Ecosystem for fostering Pharma Innovation- recent lessons from China

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TFDA ASEAN DRUG REGULATORY SYMPOSIUM
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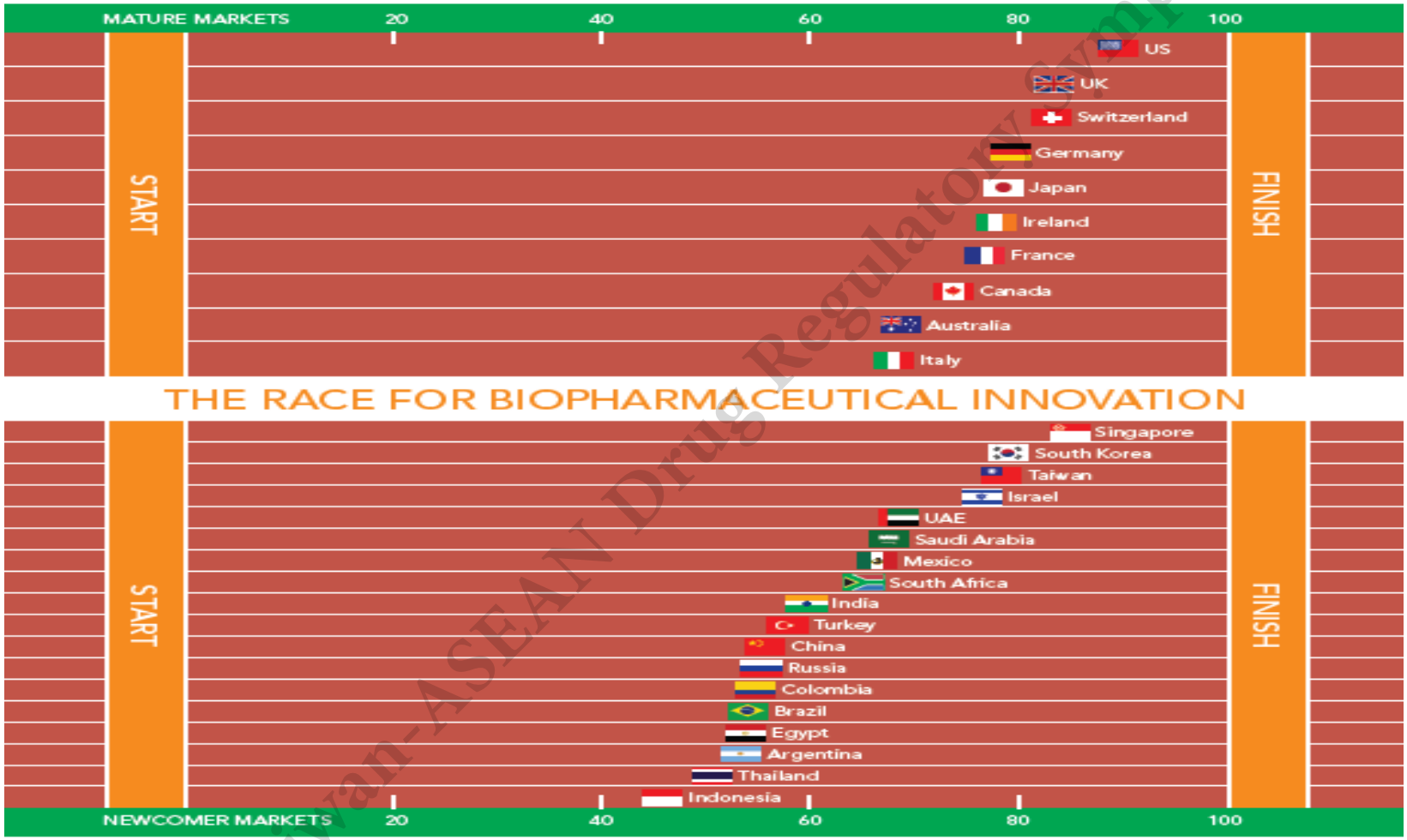
Content

- **Biopharmaceutical competitiveness and investment survey report**
- ICC on innovation ecosystem for high tech industry in 2015
- Lessons from China experience
  - 2014 eco-system for fostering pharma innovation
  - Improvement in last two years
- Key Messages to take away

世界生物醫藥產業競爭力與投資環境評比摘要-2016

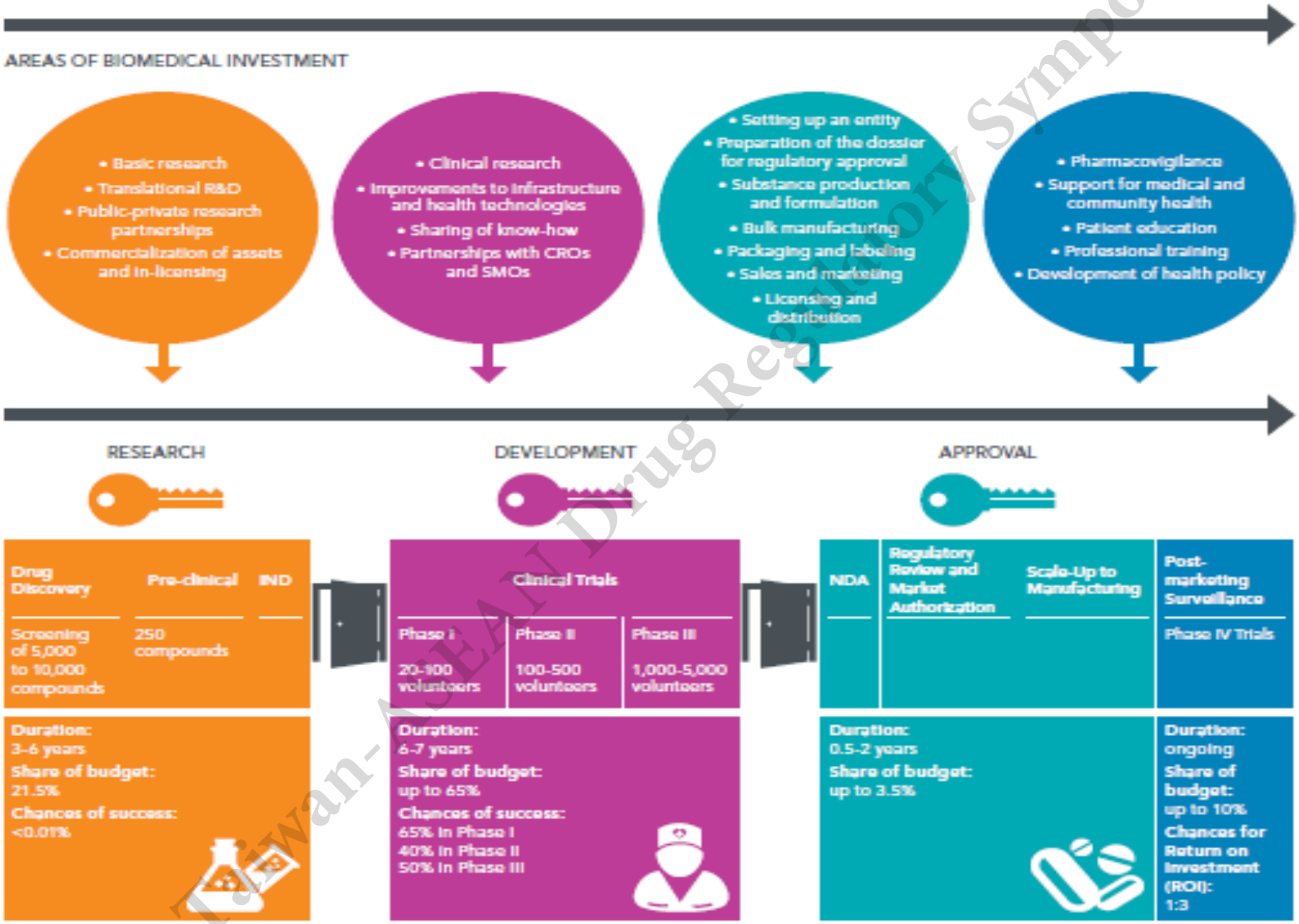
Selected summary from Biopharmaceutical Competiveness and Investment survey report -2016

The race for biopharmaceutical innovation



Biopharmaceutical Competitiveness & Investment (BCI) Survey, Third Edition, 2016

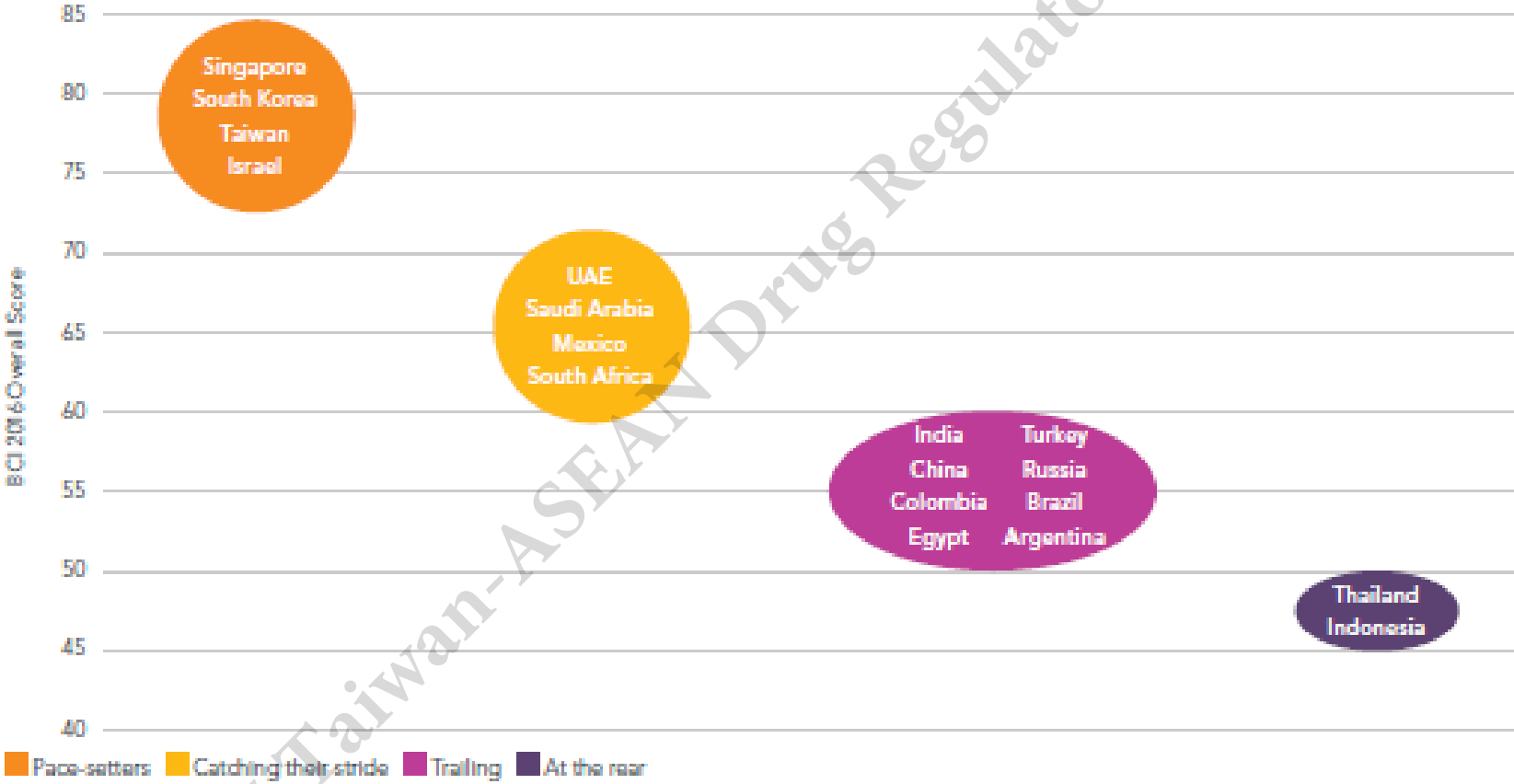
FIGURE 1 The range and value of investment across the biopharmaceutical R&D pipeline



