Fostering the China Bio-pharma R&D Ecosystem and Promoting Drug Innovation

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RDPAC, China
China has made significant progress in drug innovation over the past five years and is emerging as an increasingly important contributor on the global stage. However, it also has gaps and challenges that cannot be ignored.

**Why do Chinese patients have limited access to new drugs?** Betta’s lung cancer drug Conmana had reached only **10%** of China's late-stage lung cancer patients **three years after launch**. A similar case is that of Gardasil by MSD. Despite starting its clinical trials in China in 2007, Gardasil still failed to enter the market, where it might have helped prevent some of the 100,000 new incidences of cervical cancer a year.

**Why are the financial returns on drug R&D so low?** In China, it costs approximately **0.5–1 billion RMB to develop an innovative drug** once costs and risks are taken into account. Yet an analysis of a set of new drugs first launched in China shows their total sales five years after launch averaged less than **100 million RMB**.

**Why has government funding failed to attract private investment?** Venture capital investment in new drug R&D has been low in terms of both the number of deals (24) and their value (**1.8 billion RMB**) in the past five years. Tens of billions of government funding have failed to drive private investment.

**Why have China’s new drugs yet to go global?** Over the past five years, **13 new drugs** have been first approved and launched in China, but **none** of them has entered the international market yet.

- Focuses on the framework for a drug innovation ecosystem
- Evaluates the state of China’s industry from a global perspective and explores the factors that hold innovation back
- Examines initiatives that other countries have adopted to improve their ecosystems, and the impact these have had
- Offers a high-level proposal for establishing an innovation ecosystem for the pharma industry in China, with a particular focus on the mindsets and mechanisms needed to support it
The availability of new medicine varies widely by country and disease.

### Global New Molecular Entities 2007-11 Available to Patients in 2012

<table>
<thead>
<tr>
<th>Country</th>
<th>World</th>
<th>USA</th>
<th>Japan</th>
<th>Germany</th>
<th>France</th>
<th>Spain</th>
<th>Ireland</th>
<th>UK</th>
<th>Canada</th>
<th>South Korea</th>
<th>Brazil</th>
<th>Russia</th>
<th>Mexico</th>
<th>China</th>
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<tbody>
<tr>
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<td>65</td>
<td>70</td>
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<td>37</td>
</tr>
<tr>
<td>% of Total</td>
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<td>60</td>
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<td>Anti-infectives &amp; Antivirals</td>
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Source: IMS Institute for Healthcare Informatics, October 2013
For some high-prevalence diseases, Chinese patients account for a large portion of the global patient pool.

<table>
<thead>
<tr>
<th>Incidence of selected diseases in 2012</th>
<th>Liver cancer</th>
<th>Esophageal cancer</th>
<th>Gastric cancer</th>
<th>Hepatitis B</th>
</tr>
</thead>
<tbody>
<tr>
<td>No. of patients globally</td>
<td>782,000</td>
<td>456,000</td>
<td>952,000</td>
<td>240 million</td>
</tr>
<tr>
<td>No. of patients In China</td>
<td>395,000</td>
<td>223,000</td>
<td>405,000</td>
<td>93 million</td>
</tr>
<tr>
<td>China %</td>
<td>50%</td>
<td>49%</td>
<td>43%</td>
<td>39%</td>
</tr>
</tbody>
</table>

Source: Globocan; WHO
The number of patients with diabetes exceeds 100 million

Patients with diabetes in China (millions)

Source: National epidemiological survey statistics
China has the world’s fastest growth in pharma R&D investment

<table>
<thead>
<tr>
<th>Biopharma R&amp;D investment in 2012¹</th>
<th>CAGR 2007–12</th>
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</thead>
<tbody>
<tr>
<td>Billion RMB</td>
<td></td>
</tr>
<tr>
<td>US</td>
<td>740</td>
</tr>
<tr>
<td>Europe</td>
<td>507</td>
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<tr>
<td>Japan</td>
<td>230</td>
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<tr>
<td>China</td>
<td>52</td>
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<tr>
<td>Australia</td>
<td>38</td>
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<tr>
<td>Korea</td>
<td>37</td>
</tr>
<tr>
<td>India</td>
<td>12</td>
</tr>
</tbody>
</table>

