China Regulation for Developing Innovative Medicine

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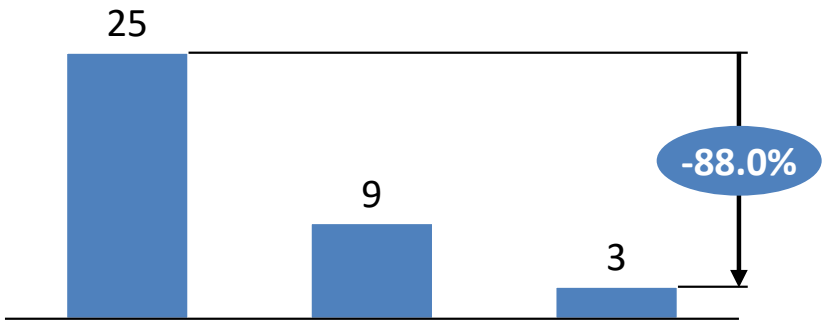
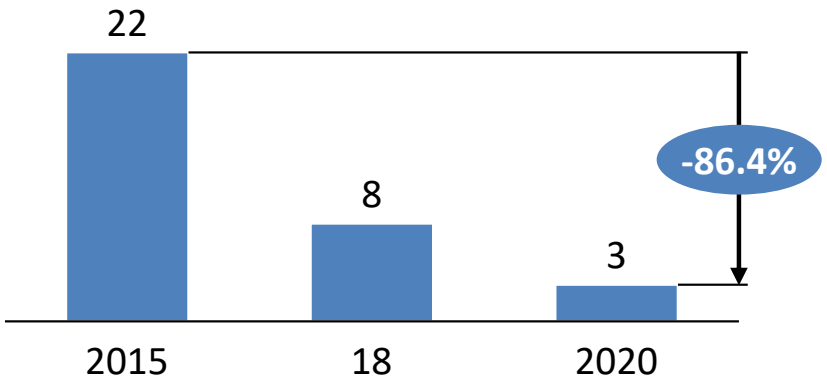
Promising regulatory reform aimed at accelerating innovation since 2015 in China

Average approval time of innovative drug clinical trial application, Month

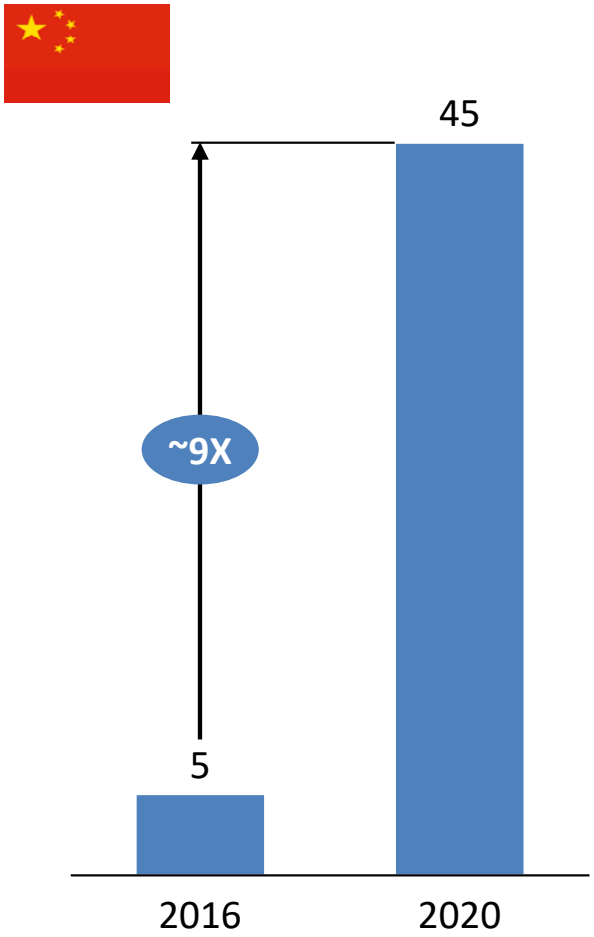
Chemical drug[1]



Biologic drug[1]



of innovative drugs[3] approved per year in China (2016 and 2020) versus other countries/regions (2020)



