Fostering a Sustainable Ecosystem for Drug Innovation in China

构建可持续发展的中国医药创新生态系统

China Pharmaceutical Enterprises Association **(CPEA)**

China Pharmaceutical Industry Association **(CPIA)**

China Chamber of Commerce for Import & Export of Medicines & Health Products **(CCCMHPIE)**

R&D-based Pharmaceutical Association Committee **(RDPAC)**

中国医药企业管理协会

中国化学制药工业协会

中国医药保健品进出口商会

中国外商投资企业协会药品研制和开发行业委员会

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FOREWORD

Pursuing innovation-driven development is a core strategy in China's 13th Five-year Plan, and the bio-pharma industry is one of the pillars. Bio-pharma innovation not only provides a long-term growth engine for the economy but also is a fundamental requirement for improving people's well-being. Globally, a vibrant and competitive drug innovation industry requires a healthy ecosystem featuring a virtuous cycle. Drug innovation is characterized by long development cycles, high risks, and large investments, thus, policy, capability and investment are three indispensable and interacting elements in the ecosystem. Specifically, policy environment remains at the core of the ecosystem. A policy environment that encourages innovation can ensure a well-functioning market mechanism, thereby boosting capital and capabilities needed to translate technology into innovative products.

China's drug innovation ecosystem has begun to take shape. Over the past two years, the aforementioned three elements of policy, capabilities and investment have been significantly improved, forming a virtuous cycle. Thanks to the improving policy environment, especially regulatory reform, private capital inflow has increased rapidly and the industry is attracting an increasing number of high-caliber professionals. These developments have allowed China's bio-pharma industry to be well poised to drive innovation. In the next 10 to 20 years, establishing a sustainable ecosystem for drug innovation will be the key to further unleashing the industry's innovation potential and enhancing the contribution of drug innovation to economic growth and people's well-being.

In this context, in order to promote drug innovation in China and serve as a reference for relevant efforts, four pharmaceutical industry associations have jointly conducted research and produced this special report. This report lays out a framework for establishing a drug innovation ecosystem, and assesses current and future trends in China drug innovation in the context of the global innovation landscape. With respect to development objectives for China's drug innovation industry over the coming 10 to 20 years, the report further examines innovation barriers relating to guiding principles, policy/mechanisms, and capabilities across multiple aspects of the industry, including top-down design, basic research, clinical research, regulatory, procurement and reimbursement, intellectual property rights protection and capital input. This report also elaborates on approaches taken by other countries towards improving their innovation ecosystems and relevant lessons for China. Last but not least, this report offers proposals to address the current challenges and build a sustainable drug innovation ecosystem.

The project group would like to take this opportunity to thank Sang Guowei, Chairman of China Pharmaceutical Association & Academician of the Chinese Academy of Engineering, and Chen Kaixian, Chairman of Shanghai Association For Science and Technology & Academician of the Chinese Academy of Sciences, as well as over 10 other members of the Advisory Committee for their guidance.

The project group has held in-depth discussions with more than 80 experts, including government officials, academic experts from the pharmaceutical communities both in China and abroad, Chinese pharmaceutical companies and start-ups that consider innovation a strategic priority, multinational pharmaceutical companies engaged in R&D investment and extensive cooperation in China, and investors from VC funds. The project group sincerely thanks all experts for their thought-provoking insights.

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Drug innovation calls for policy, capability, and investment to work together in an ecosystem characterized by a policy environment that encourages innovation, active capital inflows from diversified sources, robust capabilities, and extensive collaboration. Thanks to efforts made during the 12th Five-year Plan period, China has begun creating a virtuous cycle for this drug innovation ecosystem, and the bio-pharma industry is well poised to drive innovation. In this context, this report aims to address the following questions that are critical to further development of China's drug innovation industry.

China's bio-pharma industry has seen a surge in the "quantity" of innovation, but how can we improve innovation "quality"? 17 class-A new drugs have been approved during the 12th Five-year Plan period and the number of pipeline compounds reached 656 by 2015, indicating a strong momentum for future development. While the quantity of innovation output has been on the rise, questions remain on how to drive drug innovation to address more patients' unmet clinical needs and continue to enhance levels of innovation and globalization.

While the country's innovation-driven strategy proposes a vision of "becoming a leader among innovation-oriented countries by 2030", China is now among third tier countries of drug innovation worldwide. What is required in building its drug innovation ecosystem for China to become a second and even first tier country? As a third tier country in drug innovation, China contributes ~4%[1] of global drug innovation, lagging far behind the U.S. (~50%[1]) as the first tier country and second tier countries, such as Japan.

Over the past two years, the policy environment for drug innovation, particularly for drug reviews and approval, has improved. What additional policy improvements are needed? What changes should be made to guiding principles, mechanisms, and capabilities to ensure clear and consistent implementation of the policies? Given the complexity of the innovation ecosystem, new policies may not be able to solve all deep-rooted problems. Without systematic planning, policies in different areas would lack consistency.

In the next five years, which elements in the ecosystem will be the weakest and may become the biggest bottleneck for innovation? How can we take a forward-looking view in addressing these problems? In the past five years, a lagging regulatory environment has been the biggest bottleneck in the ecosystem. However, with the regulatory environment improving, and considering the R&D cycle, new bottlenecks may arise along the value chain (such as clinical research and reimbursement of innovative drugs), threatening R&D achievements and enthusiasm for continued investments.

In the next 10 to 20 years, how can we ensure China's innovation ecosystem will be supported by a robust source of innovation? As a form of science-based innovation, drug R&D is different from other types of innovation (e.g., engineering technology-based, customer-centric, and efficiency-driven) and must be based on the long-term accumulation of scientific research.

1 Measured by the number of pipeline molecules (at the end of 2015) and the number new drug launches (2007-2015); share of China among major drug R&D countries globally (including the U.S., Japan, the UK, Germany, Switzerland, South Korea, Canada, France, Denmark, India, Israeli and China), totaling 100.

SUMMARY

Why does China need to encourage drug innovation?