Source: Pugatch Consilium; adapted from PhRMA and Nature[22]

New comers – The race for biopharmaceutical Innovation

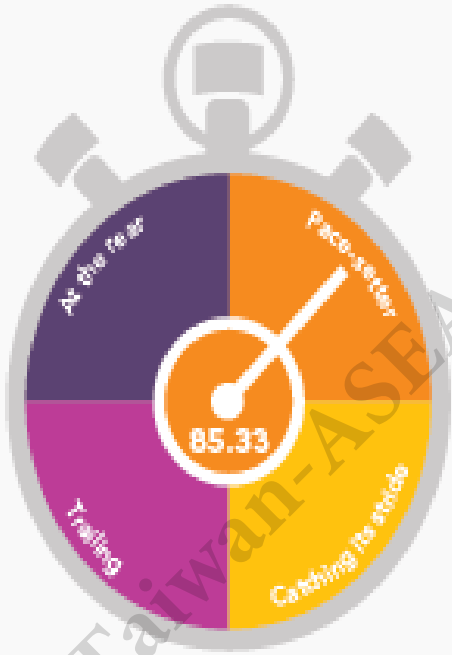
FIGURE 4 The race for biopharmaceutical innovation: Who is sprinting ahead and who is trailing among newcomer markets? - BCI 2016 Overall results

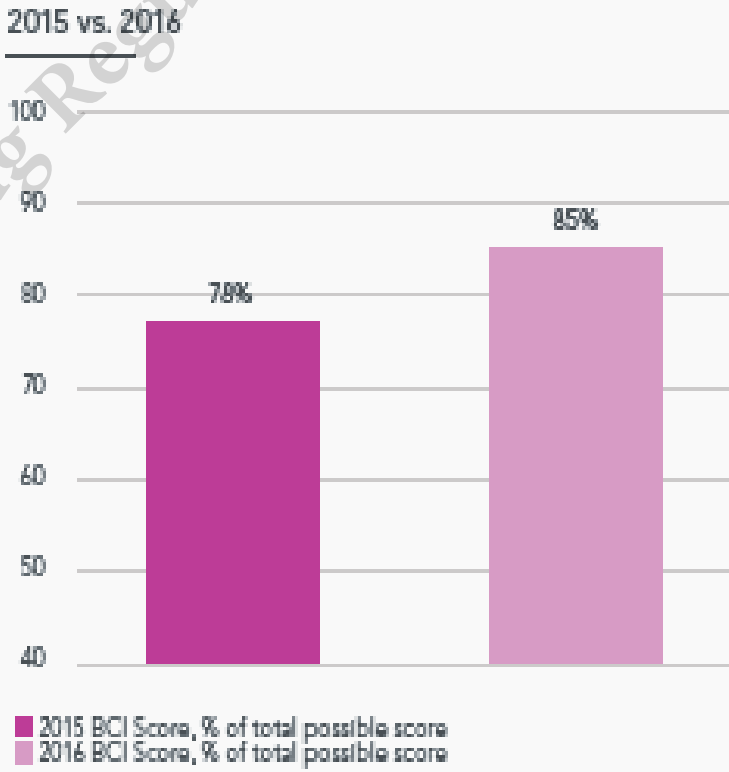


Singapore- BCI survey overall Scores 2016

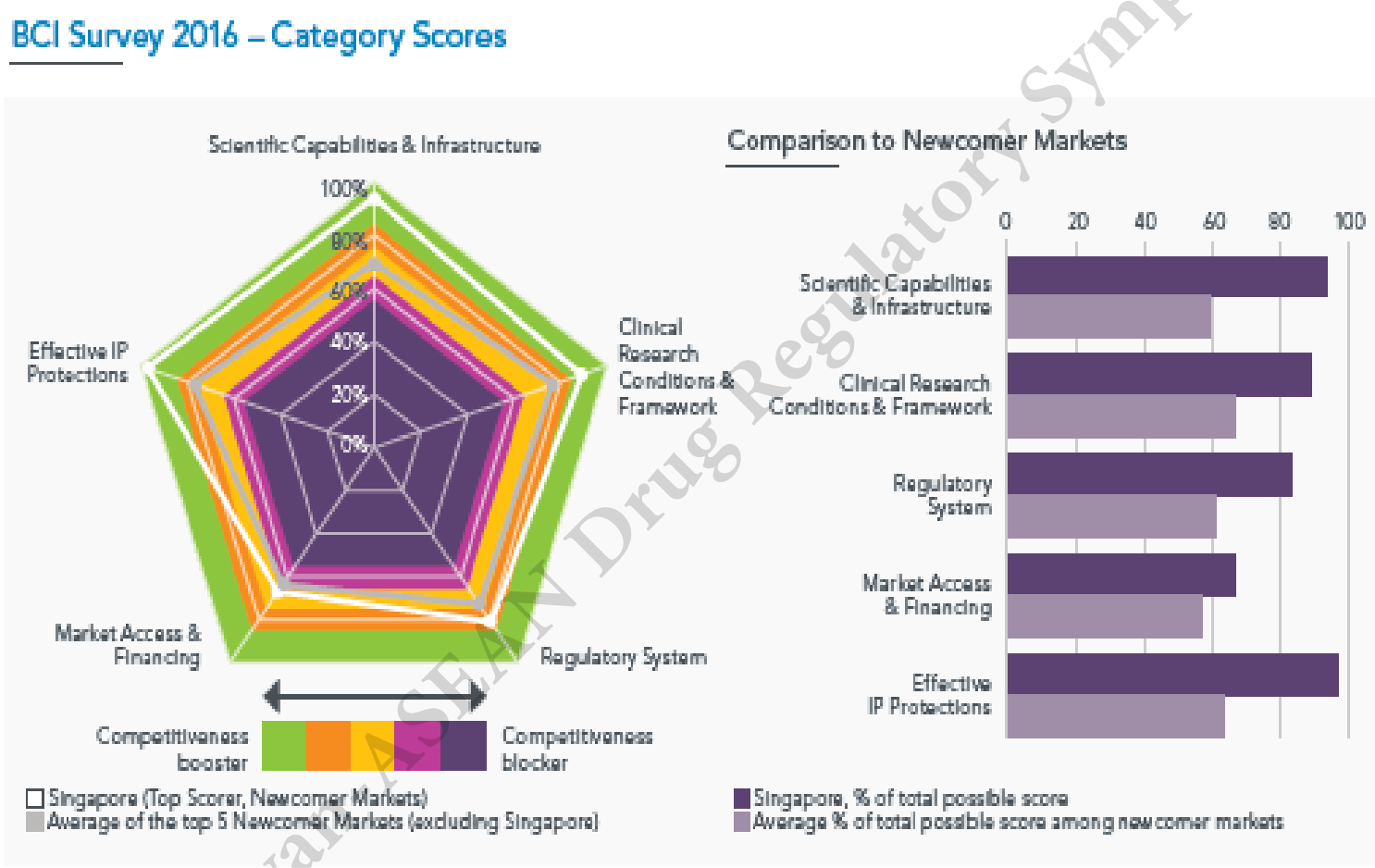
SINGAPORE

BCI Survey 2016 – Overall Scores





Singapore BCI Survey Category Scores 2016



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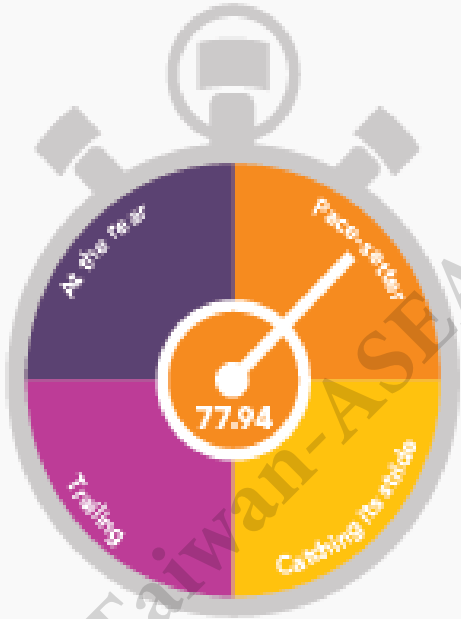
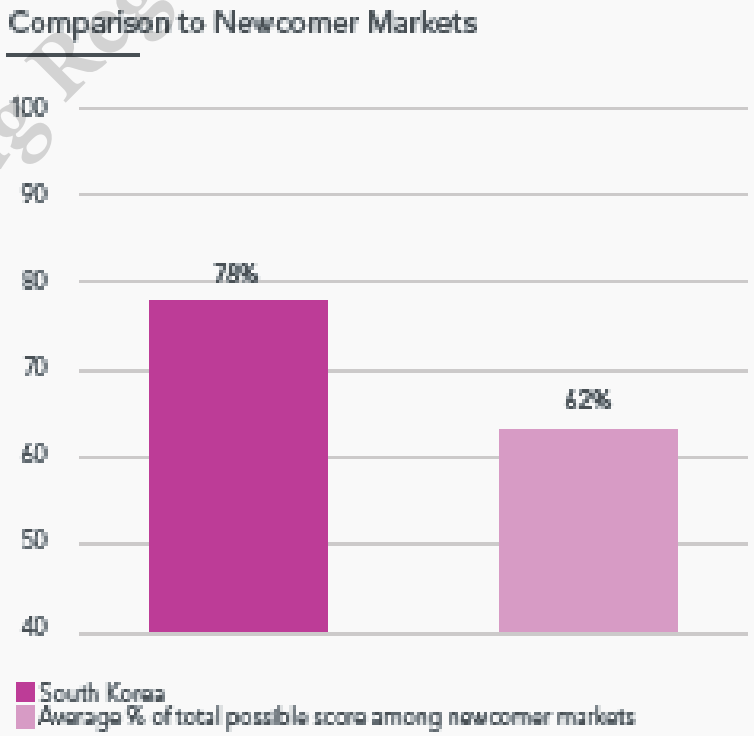
South Korea BCI survey overall scores 2016