1 Include public funding (government, education and research institutes, and NGOs) and private capital (biotech, pharmaceutical, and medical device companies)

Source: New England Journal of Medicine; McKinsey analysis
China has strong momentum in its publications, patents, and pipeline

No. of articles published in top international journals¹

<table>
<thead>
<tr>
<th>Year</th>
<th>2009</th>
<th>10</th>
<th>11</th>
<th>12</th>
<th>2013</th>
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</thead>
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<tr>
<td>No.</td>
<td>60</td>
<td>62</td>
<td>58</td>
<td>80</td>
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</table>

No. of international drug patent filings²

<table>
<thead>
<tr>
<th>Year</th>
<th>2007</th>
<th>08</th>
<th>09</th>
<th>10</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>No.</td>
<td>391</td>
<td>420</td>
<td>493</td>
<td>625</td>
<td>756</td>
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</tbody>
</table>

No. of chemical compounds under development by Chinese companies³

<table>
<thead>
<tr>
<th>Year</th>
<th>2010</th>
<th>11</th>
<th>12</th>
<th>13</th>
<th>2014</th>
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<tr>
<td>No.</td>
<td>89</td>
<td>107</td>
<td>146</td>
<td>155</td>
<td>229</td>
</tr>
</tbody>
</table>

² Patent filing after 2012 is not fully disclosed because of the 18-month confidentiality period for patents
³ Defined as companies with headquarters in China

Source: Pubmed; Patentscope; Pharmaproject; GBI; McKinsey analysis
China is leading innovation output among emerging markets

**No. of articles published in top scientific journals**

<table>
<thead>
<tr>
<th>Country</th>
<th>2013</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>132</td>
</tr>
<tr>
<td>India</td>
<td>23</td>
</tr>
<tr>
<td>South Africa</td>
<td>16</td>
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<tr>
<td>Brazil</td>
<td>16</td>
</tr>
<tr>
<td>Russia</td>
<td>4</td>
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</tbody>
</table>

**No. of international drug patent filings**

<table>
<thead>
<tr>
<th>Country</th>
<th>2011</th>
</tr>
</thead>
<tbody>
<tr>
<td>China</td>
<td>756</td>
</tr>
<tr>
<td>India</td>
<td>503</td>
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<tr>
<td>Russia</td>
<td>93</td>
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<tr>
<td>Brazil</td>
<td>75</td>
</tr>
<tr>
<td>South Africa</td>
<td>16</td>
</tr>
</tbody>
</table>
In China, there are many access hurdles which limit patient access to innovative medicines and encourage pharma R&D in China.

**Access hurdles faced by innovative drugs in China**

**National/Provincial Reimbursement**
- **Regulatory registration**
  - Long registration timelines
  - For small molecules*: 17 ± 2 months for CTA, 10 ± 2 (Type 1) months for MRCT, 18 ± 2 months for NDA
  - For large molecules*: 20 ± 2 months for CTA, 20 ± 2 (Type 1) months for MRCT, 18 ± 2 months for NDA

**Access hurdles**
- **Delays in NRDL /PRDL updates**
  - ≈ 5 years for NRDL update
  - ≈ 1.5 years for PRDL update
- **Limited negotiation mechanisms**
  - None at national level
  - Limited at provincial/city level

**Hospital access**
- **Irregular formulary reviews**
  - 3-5 months in best practices
  - Majority of hospitals take 12-24 months
- **Hospital budget control**
  - On reimbursed drugs (e.g. SH, BJ, HZ)
- **Irregular provincial bidding cycles**
  - ≈14 months per cycle

IND = Investigational New Drug, Application required prior to conducting clinical trials. NDA = New Drug Application, required prior to sales and marketing of a product. Sources: IMS analysis; RDPAC (Jan 2011)

*Registration timelines for imported drugs. CTA = clinical trial approval, MRCT = multi region clinical trials
The time taken for new drug access in China is significantly longer than other markets from a study in 2013.