- **Drug innovation is fundamental to people's well-being.** For some diseases with high incidence in China such as liver cancer, there are limited innovative drugs available globally and pharmaceutical companies need to be encouraged to develop innovative drugs in China. For chronic diseases with a high prevalence (such as diabetes and cardiovascular diseases), innovation can help unleash productivity and reduce the burden on society. For infectious diseases, China needs to build strong innovation capabilities and emergency mechanisms to protect people's lives and health.

- **Drug innovation can provide enduring impetus for sustainable economic development.** Compared to machinery manufacturing and raw material processing industries, the pharmaceutical industry is a developing industry that features low energy consumption and high technology. Currently, China's pharmaceutical industry is still dominated by the manufacturing of generic drugs. Over the past decade, the industry has sustained a high growth rate of more than 15% per year, thanks to growing demand resulting from improving living standards and improving medical insurance coverage, rather than an upgrade of the industry structure. If the pharmaceutical industry structure cannot be adjusted and an innovation industry chain cannot be established in the next decade, China's pharmaceutical industry will lack momentum for further growth.

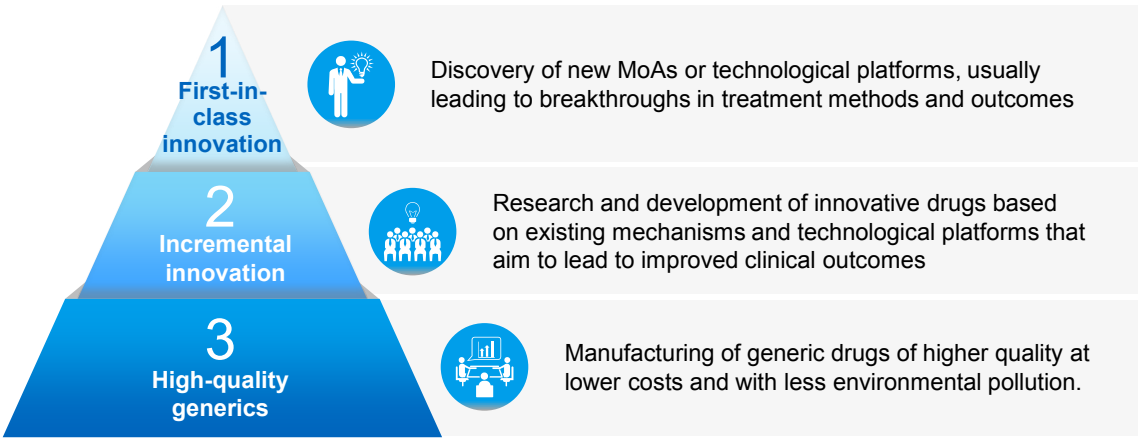
- **Drug innovation shows a country's core competitiveness:** drug innovation is a universal undertaking. In 2015, the global innovative drug market was worth almost USD 600 billion[2], to which China contributed less than USD 10 billion. Innovative products first launched in China accounted for less than USD 500 million in 2015 , with sales generated exclusively in China. China must rely on developing innovation to transform from a country with a sizeable pharmaceutical market to a country with a strong pharmaceutical industry.

China needs to plan for drug innovation at three levels. The top level is **first-in-class innovation**, which is most difficult and risky and entails identifying new mechanisms or technological platforms, and usually leads to breakthroughs in treatment methods and outcomes. The second level is **incremental innovation**, which is the research and development of innovative drugs based on existing mechanisms and technological platforms that aim to improve clinical outcomes. The drugs developed through first-in-class and incremental innovation are new molecular entities or new biotherapies. The third level is **high-quality generics**, that is, improving the production techniques of off-patent drugs. China needs to plan to develop all three levels of innovation. This means China needs to enhance drug accessibility by manufacturing generic drugs of higher quality at lower costs and with less environmental pollution. Meanwhile, China should also focus on first-in-class innovation and incremental innovation to grow from a fast follower into a leader to address the clinical needs of patients in China and around the world. The focus of this **report will be on first-in-class innovation and incremental innovation** (Figure 1).

2 IMS global medicine use

Figure 1

Three levels of innovation



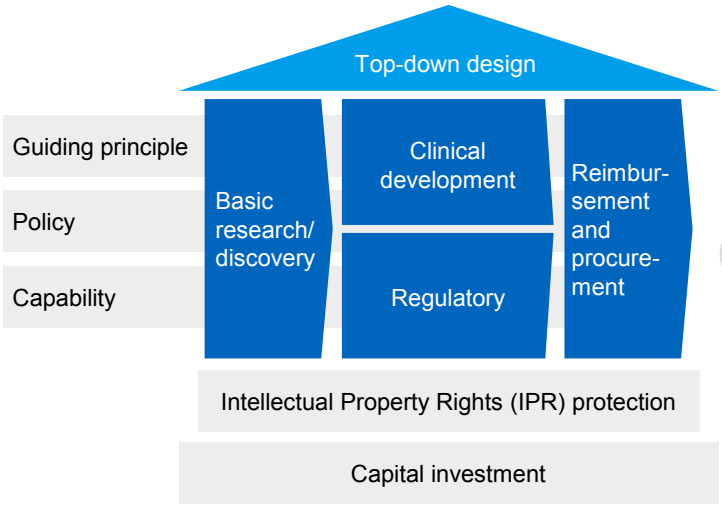
China's ecosystem of drug innovation has taken shape

The drug innovation industry chain is complex, has highly granular sub-components and involves many players. A strong and competitive drug innovation industry must rely on a healthy drug innovation ecosystem featuring a virtuous cycle. First, innovative drug R&D involves many government agencies and committees that cover regulatory, healthcare, medical insurance, finance and tax, scientific research, and others. Therefore, a **top-down design** at the central government level is critical, and should include a clear drug innovation strategy and coordination among various ministries and committees. All elements along the innovation chain, including **basic research / drug discovery, clinical research, regulatory, procurement and reimbursement** need to be supported by scientific **guiding principles**, sound **policies and mechanisms**, and strong capabilities from all parties. At the same time, **intellectual property rights protection** and **capital investment** mechanisms affect all elements along the industry chain (Figure 2).