SOUTH KOREA

BCI Survey 2016 – Overall Scores





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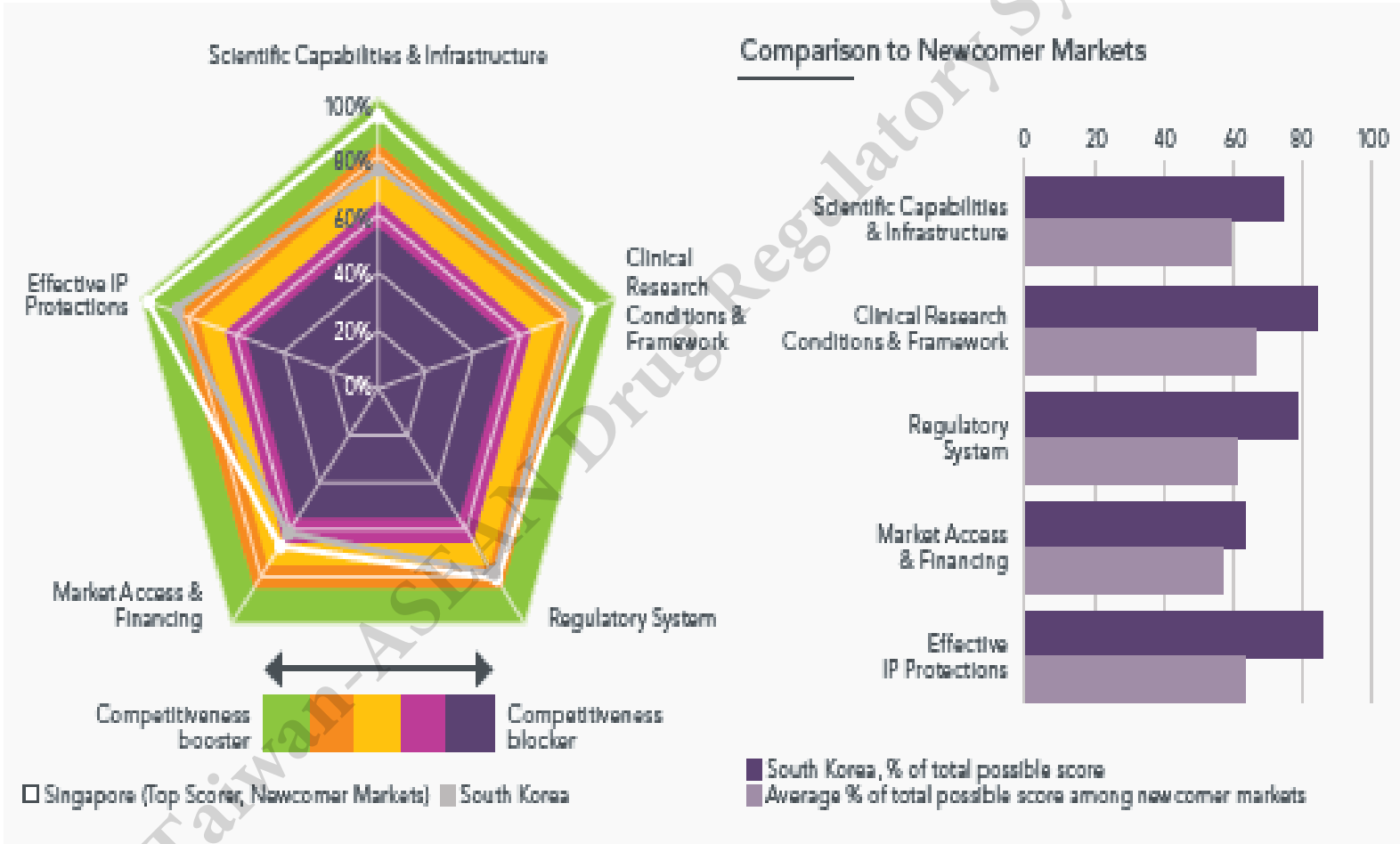
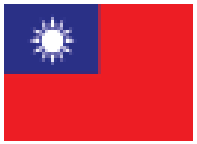
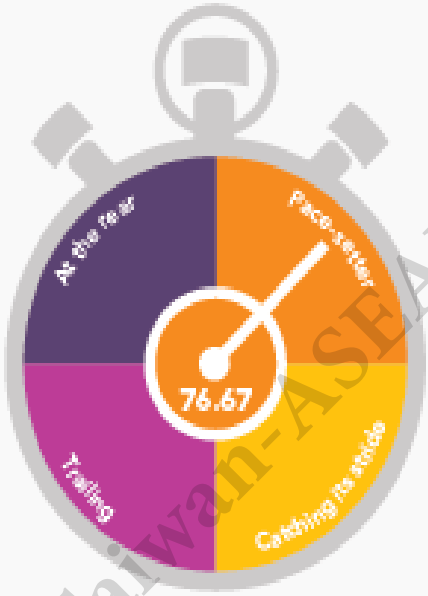


Taiwan BCI Survey overall scores 2016

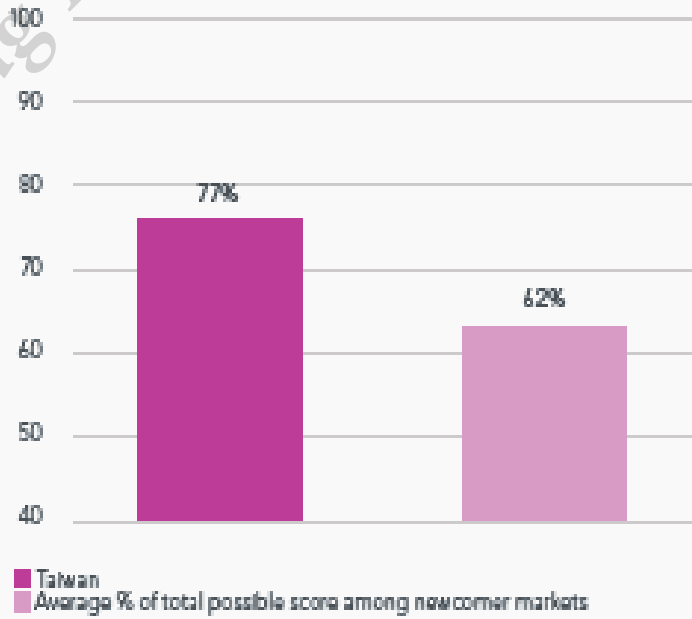


TAIWAN

BCI Survey 2016 – Overall Scores



Comparison to Newcomer Markets



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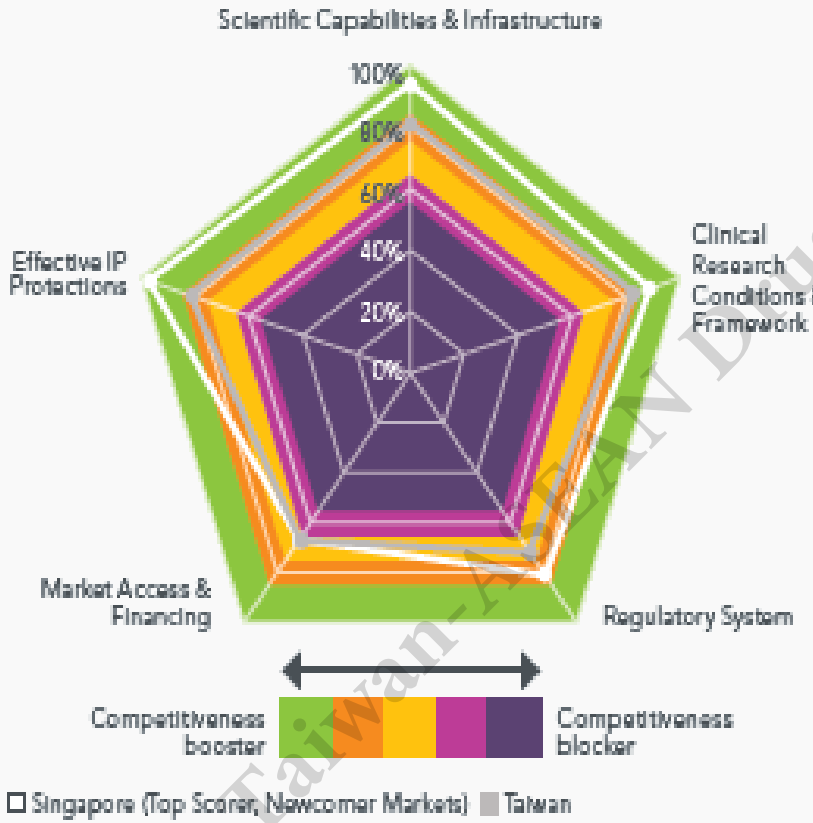