On par with development countries/ regions in 2020

53

42

39

1. Include Class 1.1 innovative drugs and Class 5.1 originator drugs
2. Including Class 1 therapeutic innovative biologics and Class 3 therapeutic originator biologics
3. US: New Molecule Entity approved by FDA; EU, EMA approved drugs containing new active substance; Japan: PMDA approved new drug containing new active ingredient; China: Class 1.1 and 5.1 chemical drugs, as well as Class 1 and 3 biologics, excluding TCM, and originator drugs of which initial approval is before 2020 or in 2020 as re-registration; excluding originators that are approved post Gx launch in China, or new indication expansion for the same product

Source: GBI

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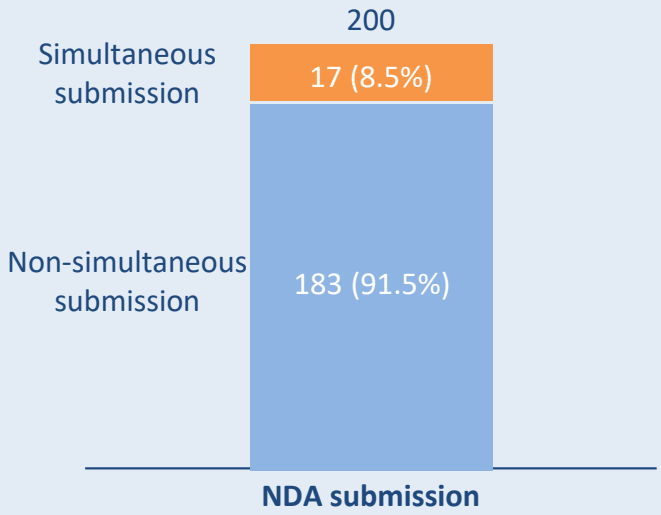
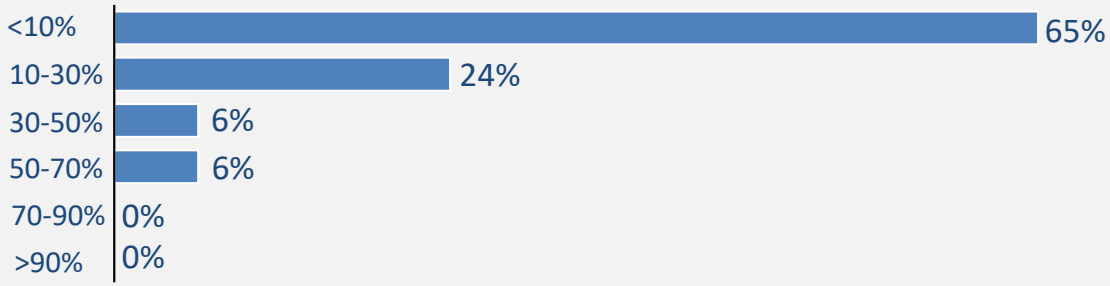
Global simultaneous submission is achievable and will grow continuously in China

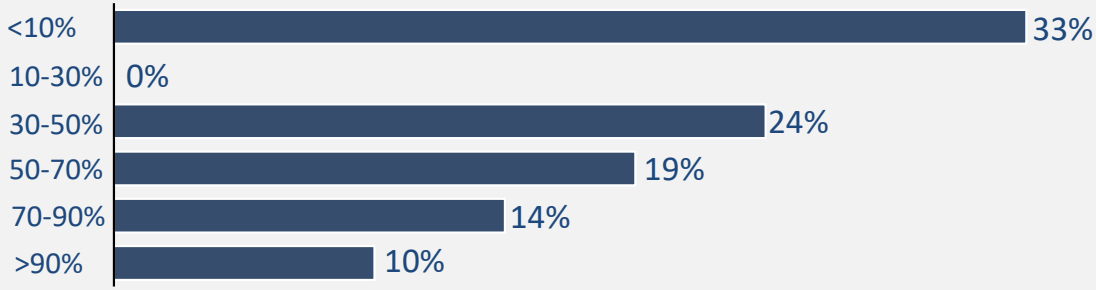
Between 2017 to 2020 Oct., less than 10% NDAs by RDPAC member companies have achieved simultaneous submission



In 2018-2021, less than 10% of simultaneous submission in more than 2/3 RDPAC member companies



Looking ahead 2022-2025, expectation on simultaneous submission is beyond 30% in more than 2/3 RDPAC member companies, which indicates a significant increase in the percentage of expectation



Simultaneous submission: China NDA submission no later than global first NDA approval
Source: RDPAC research report and internal survey