China's overall policy environment for the pharmaceutical industry has significantly improved over the past two years. In the regulatory approval stage in particular, the China Food and Drug Administration has introduced a series of policy measures to encourage drug innovation (e.g., a pilot program for marketing authorization holders to promote contract manufacturing), optimize the review mechanism, enhance review capability, enhance review efficiency and improve drug quality. These reform measures, while recent, have already had a positive and far-reaching impact on the pharmaceutical industry. Benefiting from policy improvements, key industry talents have converged on drug innovation, enhancing the capabilities of all links along the industry chain. Furthermore, the industry has witnessed an accelerated influx of private capital and a rapid increase in the number of start-ups and investment size. **China's pharmaceutical industry demonstrates strong innovation momentum and an innovative drug ecosystem has begun to take shape.**

Figure 2

Key elements for innovation ecosystem



Sustainable innovation ecosystem

- **An invigorated value chain** with diversified innovative players; **economic reward for innovation**, incentivizing pharmacos and investors to continuously invest in R&D
- A pharma industry **highly integrated with global value chain**; international standards for R&D and regulatory are widely adopted, leading to **innovations of a global standard** that benefit patients throughout the world
- **An open ecosystem,** allowing diversified sources, participants and forms of innovations

In terms of innovation output, the number of articles published in high-quality life sciences journals rose from 4,000 in 2012 to more than 6,500 in 2015[3]. The number of innovative drugs in the clinical trial phase increased from 21 in 2011 to 69 in 2015[4]. The number of pipeline compounds hit 656 in 2015[5], indicating strong momentum in the foreseeable future. **The quantitative increase in innovation is as important as the qualitative enhancement in innovation.** While accelerating innovation speed and escalating the level of innovation, China's drug innovation is focused more on addressing unmet patient needs and improving the clinical value of drugs. Moreover, drug innovation is increasingly globalized, and a group of innovative pharmaceutical companies with a global vision is committed to developing globally new drugs, including conducting clinical trials and license transfers in overseas markets.

Challenges to the sustainability of China's drug innovation ecosystem

Although China's drug innovation has achieved significant progress in a short period of time, at the global level, China remains a third tier country in drug innovation. Measured by the number of pipeline drugs and new drugs launched, China is in the third tier, contributing around 4% to global drug innovations, lagging far behind the first tier the US (~50%) and countries in the second tier such as the UK and Japan. China's innovation-driven strategy proposes a vision of "becoming a leader among innovation-oriented countries by 2030". China's efforts to become a second tier or even first tier country are bound to raise the bar on ecosystem innovation.

3 According to Nature Index statistics of number of articles published in 68 high-quality science journals (including chemistry and biology).

4 Number of CTA (chemical drug class 1.1 and therapeutical biologics class 1) approved in that year.

5 NMEs (chemical drug class 1.1 and therapeutical biologics class 1) in pre-clinical, clinical trial I-III and NDA reviewing phase at the end of the year.

China's drug innovation ecosystem still has many weak links. The top bottlenecks in the coming 5-10 years will be in clinical research, regulatory, and reimbursement and procurement. If these elements are not improved significantly in the next 5 years, the pharmaceutical industry may lose the encouraging momentum it has gained.

- **Clinical research** is an irreplaceable step in innovative drug R&D and a phase that requires significant time and capital. Since review and approval timelines are being accelerated, clinical research has become a pressing issue, potentially limiting clinical value and time-to-market of new drugs under research. The challenges facing clinical research include varying quality and limited number of clinical trials, especially early stage trials, as well as shortages of resources in more capable clinical trial sites. The root causes of these challenges include: first, low public awareness of the ultimate goal of clinical research results in it not being positioned as a hospital's key responsibility. As such hospitals and doctors are less motivated to conduct clinical trials; second, the roles and responsibilities of clinical trial participants are not clearly defined, and overall capabilities need to be enhanced, especially in early phase clinical trials; third, Good Clinical Practice (GCP) certification inhibits the effective use of clinical resources and the regulation of clinical trial processes is insufficient; fourth, clinical trial approval (CTA) is time-consuming, with the process and standards failing to accord with the norms of innovative drug R&D; fifth, the Institutional Review Board (IRB) system is problematic in certain areas, such as low review efficiency and lack of regulation.

- **Regulatory** policies and legislation need further improvement, and the implementation of policies requires scientific guiding principles, reform of mechanisms and stronger capabilities. Currently, regulatory authorities have insufficient understanding and experience in science-based regulation, overstressing "zero tolerance of risk", while the review system shows gaps in the core values of good review practice (GRP), namely, "quality, efficiency, predictability, transparency, and consistency". Meanwhile, the development of policies and regulations lacks a more comprehensive mechanism to seek and review input from the general public, laws, regulations and technical guidelines are not updated in a timely way, and the number and scope of technical guidelines needs to be expanded. The organizational structure and processes of relevant review and approval departments are not optimized, resulting in low review efficiency. Although the regulatory reform has increased the number of reviewers, the total number of reviewers and their experience in reviewing innovative drugs remain limited. Further, shortcomings of the capability building system and compensation schemes also have an impact on improving reviewer capability and stability of review teams.

- **Procurement and reimbursement mechanisms** have a direct impact on the accessibility of launched innovative drugs to patients, and are crucial to maintaining the hard-won momentum in innovation. In the next 5 years, a large batch of innovative drugs will be launched in China. However, if they fail to deliver reasonable economic returns, pharmaceutical companies' enthusiasm for investing more in R&D will be dampened. At the central government level, the Reimbursable Drug List (RDL) is not updated with enough frequency and the process to select drugs eligible for reimbursement needs to be improved. At the local government level, a scientific and common approach to selection is lacking, and as surplus for medical insurance funds vary, the willingness to reimburse and relevant capabilities also differ. The private health insurance industry that is meant to provide supplementary funding is under-developed. Slow centralized procurement of innovative drugs further postpones patient access to innovative drugs and shortens the window for innovative drug manufacturers to obtain economic returns.

Top-down design at the central government level(of overall innovative strategy and scientific guiding principles and mechanisms) will provide a solid foundation a sustainable innovation ecosystem. In addition to clinical research, regulatory, reimbursement and procurement, three other elements should also be emphasized. **Basic research and drug discovery**, while not a main hurdle in the near term, are critical as a long term source of innovation. As innovative drug R&D is characterized by significant

investment, high risk, and long cycle length, **protection of intellectual property rights** is the foundation of the innovation industry and plays a key role in ensuring the sustainable development of the pharmaceuticals industry. However, the existing intellectual property rights system lacks systematic and consistent policies and has various challenges in practice. **Capital investment** has significantly improved in recent years, but does not fully reflect the stimulating effect that tens of billions of RMB in government funding should have on private capital investment.