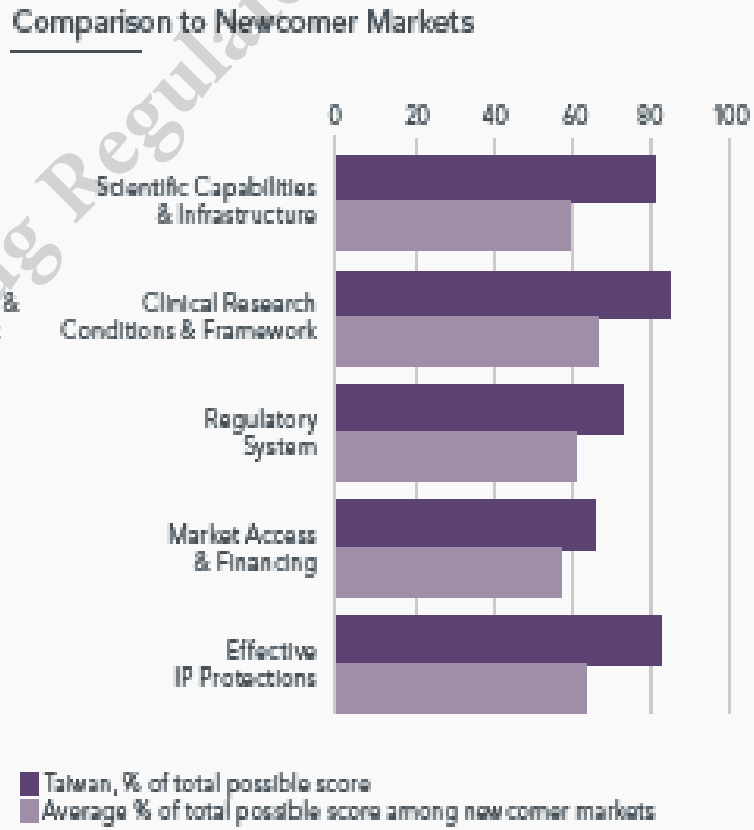

China BCI survey overall scores 2016

CHINA

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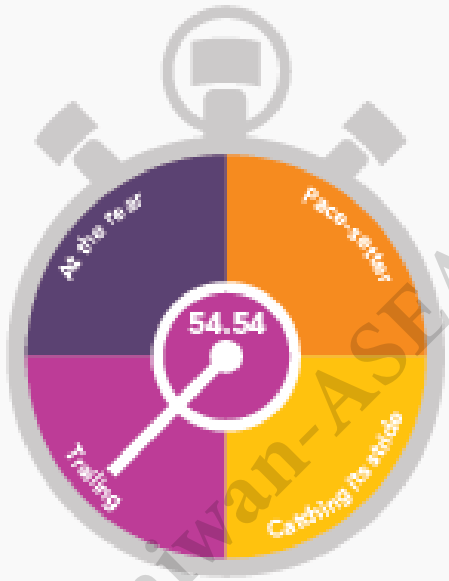
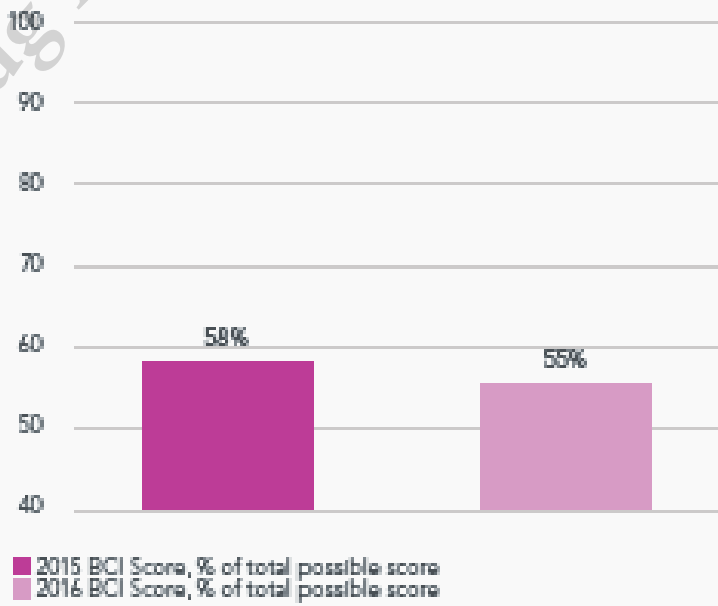


2015 vs. 2016



BCI Survey 2016 – Category Scores

China BCI survey Category scores 2016

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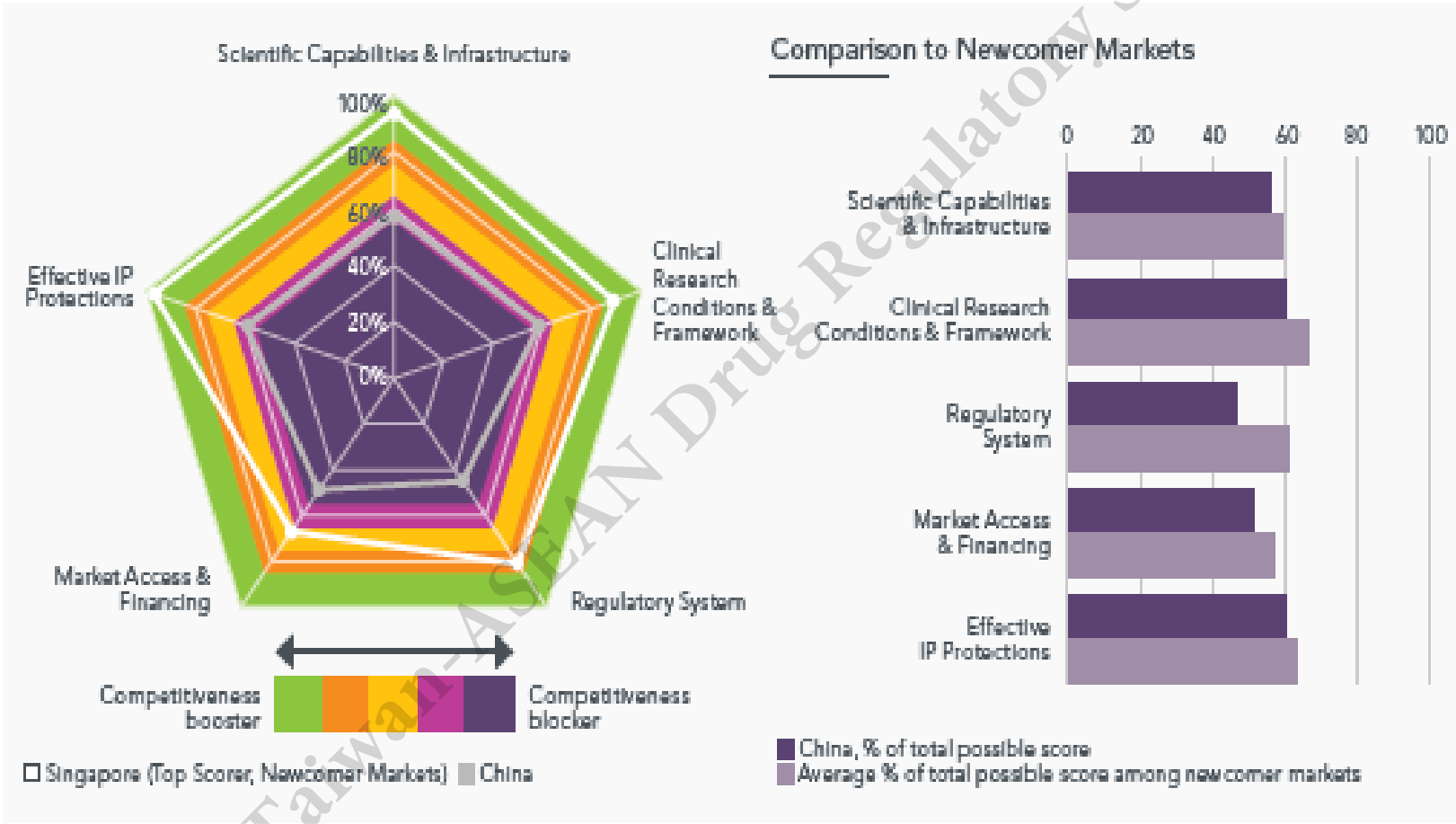
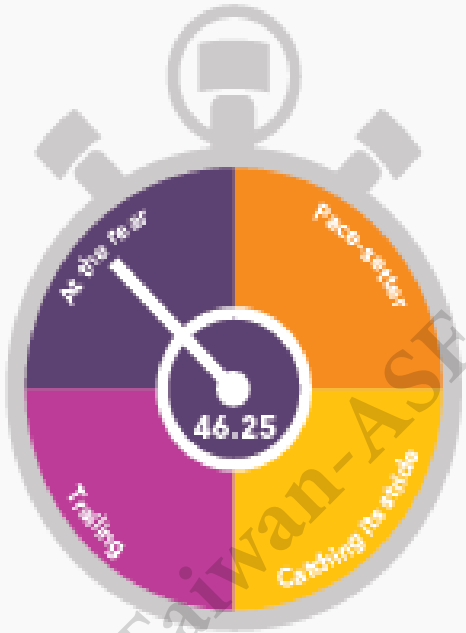


Indonesia BCI Survey Overall Scores 2016

INDONESIA

BCI Survey 2016 – Overall Scores



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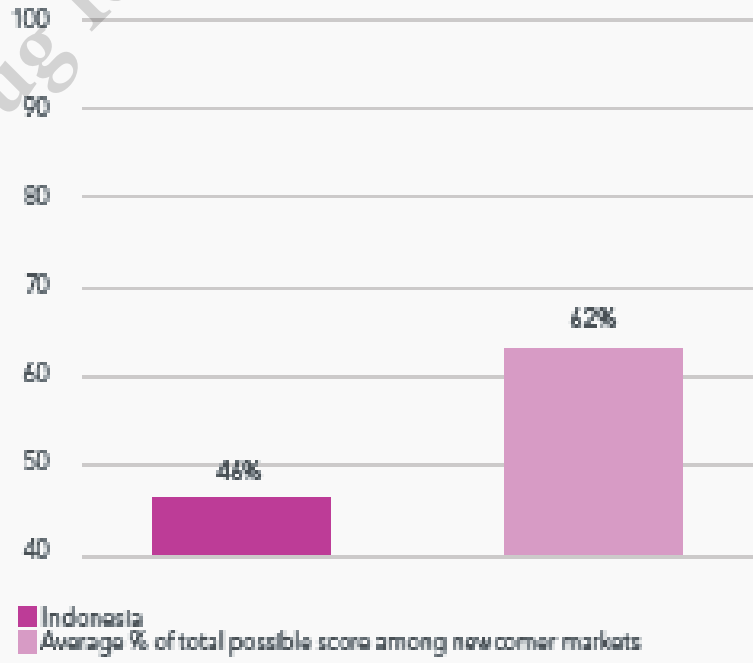