### Time to patient access for new drugs

- **Hong Kong**: 2-3 months
- **US**: 3-6 months
- **Japan**: 4-7 months
- **Taiwan**: 5-8 months
- **Italy**: 5-8 months
- **Thailand**: 6-9 months
- **China**: 1-5 yrs

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**Project definition of new drugs: All drugs launched within 5 year window**

**Time for new drugs access in China**

- **SFDA approval**
- **Provincial pricing approval**
- **Provincial bidding**
- **Hospital Formulary**
- **Patient**

1. 3-18 mos (Avg 8 mos)
2. 6-48 mos (Avg 14 mos)
3. 2-36 mos (Avg 12 mos)

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1. Time from post marketing approval to patient access, and assuming no significant barriers due to physician prescription. Based on IMS data analysis, desktop research and interview avg. of n=4 stakeholders.
2. Average timelines indicated by 17 member companies survey.
Innovative drugs first launched in China represent a tiny proportion of the global market.

Global innovative drug market
US$600 billion

China’s innovative drug market
US$20 billion

Innovative drugs first launched in China
<US$0.5 billion

1 Include patented drugs and drugs with loss of exclusivity

Source: IMS Global use of medicine; McKinsey analysis
Newly launched innovative drugs have slower uptake curve in China, largely due to lengthy and complex market access steps.

Example of the increase of sales in the domestic market of commercialized drugs

- Due to infrequent drug medical insurance (RDL) updates, China’s originator drugs usually not covered by medical insurance reimbursement in first few years of launch.
- Complex/fragmented hospital listing process further slows down sales rampup.
A thriving innovation ecosystem comprises policy, funding, and capabilities

**Policy**
- IPR
- Regulation (IND, NDA)
- Market access (Pricing, tendering, reimbursement)

**Capabilities**

**Funding**
- Government and other public funding
- Fiscal and taxation benefits
- Private capital (VC, PE, Pharmacos)

**Market**
- Unmet needs
- Economic growth
The current policy environment represents the bottle neck in China’s drug innovation ecosystem.

**Regulation:**
- Long and difficult IND process
- Limited regulatory capability and process management
- New drug registration bundled with manufacturing

**Market access:**
- Long tendering process; lack of standards across provinces
- Innovative drugs are not reimbursed in time

**IPR:**
- Lack of patent compensation system
- Patent link system to be further improved

Innovative capability still weak; the platform building still in its infancy

Private capital not willing to invest; insufficient support for early research

The current policy environment provides insufficient encouragement for innovation and represents the biggest challenge problem in China’s drug innovation ecosystem. It has also severely limited the impact of government initiatives to improve funding and capability building.
Specific recommendations – improving science-based regulation

- **Innovation review should be accelerated and IND regulations should be developed in line with the characteristics of R&D innovation.** Within drug R&D, clinical research is a process of scientific and technological discovery to evaluate the effects of drugs on the human body. Progress in clinical research is the only way to build knowledge about a drug’s attributes. Regulations governing clinical research should recognize this reality and the nature of the requirements for IND and new drug registration should be differentiated. In the early clinical stage, the IND process should be simplified while ensuring that basic safety standards are met. The responsibilities of the research owner and ethics committee should be clearly defined to enable new drugs to start clinical trials as soon as possible and allow their effects to be evaluated. Strict reviews should be applied at the registration stage for new drugs.

- **The regulation of innovation and the resources for review should be enhanced.** The inadequacy of resources for reviewing new drugs has drastically slowed new drug innovation. China can learn from the US and its PDUFA by increasing user fees for new drug applications and product registrations and finding ways to purchase third-party services to enhance its review capacity and resources without recourse to the national budget. If review waiting times could be significantly reduced, the value created for industry players would greatly exceed the fees paid. In addition, increasing fees could reduce the number of low-quality duplicate applications and eliminate idle drug approvals.

- **Barriers to innovation should be reduced and an MAH system should be introduced.** The inadequacy of resources for reviewing new drugs has drastically slowed new drug innovation. China can learn from the US and its PDUFA by increasing user fees for new drug applications and product registrations and finding ways to purchase third-party services to enhance its review capacity and resources without recourse to the national budget. If review waiting times could be significantly reduced, the value created for industry players would greatly exceed the fees paid. In addition, increasing fees could reduce the number of low-quality duplicate applications and eliminate idle drug approvals.
Specific recommendations – Expediting and expanding market access

- **For basic medical insurance (BMI)**, the NRDL should be updated more frequently. In line with the commitment made in 1999, it should be updated every two years, and a qualification review for innovative drugs should be conducted annually.