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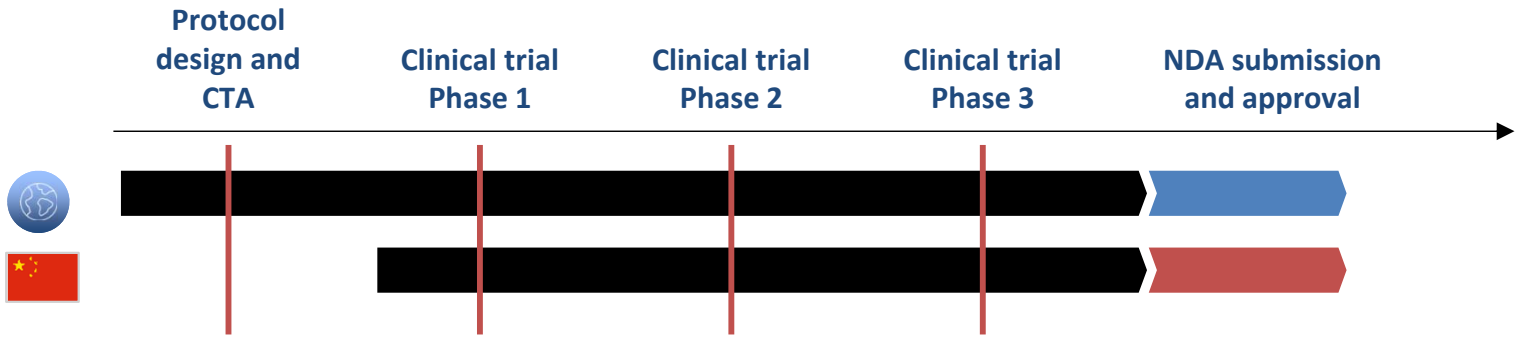
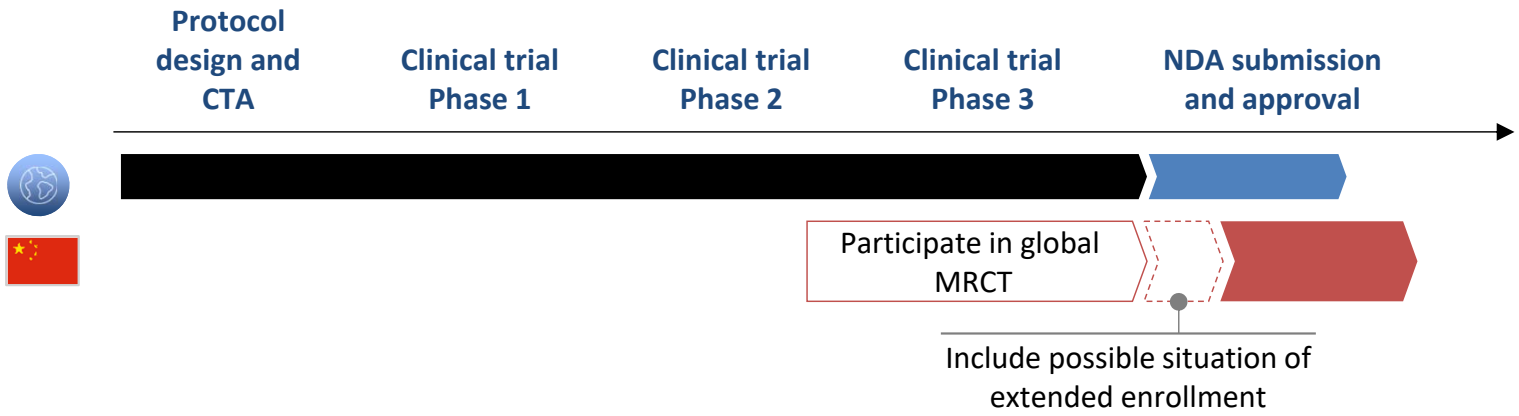
Three potential pathways to pursue simultaneous development, registration and review in China

Pathway 1: Participate in global early-stage clinical trials, ensuring synchronized development of all stages to guarantee simultaneous registration and launch



Pathway 2: Participate in global registrational MRCT, ensuring synchronized development of later stage, and strive for simultaneous registration and launch



Pathway 3: Plan early for the bridging and China standalone clinical trial needed for China registration, shortening approval lag between China and global