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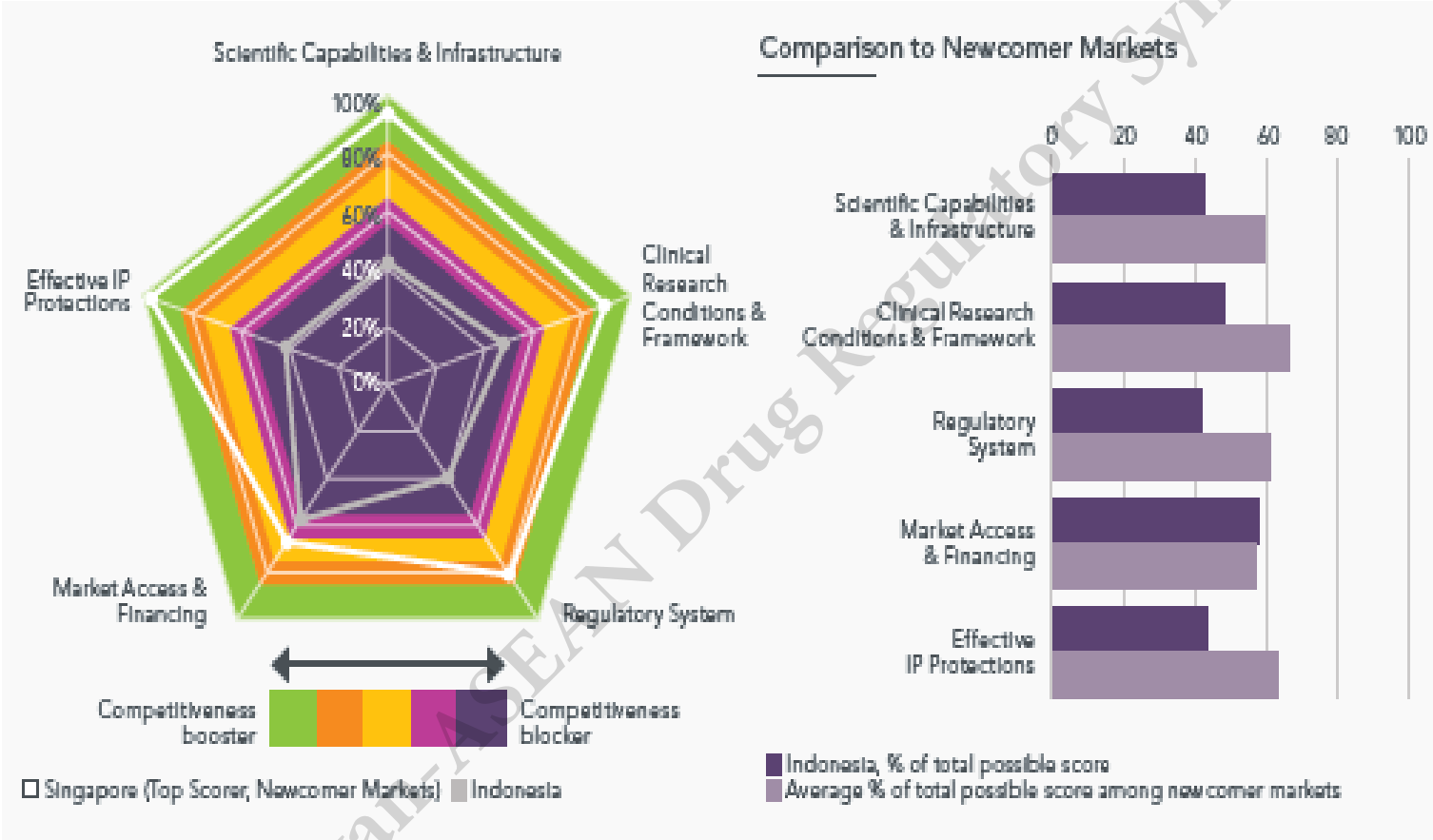

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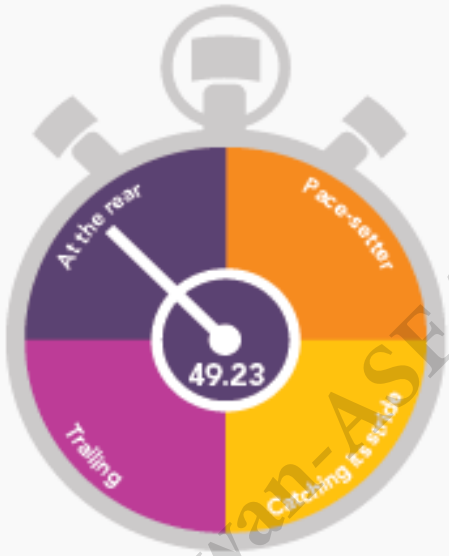
Thailand BCI survey overall scores 2016

THAILAND

BCI Survey 2016 – Overall Scores



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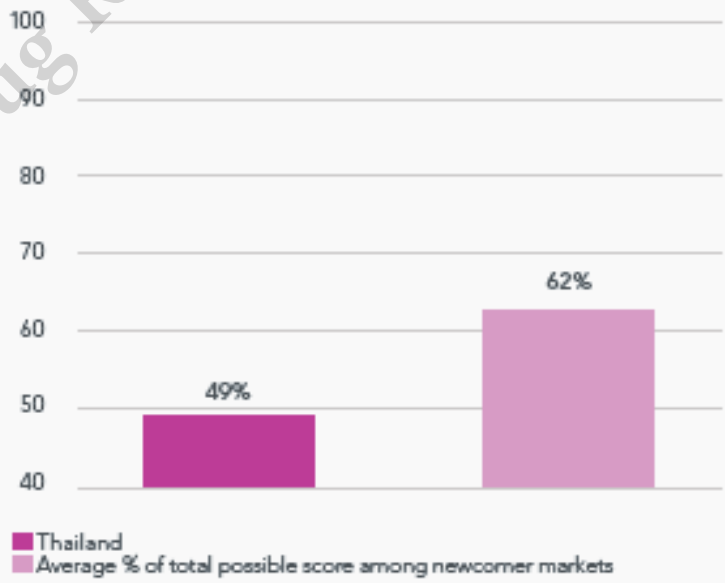

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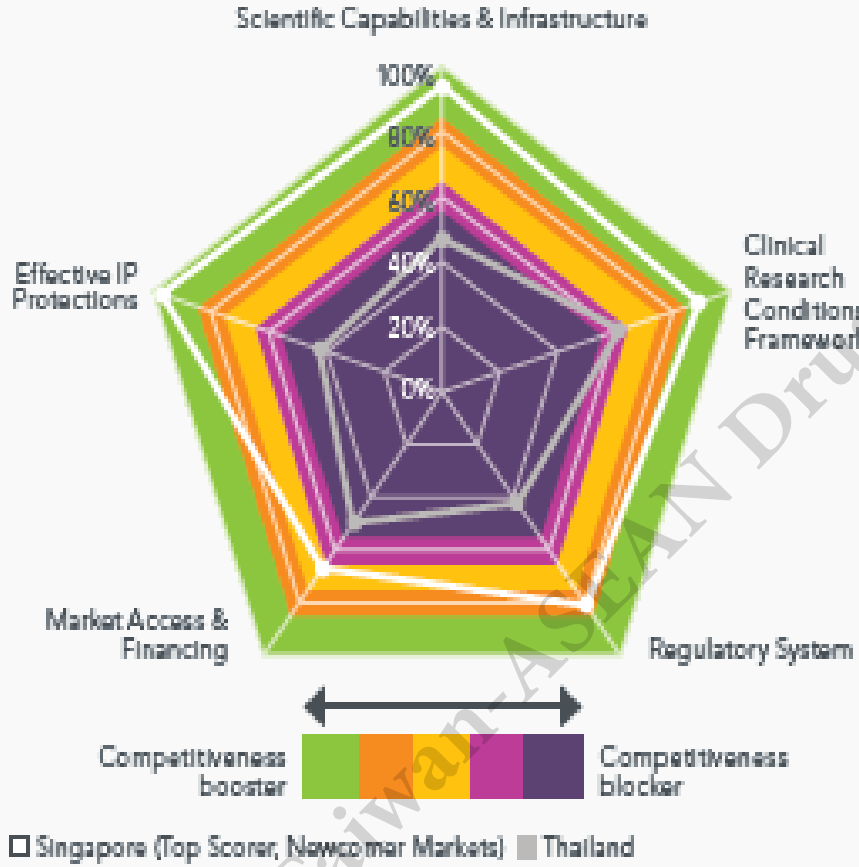

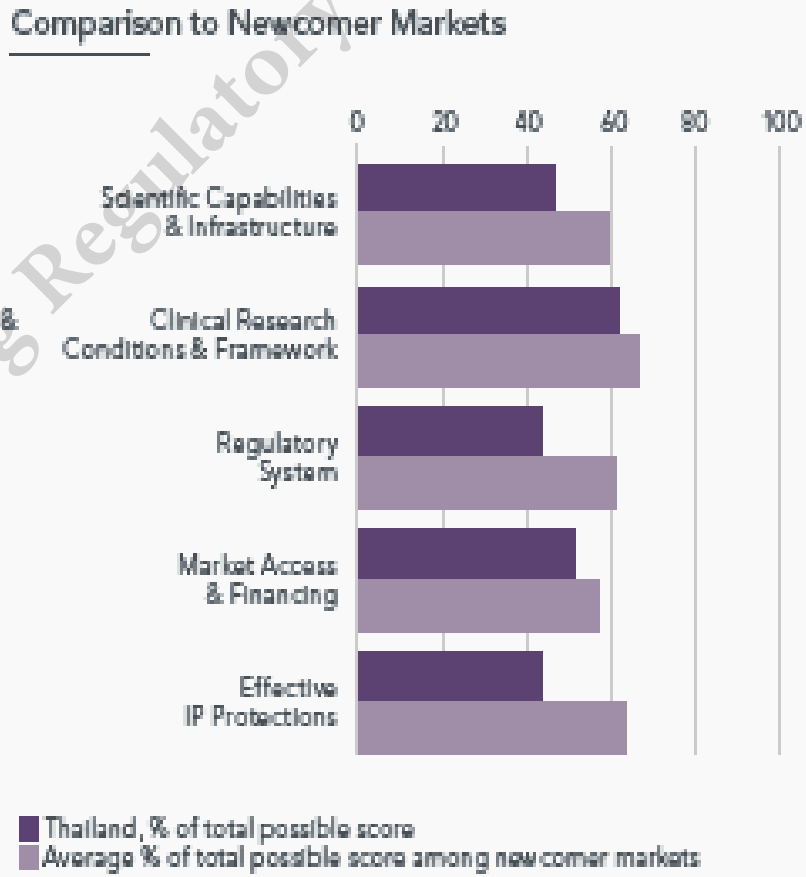

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International Chamber of Commerce on Innovation ecosystems for high tech industry

Summary and highlights

- Build investor confidence
- Train skilled workers in a climate that promotes knowledge exchange
- Open markets to trade and investment
- Ensure adequate intellectual property systems to incentivise investment in innovation and promote technological collaboration

INTERNATIONAL CHAMBER OF COMMERCE
The world business organization

450/1095
DYE/tbn 08/06/2015

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Why does China need to encourage pharma innovation?