Suggestions for building a sustainable drug innovation ecosystem

In the global R&D context and to develop a sustainable innovative drug industry in the next 10 to 20 years, a series of suggestions are hereby proposed for top-down design and six specific elements within the drug innovation ecosystem framework.

Top-down design

- **Ensure coordination and consistency between ministries and committees, and develop systematic and consistent laws and regulations:** development of drug innovation needs the establishment of a national innovation strategy that sets clear objectives and a roadmap that covers regulation, healthcare, medical insurance, taxation, finance and basic research. In implementing the innovation strategy, coordination and consistency between ministries and committees must be ensured. Efforts should be made to develop coordinated plans for the introduction and implementation of policies, with full consideration of the support needed by different elements of drug innovation.

- **Transform the government's role:** unreasonable administrative approval and unnecessary administrative intervention should be reduced and a fair and open competitive environment should be encouraged. A sound policy environment should be in place to guide capital investment and capability building.

- **Enhance industry communication and collective governance:** in the process of policy making, communication between government and industry should be strengthened, and communication mechanisms should be refined to systematically listen to industry opinions as well as review and refer to mature overseas experience. In implementing policies, industry feedback should be collected in a timely way and adjustments should be made when necessary. The communication mechanism should be normalized to ensure smooth communication channels.

- **Transform mindsets in all links along the industry chain:** the ultimate purposes and significance of clinical research should be correctly understood, and clinical research should be positioned as a key hospital responsibility. Science-based regulation should be established, with the GRP system that focuses on quality, efficiency, predictability, transparency and consistency, introduced and promoted. The standards and principles of regulation should be integrated at the international level, with ICH standards adopted and implemented, and the advanced standards and regulations of organizations such as FDA, EMA, PMDA and WHO referred to. There should be full recognition of the importance of the reimbursement and procurement system to ensuring returns on innovation and the sustainability of innovative industries, and the adoption of innovative drugs with high clinical value should be encouraged.

Basic research and drug discovery

- Encourage various parties in early R&D (including universities, research institutions, biotechnology companies, pharmaceutical companies, fund managers, and investors) to strengthen collaboration, reduce hurdles in technology sharing, promote industrialization of basic research results, thereby creating a professional, efficient innovation value chain. Enhance professionalism and transparency in managing scientific research funds and improve review and assessment mechanisms of scientific research funds.

- Identify and support more early R&D projects: Allocate some public funds to establish a seed fund that operates based on market mechanisms to stimulate venture capital investment in early R&D projects. Leverage the professional capabilities of private investment institutions to enhance professionalism in project selection, post-investment management and subsequent operational support.

- Activate and develop a well-regulated technology transfer market: Encourage universities and research institutions to build a technology transfer office. Refine the technology transaction process; based on existing preferential tax policies on technology transfer, further define the scope of technology so as to benefit technologies at different stages of R&D.

Clinical research

The development of clinical research and building its capabilities will require multiple government ministries and commissions (including the National Health and Family Planning Commission, China Food and Drug Administration, Ministry of Science and Technology, etc.) to change mindset, closely collaborate, and strengthen efforts to promote the improvement of systems and capabilities.

- Clarify clinical research as one of the important responsibilities of hospitals, improve people review and other HR policies to motivate hospitals and doctors to participate in high-quality clinical research.

- Effectively reduce restrictions around GCP certification, establish a multi-tiered system of clinical trial institutions, optimize allocation of clinical test resources and promote competition.

- Introduce a pilot program to establish central/regional IRB and improve efficiency of IRB reviews.

- Improve capabilities of all parties in clinical research by providing policy guidance, establishing capability building platforms, and fully leveraging talents and the spillover effect of ongoing R&D activities in multinational pharmaceutical companies.

- Refine relevant regulations to differentiate investigator-initiated trials (IIT) and industry-sponsored trials (IST) for registration purposes; optimize the process of IST application, simplify the data requirements and application process of clinical trial applications, increase flexibility of reviews.

Regulatory

Increase attention given to science-based regulation, ensure that the regulatory system is based on scientific guiding principles and a robust GRP system. Regulatory standards and principles should be well aligned with international practices, with international technical standards fully adopted and implemented.

- Improve the collective governance mechanism and increase transparency of policy making; refine regulations and technical guiding principles of review process; enhance and refine priority review mechanism.

- Shorten review time by optimizing organization structure, review process, and resource allocation of regulatory authorities (e.g. set up "Comprehensive CDE" and adopt a project based approach to reviewing new drugs); set budget targets, establish review systems with the rise of drug registration fees and accept public supervision.

- Establish a systematic capability building system, explore innovative services and compensation models to attract talent, and reinforce communication and cooperation with regulatory authorities of various countries and international organizations.

- Encourage pharmaceutical companies to play an active role in strengthening regulatory approvals, strengthen support and actively participate in building review capabilities of regulatory authorities, actively participate in collective governance, enhance their registration capability, develop and follow China's Good Submission Practice (GSubP).

Procurement and reimbursement

China should fully recognize the importance of the reimbursement system to rewarding innovation and ensuring sustainable development of innovation industries. China should further improve reimbursement and procurement mechanisms and support the use of innovative drugs of high clinical value.

- Accelerate updates to the National Reimbursable Drug List (at least once every two years) and ultimately realize dynamic updating of the list; set up a more scientific and clinical value-oriented assessment mechanism and optimize process management.

- Further improve local negotiation mechanisms for innovative drugs, normalize negotiations of high-value drugs for critical diseases.

- Remove bottlenecks in development of the private health insurance industry by promoting cooperation across ministries and committees including the National Health and Family Planning Commission, the Ministry of Human Resources and Social Security, and China Insurance Regulatory Commission, making medical data available to private health insurance companies, and strengthening the connections between insurers and medical institutions.

- Beyond government medical insurance and private health insurance, encourage attempts to develop innovative reimbursement models for high-value drugs.

- Optimize negotiation and procurement processes, accelerate online and supplemental procurement processes at the provincial level.

