Acta Pharmaceutica Sinica B 2023;13(6):2812–2814

Chinese Pharmaceutical Association
Institute of Materia Medica, Chinese Academy of Medical Sciences

Acta Pharmaceutica Sinica B

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NEWS

Five trends of China's pharmaceutical industry in 2022

In recent years, China has started to encourage pharmaceutical enterprises to carry out research and development of innovative drugs. From 2018 to 2021, with the capital rapidly influx into the pharmaceutical industry, there were increasing numbers of financing events with growing amount year by year[1]. The rapid development of China's pharmaceutical industry in the past five years is also accompanied by bubbles. At the end of 2021, the industry started to face adjustment due to the impact of the pandemic and the economic environment. The number of investigational new drug applications (INDs), clinical trials, new drug applications (NDAs) and drug approvals of Chinese pharmaceutical companies throughout the year of 2022 has generally declined. The following will outline the pharmaceutical industry in 2022 from four aspects.

1. An innovative environment has basically formed in China's pharmaceutical industry under the impetus of favorable policies and capital, and the industry has entered the adjustment period

In 2015, China upgraded its drug review and approval system, and four acceleration channels were established to speed up the launch of urgently needed products. At the same time, the drug Marketing Authorization Holder (MAH) system was carried out, so that the R&D and production of drugs are no longer bound together, improving the industry's innovation efficiency by facilitating marketing flexibility[2,3]. In recent years, the time for innovative drugs to be included in the National Reimbursement Drug List (NRDL) has shortened-from the previous 4–5 years to within the year of approval. At the same time, China has set up two pioneer zones-Hainan and the Guangdong-Hong Kong-Macao Greater Bay Area to accelerate the entry of urgently needed medical devices into the Chinese market, reduce the cost of clinical research for pharmaceutical companies and accelerate the commercialization of products[4,5].

In 2022, Center for Drug Evaluation (CDE) released more than 100 drug R&D guidelines and consultation drafts. It regulated the conduct of clinical trials in the field of oncology and rare diseases. For emerging therapies, such as gene therapy, antibody–drug conjugates (ADCs), CAR-T cell therapy, oncolytic virus therapies, etc., it has also provided effective guidelines and regulations.

From policies to capital support, China's pharmaceutical industry has experienced five years of rapid development. During this period, the CDE accelerated reform and actively guided the development of the industry. Various pharmaceutical enterprises in China have been improving their innovative strength and China's environment of innovative drug development has basically formed. Now, the challenges from the COVID-19 and the downward economic cycle have speeded up the industry entry into the adjustment period.

2. For the first time in 2022, the number of INDs of new drugs in China has declined; emerging therapies grow steadily

In 2022, the number of China's new drugs (including new molecular entities and new combinations; traditional Chinese medicines and COVID-19 drugs that have not been officially approved are not included) applying for their first IND fell to 600, a year-on-year decrease of 8%. In 2018, the proportion of domestic new drugs applying for their first IND was 60%, and was 79% in 2022. In the past five years, the compound annual growth rate of domestic chemical drugs was 15%, and that of domestic biological drugs is 26% (Supporting Information Fig. S1).

In terms of drug modalities, China's drugs are still dominated by chemical drugs and antibodies, while the growth of emerging therapies has become relatively stable. Among the various types of chemical drugs, the world's fastest-growing TRK-targeting PROTAC CG001419 was developed by Cullgen for the treatment of NTRK fusion-positive cancers. Furthermore, a total of 7 radiopharmaceuticals filed IND applications, and more than half were submitted by the two major nuclide drug giants in China: China Isotope & Radiation Corporation and Dongcheng Pharmaceutical. As for emerging therapies, 45 cell therapies, 32 antibody–drug conjugates, 13 gene therapies, and 6 RNAi therapeutics applied for clinical trials for the first time. In 2022, the number of INDs for cell therapies increased by 55% year-on-year, and 84% of the products were developed by China's biotechnology companies.

Peer review under the responsibility of Chinese Pharmaceutical Association and Institute of Materia Medica, Chinese Academy of Medical Sciences.

https://doi.org/10.1016/j.apsb.2023.04.004

From the perspective of therapeutic targets, PD1/PDL1, HER2, TIGIT, EGFR^{C797S}, and CLDN18.2 were popular targets in 2022 (Supporting Information Fig. S2). After 2022, there were five international pharmaceutical transactions about CLDN18.2-targeting products (1 bispecific antibody and 4 ADCs), namely Harbour BioMed's HBM7022, LaNova Medicines' LM-302, Kelun Biotech's SKB315, the CSPC Group's SYSA1801 and Keymed Biosciences' CMG901. AstraZeneca entered into collaboration agreements with Harbour and Keymed by paying USD 350 million and USD 1.188 billion, respectively.

As for enterprises filing INDs, Hengrui Pharmaceuticals topped the list with 19 filings, followed by AstraZeneca. In 2021, only 20% of the top 20 companies were overseas companies, and in 2022 it reached 35%. In addition, the proportion of biotech companies submitting INDs increased significantly (Fig. 1).