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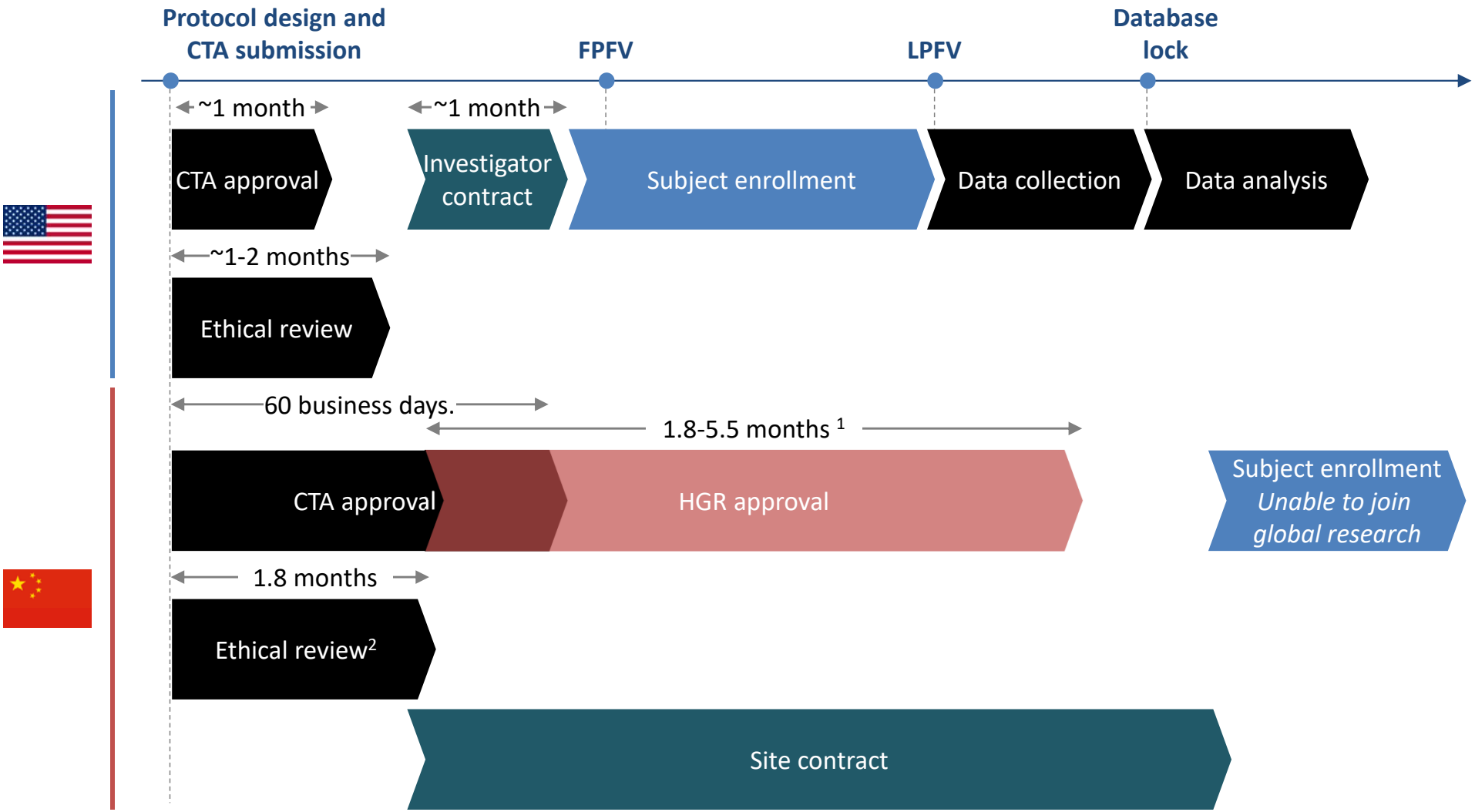
Timeline comparison of early stage clinical trials in China vs. US

Illustrative timeline of key activities in study start-up process: Phase 1 & 2 clinical trial



1. Based on 2020 clinical operation survey result of RDPAC members, top quartile as 1.8 months, median as 4.1 months, and bottom quartile as 5.5 months
2. Assume ethical review and clinical application on parallel