Intellectual property rights protection

Enhance four key areas (patent application, data protection, patent linkage system, and patent term extension system) to fully leverage intellectual property rights protection as a stimulant for drug innovation.

- Improve patent examination and ownership system: under appropriate conditions, the State Intellectual Property Office could expand the scope of patent applications, improve transparency and standardize the patent approval process.

- Promote the implementation of a data protection system: clearly define drugs with “new chemical components” that are subject to data protection. China Food and Drug Administration may allow the exclusivity of protected drugs for a given period by “not accepting or approving” new applications. Furthermore, set up a drug information disclosure platform to help implement data protection system.

- Improve the patent linkage system, including building a transparent and comprehensive drug information platform and establishing a system of patent claim and classification as well as a patent infringement complaint mechanism.

- Establish reasonable measures for extending patent term, promote interaction and cooperation between the China Food and Drug Administration and the State Intellectual Property Office, and establish patent term extension policy to offset losses incurred by drug approval.

Capital investment

Further stimulate enthusiasm for drug innovation through fiscal & taxation policies and private capital investment mechanisms.

- Develop fiscal and taxation policies specifically to promote drug innovation, including improving existing deduction policies and the taxation policy for encouraging technology transactions, reduce VAT on innovative enterprises/products, exempt VAT on pharmaceutical enterprises’ offshore services, and exempt tariff and import VAT on equipment imported by innovative pharmaceutical manufacturers.

- Further improve capital market policies to offer more exit options and adopt mechanisms to encourage participation of private capital.

Establishing a drug innovation ecosystem is a highly complex and systematic effort that requires strategic and holistic top-down design and close cooperation among ministries and commissions to address the deep-seated challenges across multiple fronts.

前言

创新驱动发展是国家十三五的核心战略，而医药产业是创新的支柱产业之一。医药创新不仅可为经济发展提供长久动力，同时也是解决民生问题的根本要求。纵观全球，具有生命力和竞争力的医药创新产业一定来自于健康的、良性循环的创新生态系统。由于医药创新周期长、风险高、投资大等特殊属性，政策、能力和投资三大要素在生态系统中缺一不可，相互作用。其中政策环境是生态系统中核心要素。鼓励创新的政策能够保证市场机制良好运转，推动资本和能力源源不断地把科技转化为创新产品。

在今天的中国，医药创新生态系统已经初步形成。过去两年间政策、能力和投资明显改善，而且三大要素之间初步形成了良性循环。受益于政策环境的改善，特别是药品审批制度改革，私人资本加速涌入，高层次产业人才加速聚集，中国的生物医药产业具备了良好的创新势头。在未来的十到二十年，提升医药创新对经济发展和民生的价值的关键是构建可持续发展的医药创新生态系统。

在这样的背景下，四家医药行业协会本着推进中国医药创新产业发展的目的，对中国医药研发展开调研，形成专门报告，为推进相关工作提供借鉴和参考。本报告基于医药创新生态系统的框架，在全球研发格局下对中国的研发现状和趋势进行审视；着眼于中国医药创新产业未来十到二十年的发展目标，从理念、政策机制和能力等层面探讨产业链各个环节阻碍创新的因素，包括顶层设计、基础研究、临床研究、监管审批、支付采购、知识产权保护和资本投入；同时，深入阐述其它国家在不断改善研发生态系统方面采取的具体做法和成效，为中国的实践提出参考；最后，就构建可持续发展的医药创新生态系统提出具体建议。

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医药创新需要政策、能力和投资三大要素共同作用的生态系统，包括鼓励医药创新的政策环境，多种来源资本的积极投入，以及专业的技术能力和广泛协作。经过十二五期间的努力，中国初步形成了医药创新生态系统的良性循环，生物医药产业具备了良好的创新势头。在这样的背景下，本项目着眼于一系列中国医药创新产业值得进一步思考的问题：

中国医药创新的“量”保持快速增长势头，而创新的“质”如何得以提升？“十二五”期间获得新药证书的一类新药数量达到17个，2015年在研化合物数量达到656个，预示着未来强劲的发展势头。在创新产出的“量”不断增长的同时，如何推动创新药物解决更多的病人未被满足的临床需求，并不断提升创新程度和全球化程度？

国家创新驱动战略提出“至2030年跻身创新型国家前列”的愿景，而目前中国在全球新药研发格局中处于第三梯队，向第二和第一梯队迈进对中国医药创新生态系统的建设提出了怎样的要求？中国目前处于第三梯队，对全球医药创新的贡献大约为4%[1]，与第一梯队的美国（大约50%[1]）和第二梯队的国家仍有很大差距

过去两年，医药创新的政策环境（特别是药品审评审批）已有改善，还有哪些政策需要进一步改变？在理念、机制和能力层面上需推动哪些变革才能确保政策的实施步骤清晰、协调一致？鉴于创新生态系统的复杂性，新政策的推出并非能够解决所有深层次问题；而且若缺少系统性的规划，不同方面的政策有可能缺乏一致性

着眼未来五年，生态系统中哪些环节最为薄弱并可能成为制约创新的最大瓶颈？如何具有前瞻性地解决这些问题？过去五年生态系统最大的瓶颈是监管审批；随着监管环境的改善，并考虑到研发周期，未来在研发产业链的其它环节（如临床，支付）可能出现新的瓶颈，对研发成果和持续投入的积极性形成风险

着眼未来十到二十年，如何确保创新生态系统具有强劲的创新源头动力？医药研发属于科学研究型创新，不同于其它很多行业的创新类型（如工程技术型、客户中心型、效率驱动型），必须基于长期积累的科学研究

1 以上市前研发（至2015年底）和新药上市数（2007-2015年）来衡量；如全球主要医药研发国家总和为100（包括美国、日本、英国、德国、瑞士、韩国、加拿大、法国、丹麦、印度、以色列和中国），其中各个国家各自所占比例