Drug innovation

People's well-being	▪ For diseases with high incidence in China (e.g., liver cancer) there are limited innovative drugs available globally and pharmacos 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 their burden on society. ▪ For infectious diseases, China needs to build innovation capabilities and emergency mechanisms to protect people's lives and health
Sustainable economic development	▪ The pharma 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. 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.
core competitive-ness	▪ In 2015, the global innovative drug market hit USD 600 billion, to which China contributed less than USD 10 billion. However, the innovative products first launched in China accounted for less than USD 500 million, with all sales generated 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's goal of drug innovation outlined in the 13th five-year-plan

Three phases for "Major New Drug Development Project"

11th five-year plan ("Spread")

- Establish innovative R&D **system/platform**
- Invest in **infrastructure**
- **Build capability**

12th five-year plan ("Streamline")

- Capability
- Identify and focus on **key products, key medical needs** and **key R&D issues**

13th five-year plan (Breakthrough)

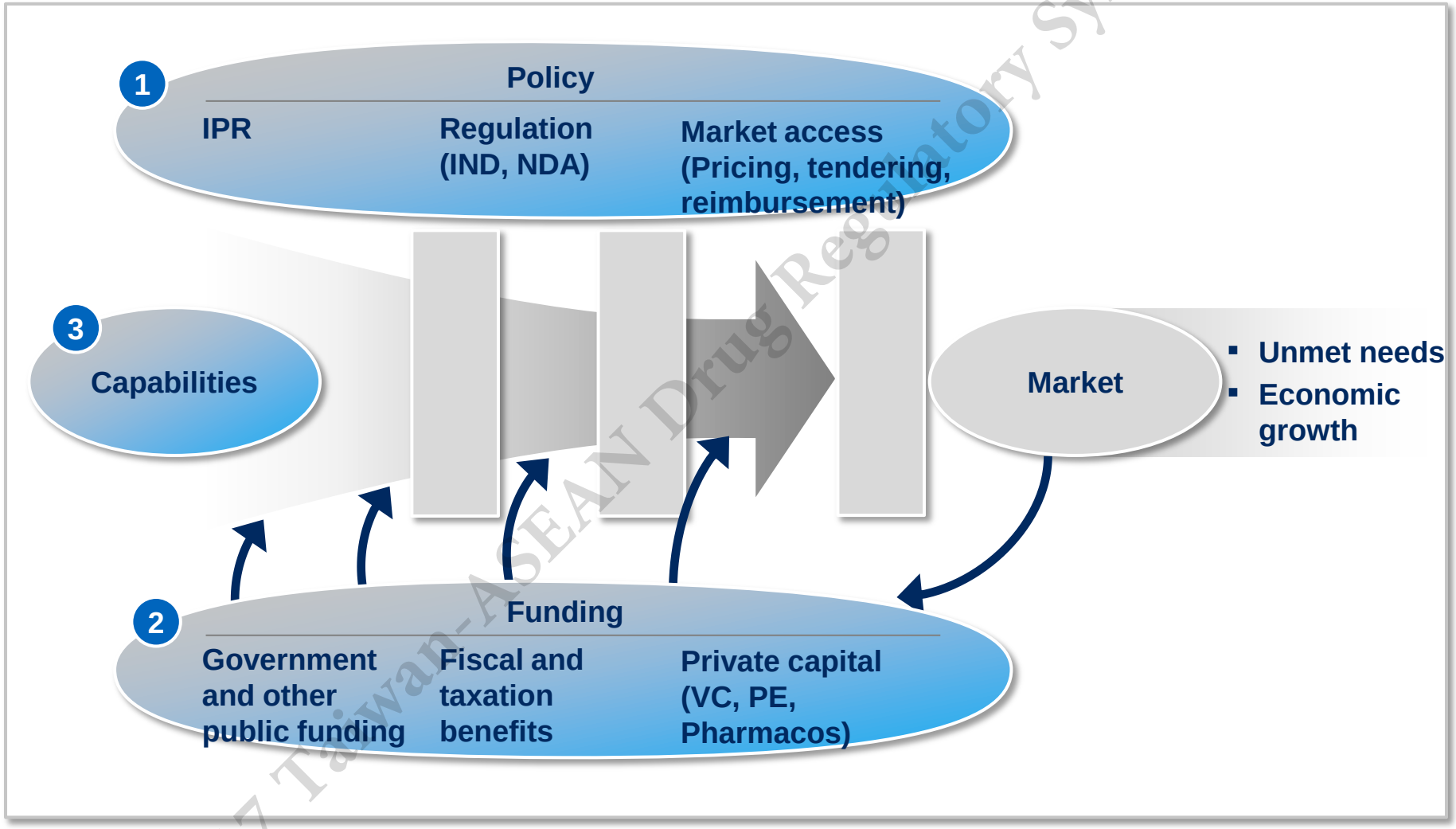
- Resources concentrated on **limited key projects**
  - Plan to develop **30 new drugs[1] including 8~10 breakthrough drugs**
  - Develop and drive **globalization** of 20~30 chemical drugs, 3~5 new TCMs and 3~5 new biologics
- Achieve **breakthrough** in a few leading areas

- **Innovative drugs**
- **Major product upgrade**
- **Start-up incubator**
- **Key technology**
- **Infrastructure platform**

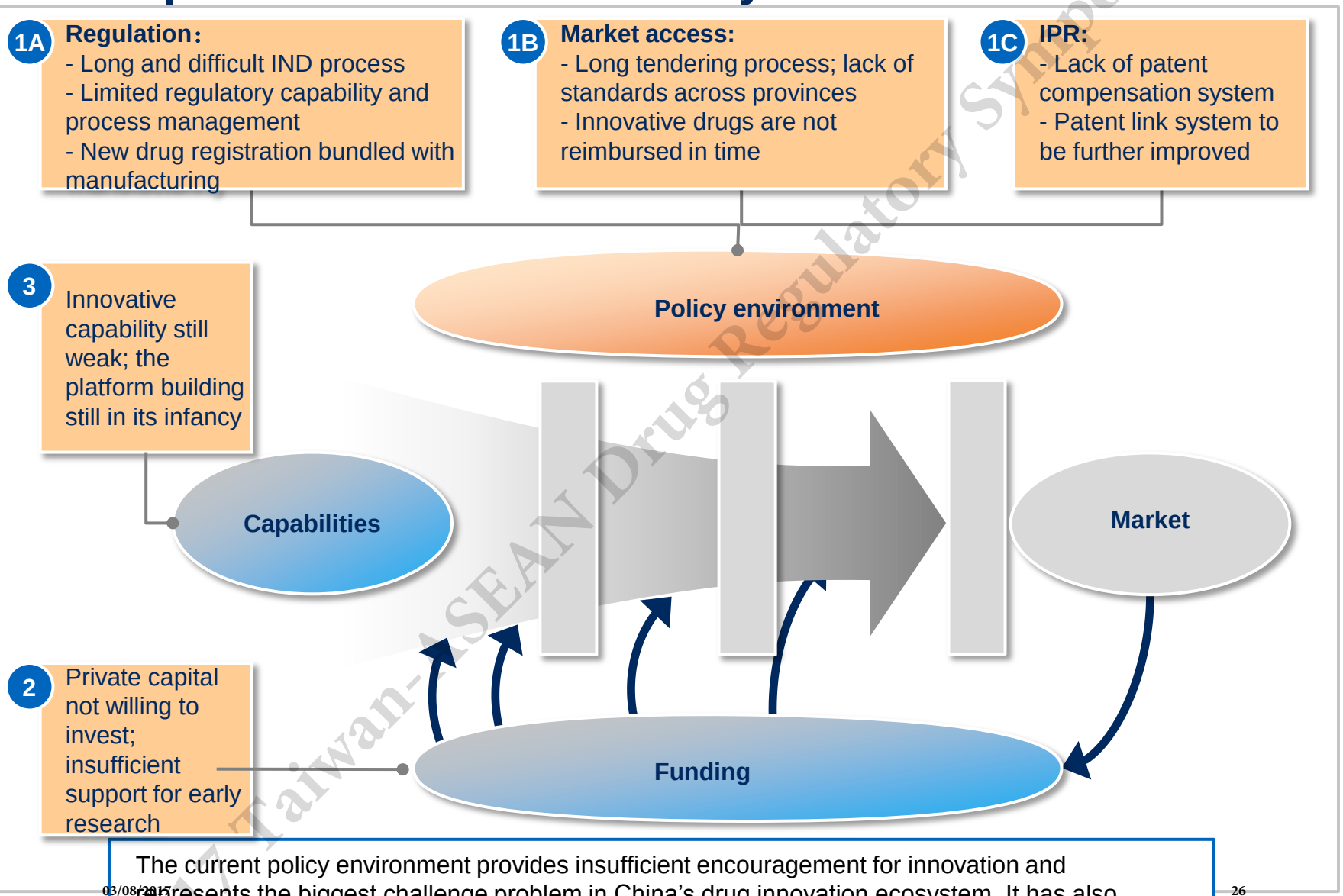
1 Including 10 chemical drugs, 10 biologics and 10 TCMs

Source: Literature search; MoST MNDDP project review

A thriving pharma innovation ecosystem comprises policy, funding, capabilities and market