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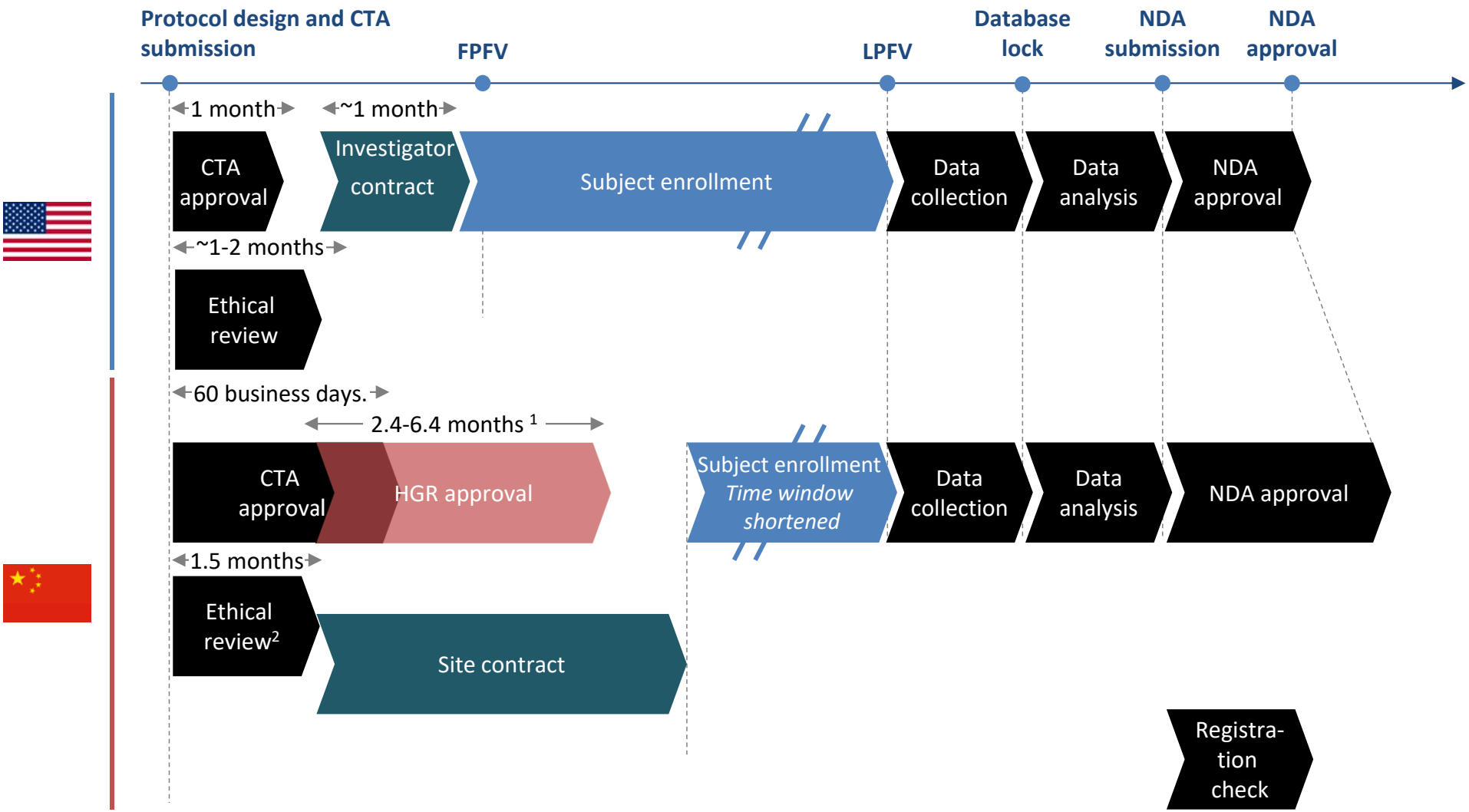
Timeline comparison of registrational clinical trials in China vs. US

Illustrative timeline of key activities in study start-up process: Phase 3 clinical trial



1. Based on 2020 clinical operation survey result of RDPAC members, top quartile as 2.4 months, median as 3.7 months, and bottom quartile as 6.4 months
2. Assume ethical review and clinical application on parallel; Data collection & analysis and NDA approval time on par with US

