations and industry standards—including consistency of, and capacity for, policy enforcement. The result is MNC pharma's hesitation to localize development programs and form local partnerships. Regardless of risk appetites and growth ambitions, decision-makers will benefit from a balanced approach where small, evolved bets build confidence and familiarity for longer-term strategic investments.

Some of Pfizer's activities demonstrate the benefits of this approach. Pfizer was able to take advantage of the CFDA's fast track program with Xalkori, largely as a go-it-alone strategy, by more proactively involving local agencies in trial design, thus allowing quicker local launch than other drugs. But Pfizer is also pursuing partnerships ranging from funding agreements with local research organizations for drug discovery to JVs with local companies for growth opportunities. This balanced approach reduces overall risk exposure while emphasizing a long-term commitment to China and to its partners.

Another critical challenge is that talent bottlenecks still exist for local R&D. Many specialized functions are hard to fill, such as pharmacologists and toxicologists, due to a lack of working experience. There is also a growing shortage of the local R&D management talent needed to rally and drive local programs. Thus, when partnering, MNC pharma should make it a priority to evaluate key capabilities required, whether they are highly specialized functions or well-rounded, and design partnerships to best complement remaining gaps.

The translational research partnerships that the Beijing Genomics Institute struck with several MNC pharma is a good illustration of how partnerships can fill these gaps. They allowed MNC pharma to take advantage of highly specialized genomic data generation and analysis capabilities that BGI has to offer for discovery of critical pathways. Similarly, a new wave of innovative local biotech companies, such as Beigene and Aslan Pharma, were able to secure top VC funding and MNC pharma partnerships primarily due to their well-rounded R&D execution capabilities.

Finally, constant change in China's Healthcare market will continue to present new challenges and opportunities. A clear and well-established governance structure is a critical factor in navigating these changes. As strategies change for both a partnership as well as each partner, a strong governance structure, that both sides understand upfront, is a necessary condition for the partnership's success.

The Simcere-Merck joint venture demonstrates the importance of a strong governance structure. Those familiar with the situation claim that despite the strategic and operational strengths of the JV designed to develop and commercialize branded drugs treating cardiovascular and metabolic diseases, its governance structure and the resulting difficulty in adapting to changing market conditions was a key factor in why it ultimately dissolved.

Summary and outlook — alternative R&D models

An accelerating shift in China's R&D landscape is already leading to increased R&D capabilities of local players, more competition for innovative programs and larger uncertainties for the regulation of clinical studies of overseas compounds. They are collectively challenging MNC pharmas' traditional, global-centric R&D models and creating a strong impetus for change.

Alternate models based on partnerships have the best chance of navigating such a dynamic landscape via increased local leaders' capabilities on multiple fronts. To make the most out of partnerships, however, decision-makers need to adopt a more balanced investment approach, access targeted capabilities and employ robust governance structures.

Building a successful R&D model is an exciting and unique challenge. Despite obstacles, positive momentum is evident as the Chinese government looks to grow a local R&D industry to improve quality and affordability of care. Capitalizing on these opportunities is possible through continued focus, experimentation and tenacity.

In summary, while developing alternate, partner-oriented R&D models, MNC pharmas need to consider the following key principles:

- Use staged, balanced R&D investments to create flexibility to co-evolve with the market
- Adopt a more capabilities-oriented mindset to ensure optimal partnering decisions
- Employ strong governance structures to ensure flexibility and continued alignment

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