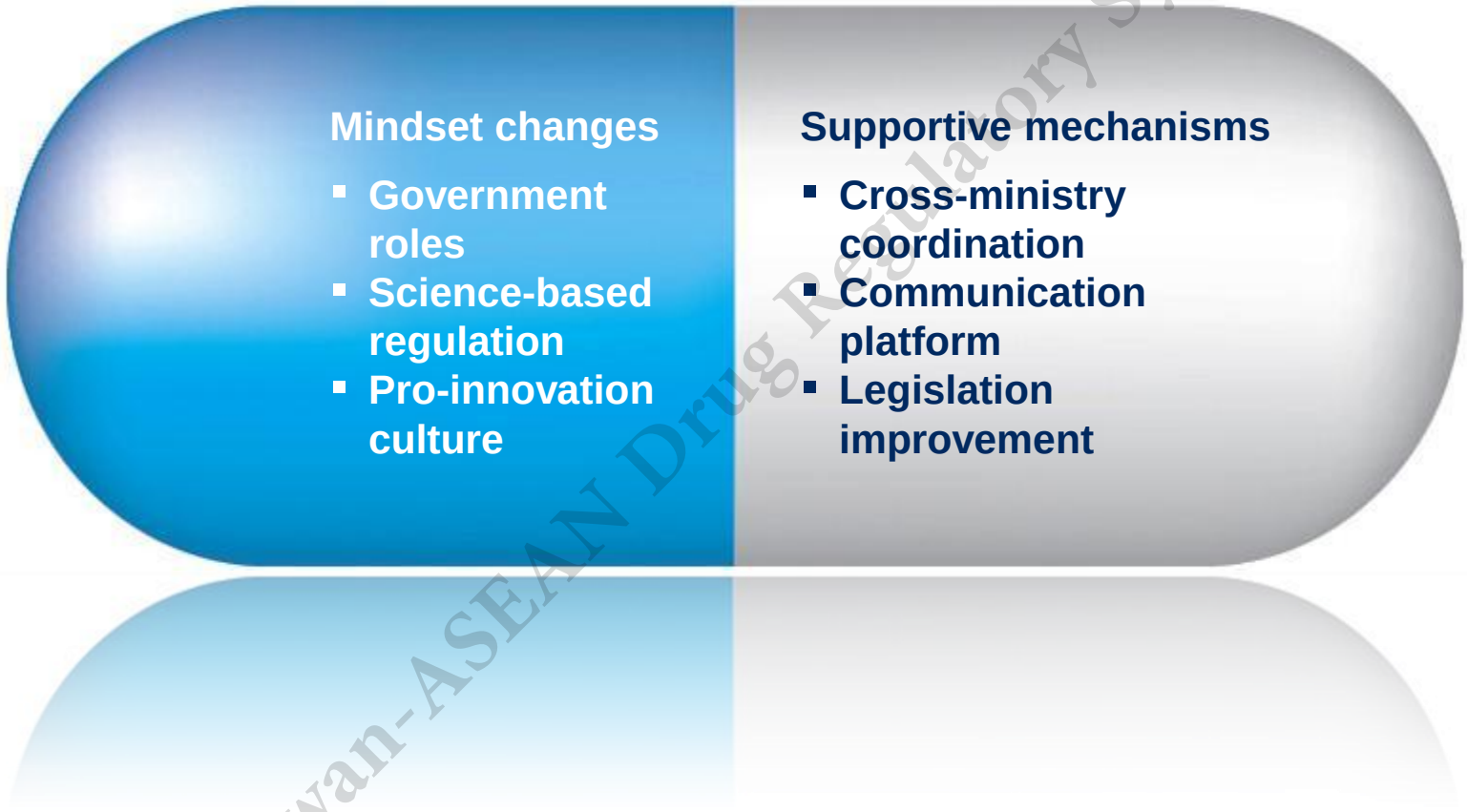


The policy environment represented the bottle neck in China's pharma innovation ecosystem in 2014



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

Fostering a pharma innovation ecosystem calls for mindset changes and supportive mechanisms



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.**

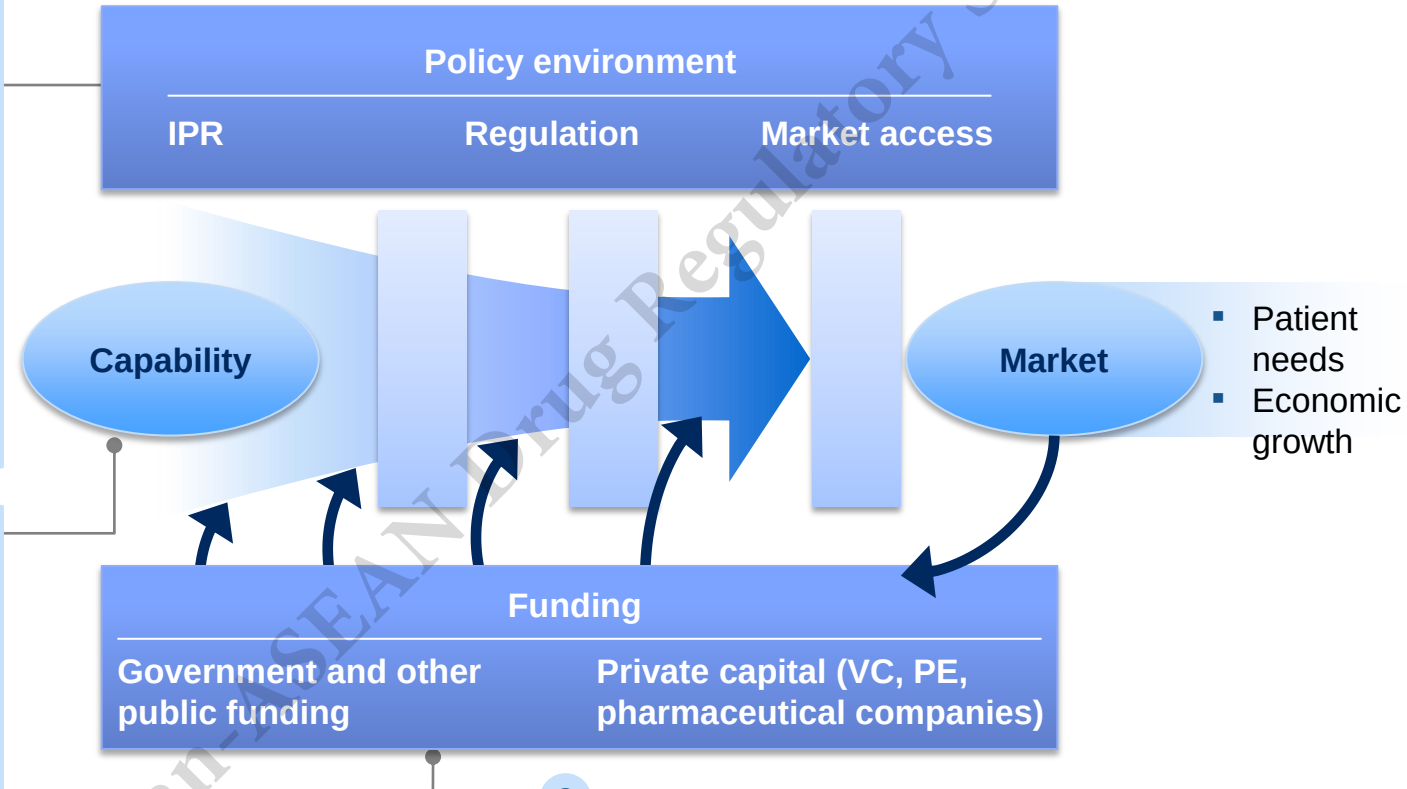
- **China should learn from the model of collaboration between industry, academia, and researchers adopted in Europe and the US, with government driving R&D collaboration.** Given China's starting point, priority should be given to high-prevalence diseases such as liver and gastric cancer and hepatitis 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.**

The three key elements in China's Pharma innovation ecosystem have improved and evolved out of a virtuous circle since 2014

1 **Policy environment significantly improved:** a series of policies have been issued to push forward regulatory reform, including improved drug review quality, backlog clearance, MAH, etc.

2 **Talent:** overseas returnees and local talent actively join together in building start-ups, with clearly improved overall capabilities



3 **Private capital investment** increasingly invested in biopharma industry, leading to lowered financing barriers and rapid growth both in the **number of start-ups and deal size**

China's Pharma innovation has strong momentum- rapid growth in 'quantity', gradual improvement in quality

Key ecosystem drivers

1. **Policy environment significantly improved:** a series of policies have been issued to push forward regulatory reform, including improved drug review quality, backlog clearance, MAH, etc.
2. **Overseas returnees and local talent** actively join together in building start-ups, with clearly improved overall capabilities
3. Private **capital** investment increasingly invested in biopharma industry, leading to lowered financing barriers and rapid growth both in the number of start-ups and deal size

"Quantity" grows rapidly and "Quality" gradually improves

A Innovation output steadily increases

- **Academic publications** in top international journals increasing by 16% CAGR, and annual **PCT** applications growing
- Innovative drugs approved for clinical trials increased from 21 in 2011 to 69 in 2015, and molecules in pipeline reached to 656 by year-end 2015

B Marketed **innovative drugs** are mostly incremental innovation built upon known targets or MOA; while some innovative pharmacos aspire to develop "breakthrough drugs", they also have more focus on unmet clinical needs, and strengthening R&D quality

C **Globalization** of drug innovation accelerates, with a more open pharma industry value chain

- No real "global new" drugs yet, as marketed class 1 drugs **have not be approved / launched in ICH markets**
- **A group of local innovative pharmacos with global vision** are striving to develop drugs for the global market, with more global trials and licensing activities

Clear improvement in policy environment with CFDA regulatory reform

Encouraging innovation

- **MAH pilot launched** to encourage drug R&D in academia
- **Local clinical trial centers encouraged to participate in MRCT**, and eligible trial data allowed to be used in NDA

Optimizing drug review and approval system

- Established **priority review and approval** mechanism to encourage the development of innovative drugs that can address significant unmet medical needs
- Issued ***Administrative Measures for the Communication on Drug R&D and Technical Review*** to institutionalize and encourage communication between applicants and CDE
- Established **advisory committee** based on FDA's approach to provide scientific input on relevant topics

Building up review capabilities

- Collaborated with APEC and Peking University to found **Peking University & APEC Center of Excellence in Regulatory Science** focused on science-based regulation and capability building
- Actively **collaborated with international regulatory authorities** to improve review capabilities and gear towards global standards

Improving review efficiency

- CDE reviewer team capacity increased to improve overall review capability of CDE
- Accelerated review and approval and addressed CTA and NDA backlog issues