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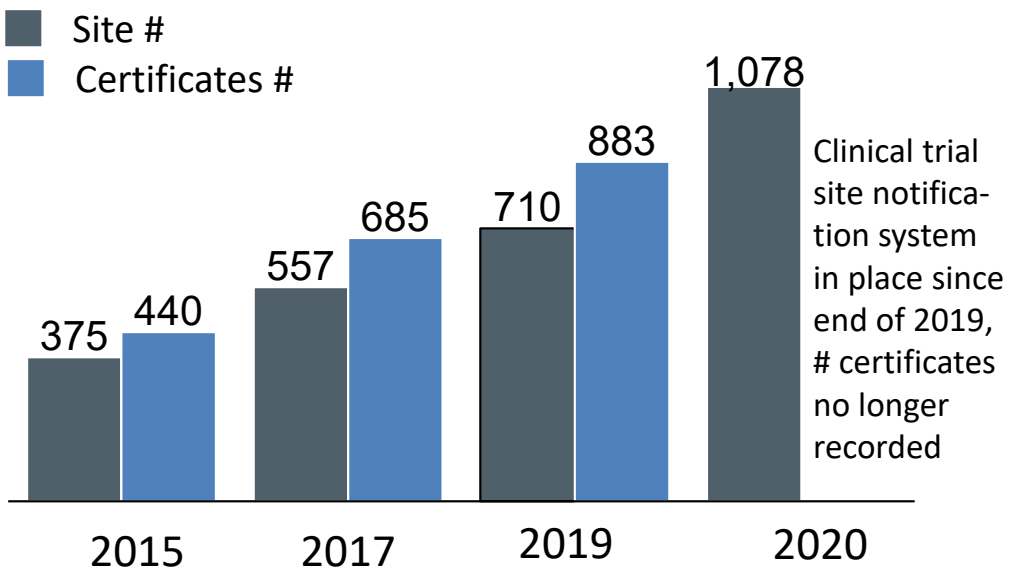
Clinical research system improvements and challenges

History and progress

- 2015-2016: About 80% CTA applications (over 1200) withdraw after the “Announcement of Clinical Trial Data Self Inspection and Verification” released by NMPA on July 22, 2015
- 2016-present: China clinical quality improved a lot after the “722 event”

2015-2020, # of clinical trial certified sites and # of certificates, China

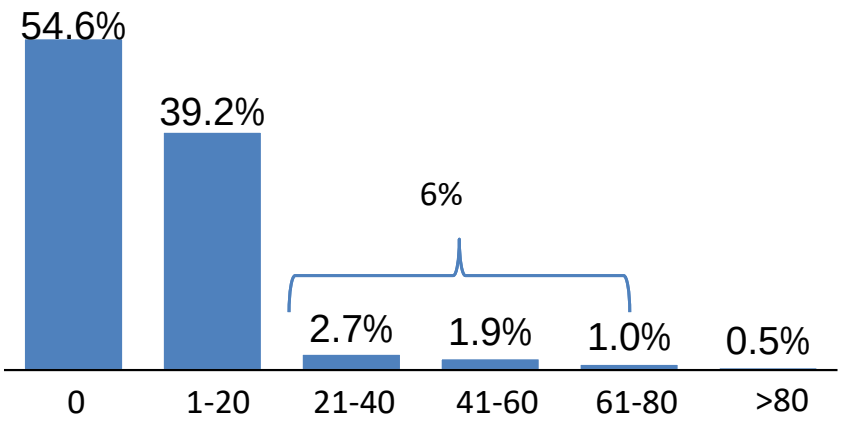


China sees steady growth of clinical trial sites in recent years

Capability competition

# of sites by # MRCT conducted

2019-2020, total # = 1,078



Only ~ 6% of sites have conducted 20+ MRCT in last 2 years

Data source: platform of drug clinical trial registration and information disclosure, as of July 2021