  For high-value drugs, regions should be encouraged to **develop a negotiation and reimbursement mechanism** based on their local BMI surplus, residents’ incomes, and healthcare service infrastructure. This would help to expand coverage and depth to lift the burden on patients. Negotiation mechanisms should be explored to set pricing by volume, by therapeutic outcome, or within expenditure caps.

- **The development of private health insurance should be encouraged** in order to satisfy diverse consumer needs and explore reimbursement mechanisms for innovative drugs. One of the factors inhibiting the development of private health insurance in China is the absence of a mechanism for disclosing medical information, which deprives private health insurance companies of data and increases their risks and costs. The government should legislate for medical information disclosure and create a standard process for it so as to enable restrictions on private health insurance development to be lifted without compromising patient privacy.

- **In tendering and procurement, the process for innovative drugs should be optimized.**
  The purpose of innovation is to benefit patients. Existing market-access processes should be improved so that new drugs can be offered to more patients more quickly after launch

  The drug tendering system that has developed over the past 15 years does not take full account of the accessibility of innovative drugs, and represents an obstacle to innovation. It should be improved by allowing new drugs to be listed online for hospital procurement, setting up a real-time off-cycle procurement mechanism, and standardizing the centralized tendering cycle across provinces, and eliminate idle drug approvals.
Specific recommendations – Funding

- **The most critical role for the government is to encourage private capital to invest in those strategically important areas in which it is unwilling to invest itself so as to ensure the sustainable development of the drug innovation ecosystem.** China has a state-driven “Major New Drug Development Project” for drug innovation, but does not offer preferential fiscal or taxation policies for R&D. Meanwhile private capital’s support for start-ups is still limited. These issues could be addressed by three measures.

- **The professionalism and transparency of fund management should be enhanced and the efficiency of government funding should be maximized.** New drug R&D is a complex project with high risks. **Industry experts who have been involved in drug R&D** need to be invited to review projects to ensure the best projects are selected for funding. As funding comes from the public budget, pharma companies and administrative agencies should provide details of how funds are used and how projects are progressing to enable fund allocation to be publicly monitored to ensure it is fair and effective.

- **Fiscal and taxation policies should be improved and tax credits should be introduced for the pharmaceutical industry.** The range of R&D expenses should be expanded and clarified, a clear definition of reasonable R&D costs should be provided, and the ratio of pre-tax deductions for SMEs should be increased. The government should provide pharma with the same support as the software industry and include it in the national list of high-tech industries to reduce VAT rates and encourage innovation.

- **Private capital investment and support for small- and medium-sized innovative companies and early research should be enhanced.** Government funding should focus on supporting start-ups and early-stage projects. These projects have high risks and require greater expertise. The government can learn from Israel and Korea and allocate part of its funding for collaboration with venture capital firms so as to motivate private capital investment. In this way, project evaluation, management, and follow-up support will be more professionally handled. The government also needs to improve financial market mechanisms by reducing the cost of access to capital and adding exit options to encourage private capital investment.
Specific recommendations – Capabilities

- The government should play a key role in attracting and fostering qualified talent and promoting a collaborative model that serves public interests and transcends the interests of individual companies.

- China should learn from the model of collaboration between industry, academia, and researchers adopted in Europe and the US, with government driving R&D collaboration. Given China’s starting point, priority should be given to high-prevalence diseases such as liver and gastric cancer and hepatitis B, and to chronic and critical diseases such as diabetes and stroke. China should consider establishing a clinical data platform or other collaborative platform for developing standards and collecting and sharing data on industry requirements.

- Research institutes should be encouraged to set up a technology transfer office to protect inventors’ rights and interests and promote the business development and market application of academic research.
Fostering a drug innovation ecosystem calls for mindset changes and supportive mechanisms

**Mindset changes**
- Government roles
- Science-based regulation
- Pro-innovation culture

**Supportive mechanisms**
- Cross-ministry coordination
- Communication platform
- Legislation improvement
THANKS