Improving drug quality

- **Self-inspection of clinical trial data launched** to ensure data quality
- **Quality Consistency Evaluation (QCE) now required for generic drugs** to improve Gx quality

SOURCE: CFDA; team analysis

Key elements of innovation ecosystem for fostering pharma innovation

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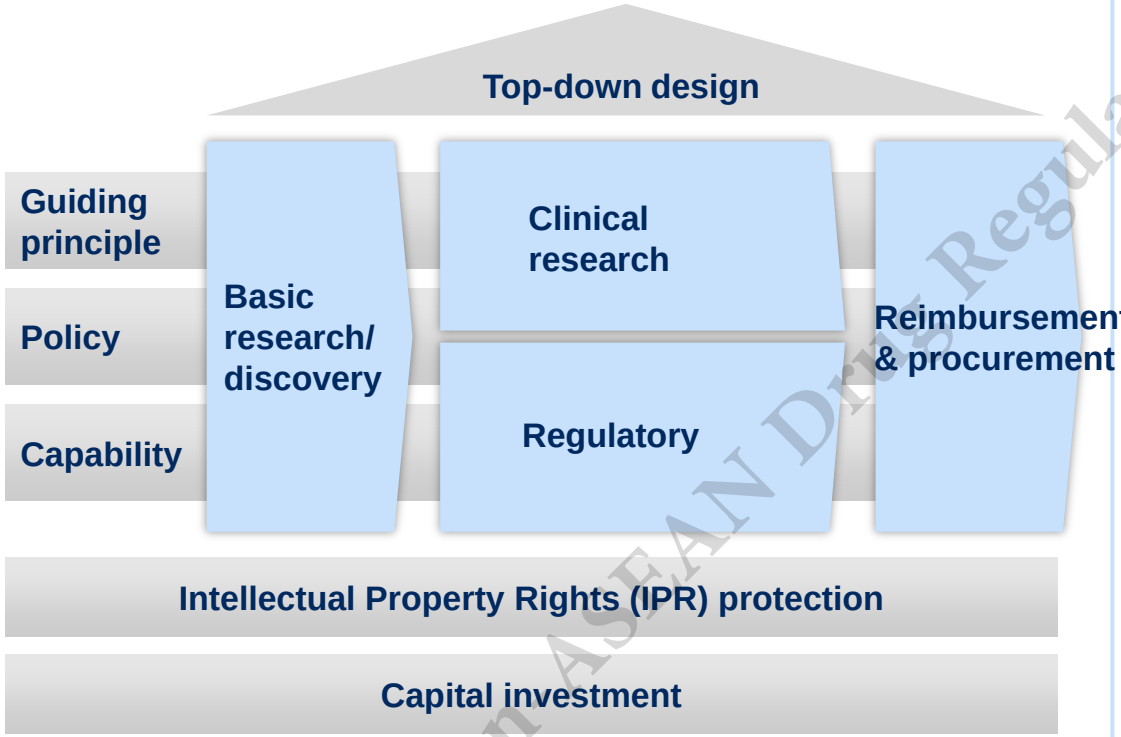
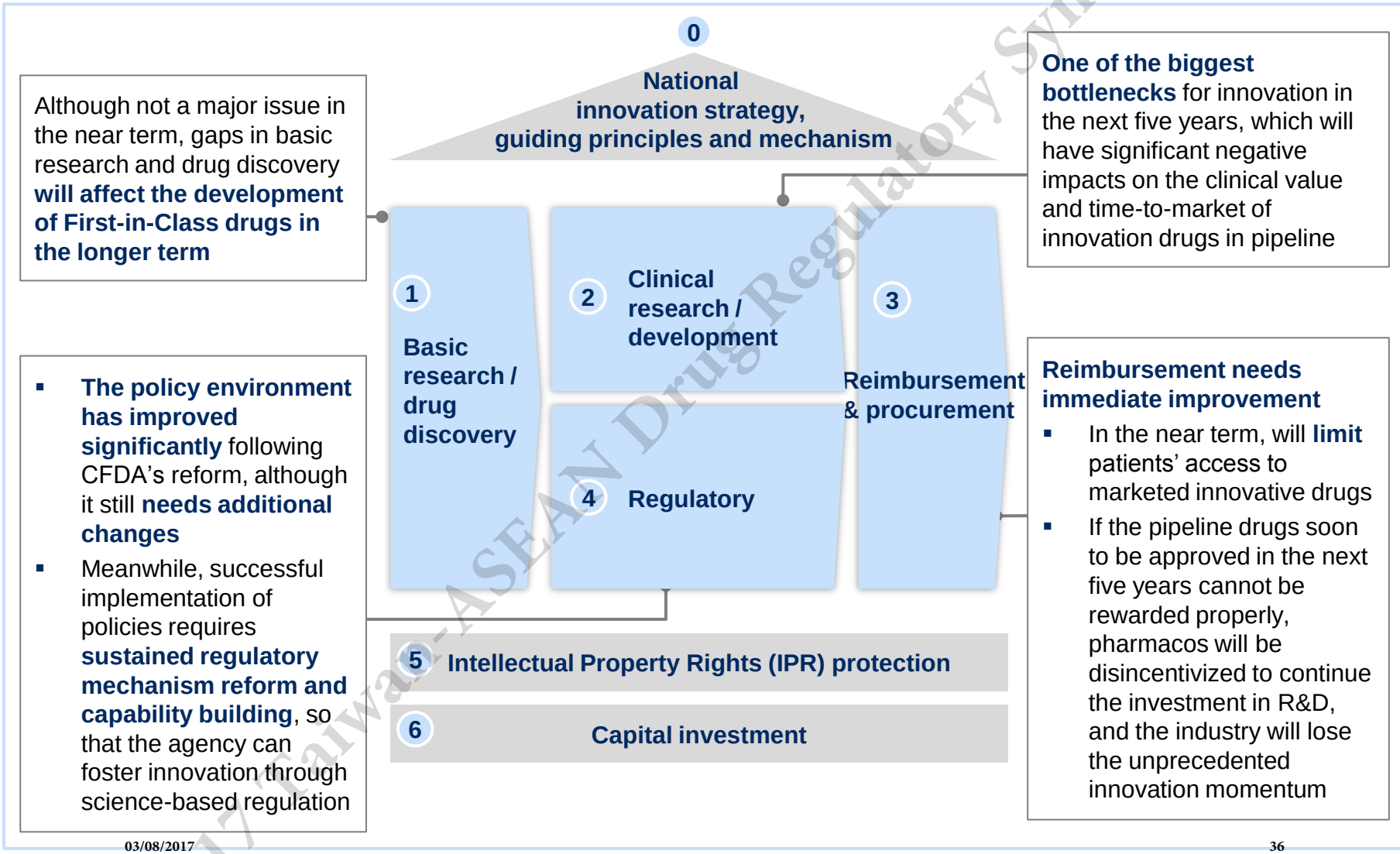


Sustainable innovation ecosystem

- **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

China is facing challenges of various natures across key steps of pharma innovation: clinical research, regulation, and market access are the biggest bottleneck



Although not a major issue in the near term, gaps in basic research and drug discovery **will affect the development of First-in-Class drugs in the longer term**

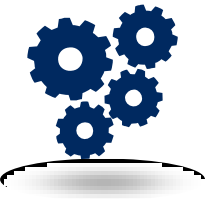
- **The policy environment has improved significantly** following CFDA's reform, although it still **needs additional changes**
- Meanwhile, successful implementation of policies requires **sustained regulatory mechanism reform and capability building**, so that the agency can foster innovation through science-based regulation

One of the biggest bottlenecks for innovation in the next five years, which will have significant negative impacts on the clinical value and time-to-market of innovation drugs in pipeline

Reimbursement needs immediate improvement

- In the near term, will **limit** patients' access to marketed innovative drugs
- If the pipeline drugs soon to be approved in the next five years cannot be rewarded properly, pharmacos will be disincentivized to continue the investment in R&D, and the industry will lose the unprecedented innovation momentum

Overarching design for Pharma innovation is fundamental to foster a sustainable ecosystem



1 Cross-Ministry collaboration and policy/regulation consistency

- **Develop a national innovation strategy** with clearly stated goals and defined implementation road map, covering all the key aspects including regulatory approval, healthcare provider administration, reimbursement, taxation, financing, research, etc.
- **Facilitate cross-ministry collaboration** taking into consideration the support needed in different areas of the drug innovation ecosystem for policy making and implementation, and **ensure comprehensiveness and consistency of laws and regulations**

2 Shift government roles

- **Reposition the government roles** to create an effective policy environment that will guide investment and support capability building
- **Eliminate unnecessary administrative approvals and administrative interventions,** and encourage open and fair competition

3 Enhance communication and collective governance

- **Enhance government-industry communication and increase transparency of policy making** by systematically soliciting opinions from industry and learning from global practices; make timely adjustment during policy implementation based on industry feedback
- **Establish a formalized communication mechanism** to ensure timely and open communication between government and industry

4 Transformation of guiding principles

- **Establish scientific guiding principles across all aspects of the innovation ecosystem**
  - **Clinical research and development**: fully recognize the fundamental goals and importance of clinical research; clinical trial is the only way to evaluate the safety and efficacy of a new therapy
  - **Regulation:** establish science-based regulatory system, implement and practice Good Review Practice (GRP) building upon quality, efficiency, specificity, transparency and consistency; integrate with international practice on scientific standards and principles, adopt and implement ICH guidelines, and learn from FDA, EMA, PMDA, WHO, etc.
  - **Market access:** fully recognize the importance of market access to sustainable development of an innovative industry, and encourage adoption of innovative drugs with proven clinical value

Content

- Biopharmaceutical competitiveness and investment survey report
- ICC on innovation ecosystem for high tech industry in 2015

- Lessons from China experience
  - 2014 eco-system for fostering pharma innovation
  - Improvement in last two years

- Key Message to take away

Key Messages to take away

1. 5 Imperatives for improving competiveness in Biopharmaceutical investment
2. Ecosystem for fostering pharma innovation composed of policy environment (regulatory, IPR protection, market access), capabilities, funding and market.
3. Policy makers in China accepted the recommendations from industry and academics, major regulatory reforms had been initiated and significant improvement have been observed.
4. ASEAN has set ambitious goals for regulatory harmonization, Taiwan can be a good partner through more effective collaboration, together we may develop sustainable ecosystem for pharma innovation for mutual benefit .

Thank you for you attention.

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