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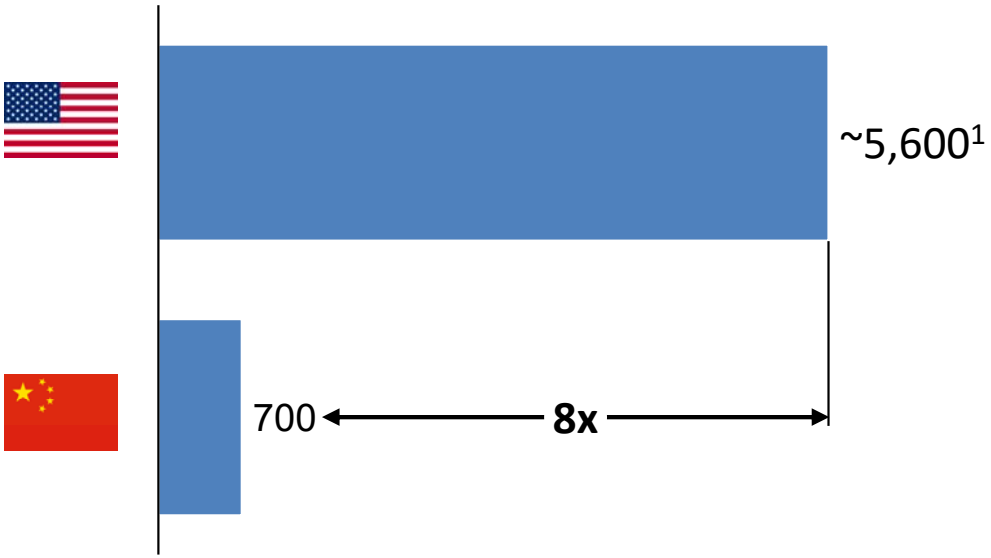
China still has large improvement room for drug review in terms of both team size and expertise level

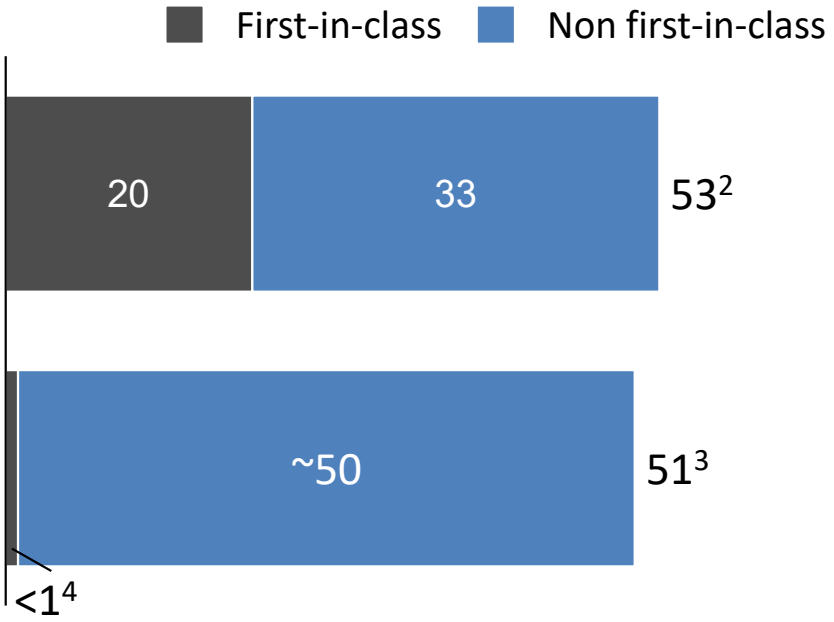
Reviewer team size comparison, China vs. US