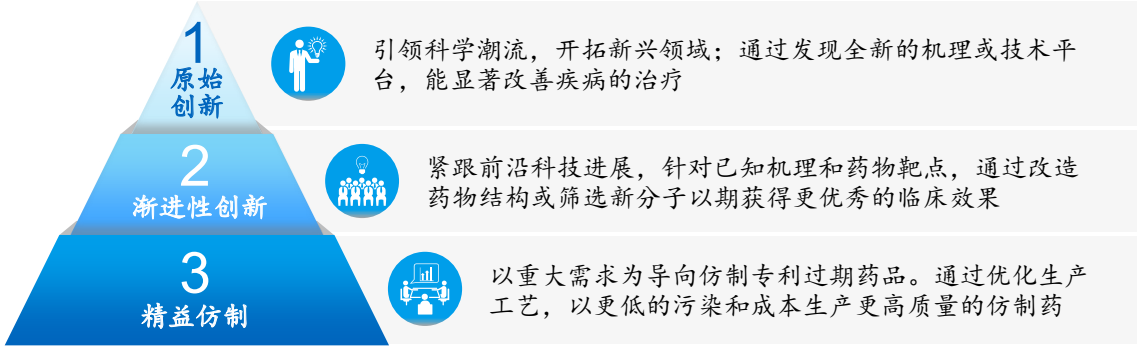
概要

中国为什么要大力发展医药创新?

- **医药创新是解决民生问题的根本需要。**对于在中国发病率较高的一些疾病（如肝癌），在全世界范围内都缺少创新药，需要鼓励医药企业在中国进行创新研发；对于患者基数巨大的慢病和重病（如糖尿病，心脑血管疾病），创新可以释放社会生产力并减轻社会负担；对于突发性传染病，中国需要建立起强大的创新能力和应急机制，保护人民生命健康。
- **医药创新可为经济可持续性发展提供长久动力。**与机械制造、原材料加工等行业相比，医药产业是低能耗、高科技的朝阳产业。中国医药产业目前仍然是以仿制药生产为主。过去十年医药产业年均15%以上的高速增长，主要得益于人民生活水平提高而释放的健康需求和医保覆盖，而非产业结构升级所致。如果不能在今后十年调整医药产业结构，建立起创新产业链，中国医药产业的发展将后劲不足。
- **医药创新体现国家的核心竞争力：**医药创新是无国界的。2015年全世界创新药的市场近6000亿美元[2]，其中中国市场占了不足100亿美元。而其中在中国首发上市的创新产品贡献不到5亿美元，且这些产品的销售全部来自于中国市场。中国必须依靠发展创新产业，实现从医药大国向医药强国转变。

中国需要在三个层次的医药创新上布局。最高层次为**原始创新**，是难度最高、风险最大的创新，原始创新药物是对全新机理或技术平台的发现，往往能够在疾病的现有治疗手段和水平上获得突破。第二个层次为**渐进性创新**，即紧跟前沿科技进展，针对已知机理和药物靶点，通过改造药物结构或筛选新分子以期获得更优秀的临床效果。原始创新和渐进性创新的药物都属于新分子实体或新生物疗法。第三个层次为**精益仿制**，即针对专利过期药品实现工艺改善。中国未来需要同时在三个层次上布局，即通过精益仿制，以更低的成本和环境污染生产更高质量的仿制药，增加药物可及性；同时聚焦原始创新和渐进性创新，并逐步实现从快速跟随变为领跑者，解决中国和全球病患的未满足临床需求。**本报告关注的重点是原始创新和渐进式创新这两个层面**（图1）。

图 1
创新布局的三个层次



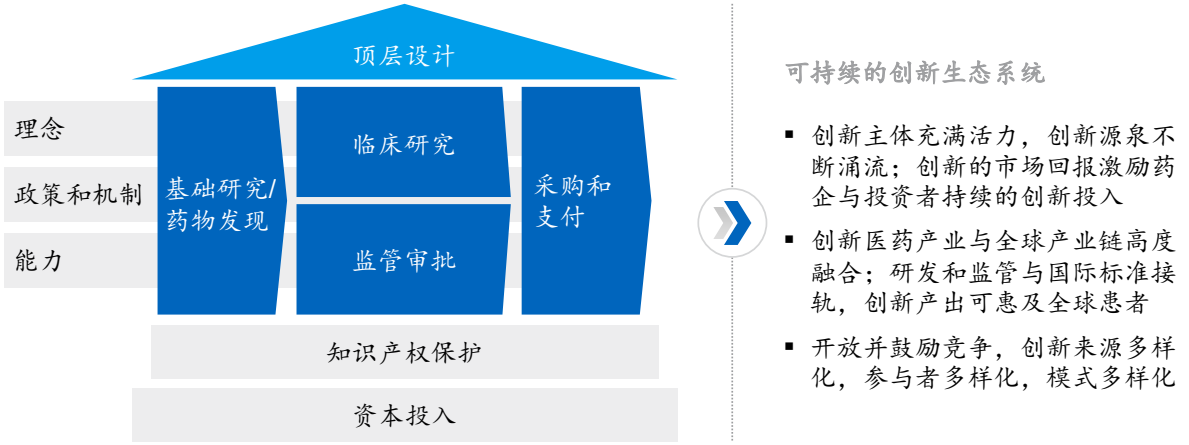
2 IMS global medicine use

中国医药创新生态系统初步形成

医药创新产业链复杂，分工高度细化，涉及主体繁多。具有生命力和竞争力的医药创新产业一定来自于健康的、良性循环的医药创新生态系统。首先，创新药研发涉及多个部委和监管机构，涵盖监管、卫生、医保、财政税收、科研等各方面，因此，国家层面的顶层设计至关重要，包括清晰的医药创新战略和部委间的统一协调。在产业链的各个环节，包括基础研究和药物发现、临床研究、监管审批和采购与支付，都需要科学的理念、完善的政策和机制以及参与各方的能力作为支撑。而知识产权保护和资本投入机制贯穿产业链各个环节（图2）。

图 2

创新生态系统要素



过去两年中国医药整体的政策环境有了明显改善。特别是在监管审批环节，食药监总局出台了一系列政策措施，鼓励医药创新（如上市许可人制度试点），优化审评机制，提升审评能力，提高审评效率，提升药品质量。这些改革举措对医药行业产生了积极而深远的影响。受益于政策的改善，高层次产业人才加速聚集医药创新，产业链各环节的能力有所提升；而且私人资本加速涌入，初创企业数量和融资体量增长迅速。中国医药产业具备了良好的创新势头，医药创新生态系统已经初步形成。

