nature portfolio

https://doi.org/10.1038/d41573-022-00077-3

Supplementary information

Trends in innovative drug development in China

In the format provided by the authors

Supplementary Box 1 | Data sources and analysis

Data characteristics and sources

Innovative drugs included in the analysis are as follows: chemical substances in Classes 1.1 and 1.2, biological products in Class 1 of the former drug registration classification; Class 1 chemical drugs and Class 1 biological drugs of the existing drug registration classification. COVID-19 vaccines and treatments under emergency approval procedures were excluded from the analysis.

The data on investigational new drug (IND) applications and new drug applications (NDAs) for innovative drugs (that were applied for and approved in China between January 1, 2010, and December 31, 2020, were collected from multiple sources, including the National Medical Products Administration (NMPA) marketed drug database, the *Drug Review Annual Report* released by the Center for Drug Evaluation, NMPA, Chinadrugtrials.org.cn, Chinese Clinical Trial Register (ChiCTR), the ClinicalTrials.gov clinical trial registry, scientific conferences, company press releases, published reports, investor presentations and other sources.

Analysis of INDs and NDA for innovative drugs that were applied for and approved

Data were stratified by the year of submission or approval, therapeutic category and type of sponsor (local or foreign). When multiple INDs and NDAs were applied by a sponsor for the same drug, the earliest effective date was used for analysis. Fixed-dose combination products often had one IND for the combination product and an earlier IND or NDA for the single active ingredient drug. Drugs that were originally discovered outside China and licensed-in to domestic pharmaceutical companies after entering the clinical phase were counted as imported drugs in this analysis. We only calculated the approval rate of drugs that had completed review, excluding drugs that were voluntarily terminated by the sponsor. The summary of the reasons for disapproval is according to *Drug Review Annual Report* released by the Center for Drug Evaluation.

According to ICH related guidelines, a new molecular entity (NME) in our study was defined as an active ingredient that contains no active moiety that has previously been approved or marketed worldwide, including not only pharmaceuticals, but also biological drugs with well-characterized molecular formulas (traditional vaccines, blood products and cytokines with no well-defined molecular formulas are excluded, but monoclonal antibodies and recombinant proteins that have well-defined primary sequences are included). For drugs for which the NDA was approved and the priority approval process was adopted, the priority procedure could be applied not only at the NDA stage but also at the IND stage.

Analysis of innovative drug therapeutic categories and targets

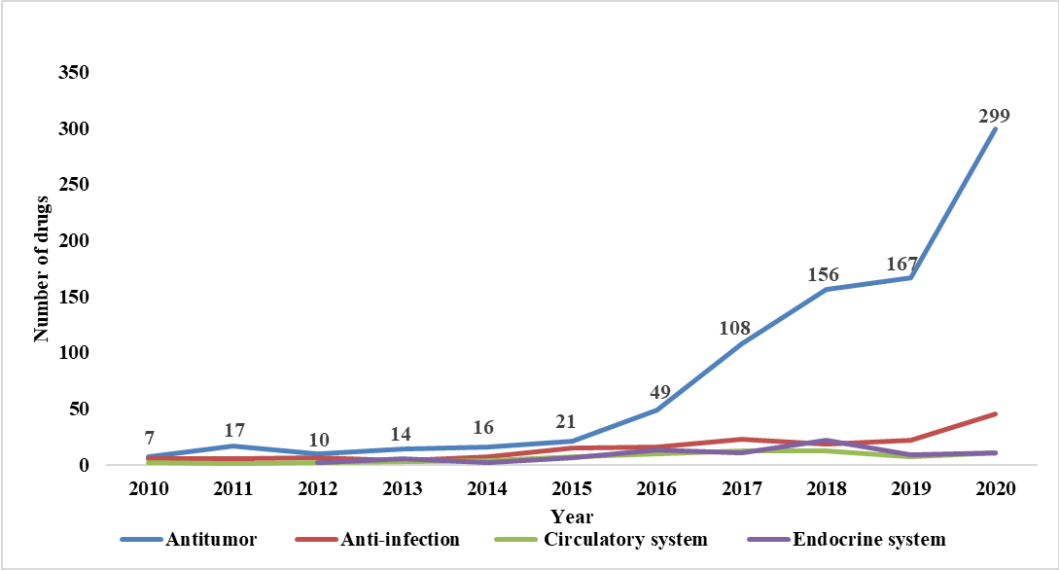
The therapeutic categories of the drugs were classified according to the International Classification of Diseases 10th Edition (ICD-10). When multiple indications were applied for the same drug, we used the earliest one for analysis. “First in class” was defined as a new and unique drug with a mechanism of action to treat a certain disease, which is determined

and classified according to the global progress of drug research and development. The "preclinical" stage is defined as the time during which IND approval has been obtained but the clinical trial had not been started (that is, the informed consent form of the first subject had not been signed).

Analysis of times for IND and NDA approval, clinical phases and trial starts

In July 2015, China Food and Drug Administration (now known as NMPA) issued the *Announcement on Carrying out Self-inspection & Verification of Drug Clinical Trial Data* ([2015] No. 117), which marked the beginning of deepening the reform of review and approval system in China. In August 2015, the State Council issued the *Opinions on Reforming the Review & Approval System for Drugs and Medical Devices* (the State Council [2015] No. 44), which promoted priority review. In our study, we selected June 2015 as the midpoint, so as to compare the pre-reform period (January 2010 to June 2015) with the post-reform period (July 2015 to December 2020). The implied license system has been conducted since 27 July 2018, according to *Announcement on Adjusting the Review & Approval Procedures of Drug Clinical Trials* ([2018] No. 50) issued by the NMPA.

The time for IND and NDA approval, clinical phase and clinical trial starting were analysed. Numerical data are presented as medians and interquartile ranges. The nonparametric Mann–Whitney Wilcoxon (MWW) test was performed to examine the differences in phase lengths between pre- and post-reform periods. Statistical analyses were performed using GraphPad Prism version 8.0. A two-tailed *p*-value of <0.05 was considered statistically significant.



Supplementary Fig 1 | Trends in therapeutic categories of innovative drugs in China from 2010–2020. Therapeutic categories were assigned based on the product's first approved indication. No analysis was performed for any cohort that included <50 products.