FTE # for drug review, 2020



innovative drug approvals, China vs. US

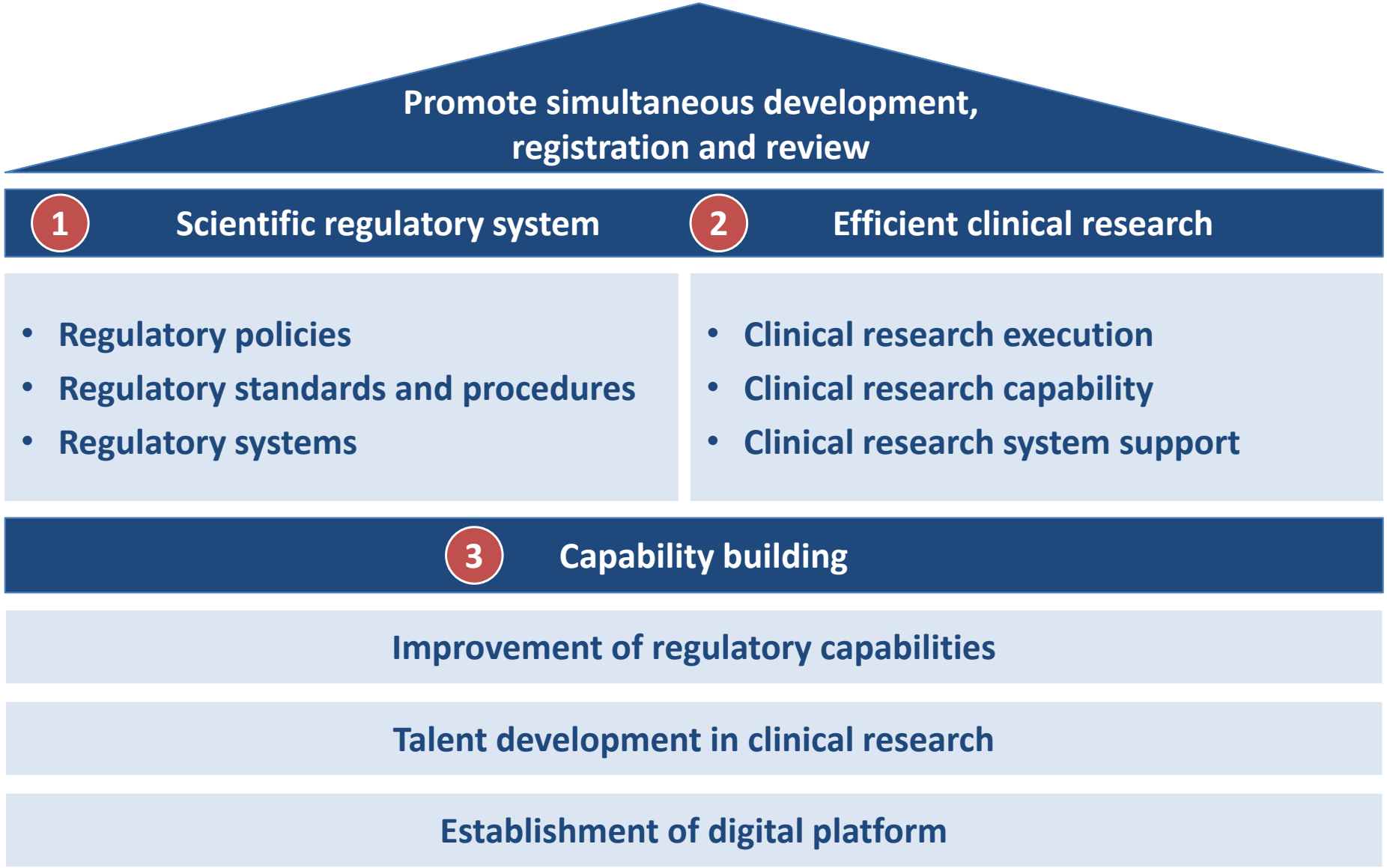
2018-2020 average # of drugs approved per year



1. US drug review team includes CDER staff only. Total FTEs of FDA as 18,062 ppls; in addition to CDER, also 10 other departments, e.g. biologics Research Center (1,191 FTEs), Regulatory Affairs Office (4,997 FTEs)
2. Including new molecular entities and new therapeutic biologics only; excluding vaccines, blood products approved by CBER.
3. Including Class 1.1 innovative drugs and Class 5.1 originator drugs; biological drugs including Class 1 therapeutic innovative biologics and Class 3 therapeutic originator biologics
4. Excluding First-in-class innovative drugs approved in US before approval in China

Source: CDE; FDA; GBI

Three dimensions are key to the promotion of simultaneous development, registration and review in China



4. PANEL DISCUSSION

Promote simultaneous development, registration and review of innovative drugs via…

"Three initiatives"

…to **debottleneck current challenges**

- Rationalize requirements for **HGR** application and optimize process efficiency
- Define more scientific requirements for the **Chinese subject enrollment** and enhance mutual recognition of global data
- Promote unified, standardized, and **collaborative processes for clinical trial sites** and ensure efficient implementation

"Five levers"

…to **ensure a sound system**

- Optimize review-related processes and encourage **clinical value-oriented reviews**
- Rationalize the requirements for dossier submitted for review and approval to further **harmonize with global standards**
- Fully implement the drug **MAH** (marketing authorization holder) mechanism in harmonization with global
- Establish **clinical study platforms** and **dedicated study teams**
- Improve the **incentive mechanism** and **resource investment** for clinical studies

"Two enablers"

…to **drive continuous development**

- Develop **clinical research professionals** and diversify the source of **regulatory talents**
- Develop a scientific, transparent, and predictable **regulatory system**, and promote the development of the **digital tool & platform** for clinical research

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