以创新产出来看，中国发表在生命科学高质量期刊上的文章数量从2012年的4,000余篇增加到2015年的6,500余篇[3]；进入临床阶段的创新药从2011年的21个增长到2015年的69个[4]，在研化合物数量2015年达到656个[5]，预示着未来几年强劲的发展势头。与创新“量”的增长同样重要的是创新“质”的提升。在不断加快跟踪创新速度和提高创新程度的同时，中国的创新研发对未满足的病人需求和药物的临床价值更加关注。而且医药创新全球化程度不断提高，一批具有国际视野的创新型医药企业正在致力于开发全球性新药，包括中国境外市场的临床试验和产品许可转让。

3 来自于Nature Index 统计的发表在68个高质量科研杂志中的文章数量，包括化学和生物学科杂志

4 当年获批临床的化药1.1类和治疗用生物1类分子数；数据来源为GBI

5 2015年在中国处于临床前、临床I-III期及上市注册（未上市）期的化合物数量；数据来源为Pharmaprojects

中国医药创新生态系统可持续发展的主要挑战

中国医药创新虽然在短时间内取得了很大进展，但在全球创新的格局下来看，仍处于医药创新的第三梯队。以上市前研发和新药上市数来衡量，中国目前处于第三梯队，对全球创新的贡献大约为4%，与第一梯队的美国（大约50%）和第二梯队的国家（如英国、德国、日本等）仍有很大差距。国家创新驱动战略提出“至2030年跻身创新型国家前列”的愿景，未来中国医药创新向第二甚至是第一梯队迈进必然对创新生态系统的建设提出了更高的要求。

当前中国医药创新生态系统中还存在诸多薄弱环节。今后5-10年最大的瓶颈问题集中在临床研究、监管审批和支付环节。如果这些要素没有在今后五年得到显著改善，医药行业将有可能失去当前来之不易的良好创新势头。

- **临床研究**是创新药研发过程中无法替代的一步，也是投入时间和资金最多的阶段。审评审批加快之后，临床研究的机制和能力问题变得愈发突出，对在研新药的临床价值和上市速度可能起到极大的制约作用。临床研究的当前挑战集中表现在临床试验质量参差、数量偏低（尤其是早期临床数量）以及高水平临床试验机构资源紧张，特别是部分研发热门领域和专业。导致这些问题的深层次原因包括：社会各界对于临床研究根本目的的认知程度很低，没有意识到临床研究是发展医学水平、满足未满足临床需求的必经途径，没有将临床研究明确定位为公立医院的重要职责之一，医疗机构和医生从事临床试验的动力不足；临床试验参与各方权责不清，且各方的综合能力有待提升，其中早期临床相关能力尤其薄弱；临床试验机构资格认证限制了临床资源的有效利用，同时临床试验过程监管不足；临床准入审批（IND）耗时长，且流程和标准不符合创新药研发规律；部分伦理委员会存在审评效率低和监管缺失等问题。

- **监管审批**的相关政策和法律法规仍需继续完善；同时，政策的落实需要科学理念、机制改革和能力提升的配套支持。在理念方面，当前社会各界对医药创新研发风险的认知水平不足，从公众到媒体都缺乏对研发过程中的科学探索精神以及相关风险的关注和重视，公共教育和宣传非常匮乏。监管部门对科学监管理念的认识及经验不足，风险管控机制不够完善，过度追求“零风险”。在机制方面，当前的审评体系相较于GRP（审评质量管理规范体系）的核心价值——“质量、效率、可预见性、透明、一致”仍有较大差距。同时，政策法规的制定过程中缺乏社会共治机制，且法律法规及技术指南更新不及时，技术指南的数量和涵盖范围有待增加。审评审批相关部门的组织架构与流程不够优化，导致审评效率较低。在能力方面，药审改革逐步增加了审评人员的数量，但人员总量及创新药审评经验水平仍然不足；而能力培养体系的缺失和不合理的薪资水平也影响了审评人员能力提升和审评队伍的稳定性。

- **采购和支付机制**直接影响到病人对已上市创新药的可及性，并且对保持行业来之不易的创新动力十分关键。未来五年内将有一批创新药获批上市，若不能及时获得合理经济回报，会严重打击企业对研发持续投入的积极性，在中央层面，医保目录更新不及时，且目录遴选方法有待改进。在地方层面，缺乏科学统一的遴选方法；且由于医保资金盈余参差不齐，报销创新药的意愿和能力存在差异。本应作为重要的补充资金来源的商业健康险体系尚不健全。而创新药的集中采购进度缓慢进一步拉长了创新药惠及患者的时间和创新药企业获得经济回报的周期。

当然，国家层面的**顶层设计**（包括创新总体战略、科学的理念和机制等）是可持续发展的生态系统的基础。而除了临床研究、监管审批和支付采购机制之外，生态系统的其它三个

要素也不容忽视：**基础研究和药物发现**虽然短期内不是最主要的制约因素，但对于着眼长期的原始创新至关重要；由于创新药研发的高投入、高风险、长周期等特性，**知识产权保护**是创新性产业的根基，对于医药产业的可持续发展尤为重要，而目前的知识产权制度不仅在法规层面仍然缺乏系统性和一致性，在实际操作和执行过程中也存在诸多问题：**资本投入**近几年已有很大增长，但尚未充分地体现数百亿政府资金可起到的对私人资本投入的催化作用。

构建可持续发展的医药创新生态系统的主要建议

在全球研发格局的大背景，着眼于中国医药创新产业未来十到二十年的可持续发展，基于医药创新生态系统的框架，对顶层设计及六大要素提出一系列具体建议：

顶层设计

- **确保部委间协调一致和法律法规的系统性和一致性：**医药创新的发展，需要制定国家层面的创新战略，目标明确，步骤清晰，涵盖监管、卫生、医保、税收、财政、科研等各环节。创新战略实施过程中，应确保部委间协调一致；在政策出台和落实过程中统筹规划，充分考虑促进医药创新各环节所需要的支持。
- **转换政府角色：**减少不合理的行政审批和不必要的行政干预，鼓励公平、开放的竞争环境，通过建设良好的政策环境来引导资本投入和能力建设。
- **加强行业沟通和社会共治：**在政策制定过程中，加强政府与行业间沟通，并完善沟通机制，系统地听取行业意见，充分论证并参考国外成熟经验；在政策执行过程中，及时收集行业反馈，并做出必要调整；将沟通机制常态化，保持多种沟通渠道的顺畅。
- **在产业链各环节转变理念：**正确认识临床研究的根本目的和重要性，将临床研究的定位上升到医院的重要职责之一；贯彻和实践基于科学的监管理念，认识到新药研发的风险性，加强对新药研发的公共教育并完善风险管控机制，引入和推行以“质量、效率、可预见性、透明、一致”为核心的GRP体系；监管标准和原则与国际接轨，采纳并执行ICH（国际协调会议）标准，同时借鉴FDA（美国食品与药物管理局）、EMA(欧洲药物管理局)、PMDA（日本药品与医疗器械管理局）和WHO（世界卫生组织）等机构的先进标准和规范；充分认识支付体系对于创新回报和创新产业持续发展的重要性，鼓励具有高临床价值的创新药的使用。

基础研究和药物发现

- 促进早期研发的各参与方（包括高校、研究机构、生物技术企业、药企、基金管理和投资机构）加强互相协作，减少技术流通障碍，促进基础研究向产业的转化，从而形成专业化、高效率的创新产业链。加强科研基金管理的专业性和透明性，完善科研基金评审和考核机制。
- 发掘并支持更多早期项目：分拨部分公共资金成立以市场机制运作的种子基金，撬动风险资本投资早期研发项目；借助私立投资机构的专业实力，加强项目筛选、投后管理和后续运营支持的专业性和效率。

- 激活和发展规范的技术交易市场：鼓励高校和研究机构建立技术转移办公室，规范技术交易过程，鼓励科技成果转化；完善鼓励技术交易的税收政策：在现有技术转让税收优惠政策的基础上，进一步明确受惠技术的范围，从而让处于研发不同阶段的技术转让也可以受益。

临床研究

临床研究的发展和能力建设需要各部委（包括卫计委、食药监总局、科技部等）转变观念，统筹配合，加大力度推动体系完善和能力提升：

- 明确临床研究是医院的重要职责之一，并改进考核和人事制度以提高医院和医生从事高质量临床研究的积极性。
- 有效放开临床试验机构GCP 认证，建立多层级的临床试验机构体系，优化临床试验资源配置，同时引入竞争。
- 设立中心或区域伦理委员会制度试点，提高伦理委员会审查效率。
- 通过政策引导和搭建平台，同时充分利用跨国药企人才和研发活动的溢出效应，多种方式提升临床研究参与各方综合能力。
- 应从法规入手，明确区分研究者发起的临床试验（IIT）和以注册为目的的由药企发起的临床试验(IST)；其次，优化由药企发起的临床申请的流程,简化临床申请的数据要求和申请流程，并增加审评灵活度。

监管审批

提高对监管科学的重视，监管体系要建立在基于科学的监管理念和合理规范的审评质量管理体系（GRP）的基础之上；监管标准和原则与国际接轨，全面采纳并执行国际技术标准：

- 完善政策制定过程中的社会共治机制，增加透明度；完善法律法规及审评技术指导原则，丰富和完善优先审评机制。
- 优化监管机构组织架构（如“大药审中心”，以项目组形式开展新药审评）和审评流程与资源配置，缩短审评时间；随着药品注册费用的提高，设定预算目标和评估体系，并接受公众监督。
- 建立系统的能力培养体系，探索创新服务和薪资模式以吸引人才，并加强与各国监管机构和国际组织的交流合作。
- 企业在加强监管审批中也应发挥积极作用，大力支持并积极参与药监部门的审评能力建设，积极参与监管的社会共治，提升注册能力，建立并遵守中国的良好注册规范（Good Submission Practice, GSubP）。

采购和支付

充分认识支付体系对于创新回报和创新产业持续发展的重要性，完善采购和支付机制，支持具有高临床价值的创新药的使用：

- 加快医保目录更新的频率（至少每两年一次），并最终实现动态更新目录； 建立更加科学、临床价值为导向的评估机制，同时优化流程管理。
- 进一步鼓励和完善创新药地方谈判机制，推进针对重大疾病的高价值药品的谈判常态化。
- 针对制约商业健康险发展的瓶颈，促进包括卫计委、人社部和保监会等在内的跨部委协作，开放商业健康险所需的医疗数据，并加强保险机构与医疗机构的衔接。
- 鼓励医保和商业健康险之外的、针对高价值药品创新支付模式的尝试。
- 优化谈判采购流程，加快省级挂网和备案采购进度。

知识产权保护

建议从专利申请、数据保护执行、完善专利链接制度和建立专利期延长制度四个方面着手，发挥知识产权保护对医药创新的激励作用：

- 改进专利审批及所有权制度：知识产权局应当在一定条件下，允许通过合理概括适当扩大专利的申请范围；并推进专利审批过程的规范化与透明化。
- 推动数据保护制度执行：将受数据保护的“新型化学成份”的药物明确定义，食药监总局可通过“不受理、不批准”授予受保护药品一定时期的市场独占权，同时建立药品信息公示平台，帮助数据保护制度落地。
- 完善专利链接制度，包括搭建透明全面的药物信息平台，建立专利声明分类制度和专利侵权可诉机制。
- 制定合理的专利延长期限确定办法，并促进食药监总局与知识产权局的联动合作，推动专利期延长制度的建立以弥补药品审批带来的损失。

资本投入

从财税政策和私人资本投资机制两个方面，进一步激发医药创新的积极性：

- 针对医药创新的财税政策建议，包括完善现有“加计扣除”政策，完善鼓励技术交易的税收政策，降低创新企业或创新产品的增值税，免除医药企业境外服务的增值税，免除医药创新企业进口设备的关税和进口增值税，扩大医药创新企业亏损的抵扣年限。
- 进一步完善金融市场制度，增加退出选项，从机制上鼓励私人资本的参与。

构建医药创新生态系统是一项高度复杂的系统工程，需要战略性、全局性的顶层设计，以及各部委之间的密切配合，才能解决各个环节面临的深层次挑战。