3. The number of clinical trials related about new drugs declined, with a significant fall in the number of phase III trials

From 2017 to 2021, the number of clinical trials related to new drugs were growing year by year. In 2022, the upward trend stopped. There were 1466 clinical trials over new drugs throughout the year, a year-on-year decrease of 5% compared with 2021 (693 phase I trials, 472 in phase I/II and phase II, and 301 in phase II/III and III). Among them, the number of phase III trials faced the greatest decline, down nearly 26% year-on-year. The speculated reason was that the clinical pipelines shrank due to insufficient cash flow. To view from the company type, in 2022, the number of China's pharmaceutical companies that carried out Phase III studies fell by 35% year-on-year, and that of biotechnology companies reduced by 9% year-on-year. The fading enthusiasm for the launch and R&D of PD1/PDL1 products should be one of the reasons behind.

4. The number of NDAs dropped, and out-licensed products were ready for marketing filings

In 2022, a total of 64 new drugs filed marketing applications in China, of which 24 were domestic drugs, 11 in-licensed, 5 ones licensed out (Supporting Information Table S1), including vorolanib, a small molecule drug and 4 CAR T-cell therapies, namely Equecabtagene autoleucel (IASO Biotherapeutics' BCMA-targeting therapy), Ciltacabtagene autoleucel (Legend Biotech's BCMA-targeting therapy), Zevorcabtagene autoleucel (CARsgen's BCMA-targeting therapy) and Inaticabtagene autoleucel (Juventas' CD19-targeting therapy). On the one hand, the out-licensing deals mean that some of China's domestic drugs have obtained recognition from the overseas market. On the other hand, as it is hard for China's market to cover the R&D expenditures of pharmaceutical companies due to the high treatment costs of cell therapies, Chinese enterprises should seek for a wider market. At present, the research on cell therapies in China are dominated by biotechnology companies, and the collaboration with pharmaceutical companies can be a reasonable way to reduce commercialization costs.

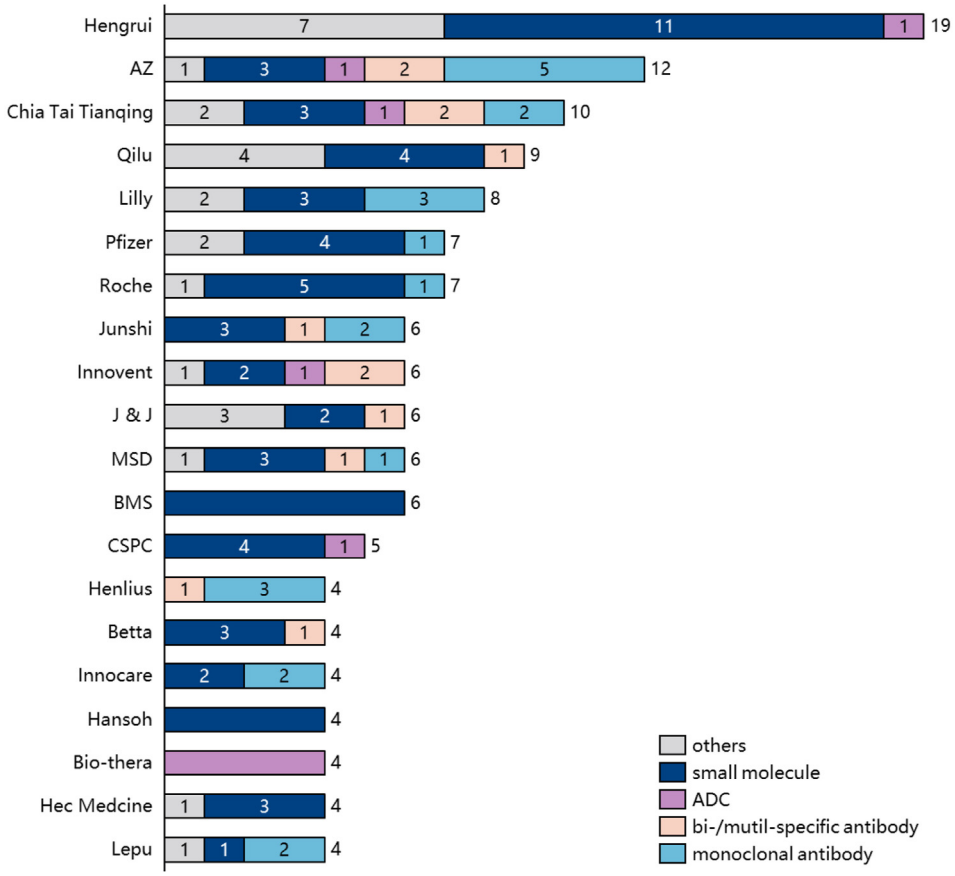

Figure 1 Top 20 companies of INDs in 2022. Source: PharmaGOTM database, NextPharma® database.

5. The number of new drug approvals shrank, and domestic pharmaceutical companies were eyeing overseas markets

The year 2022 saw a total of 50 new drug approvals (a year-on-year decrease of 35%), including 15 homegrown drugs and 35 in-licensed drugs (Supporting Information Fig. S3). Among the approved homegrown drugs, there were 6 small molecule drugs, 2 combinations, 4 monoclonal antibodies, 1 bispecific antibody, and 2 vaccines (Fig. 2). About half of these drugs were developed to target oncology. For example, candonilimab is the world's first marketed bispecific antibody targeting PD1/CTLA4, which was granted fast-track and orphan drug designations by the US FDA. Candonilimab demonstrated better efficacy and safety than PD1-targeting monoclonal antibody used in combination with CTLA4 inhibitors. Within 6 months after its approval in China, the sales reached 546 million yuan. Another example is Luye Pharma's independently-developed toludesvenlafaxine, the first triple reuptake inhibitor for the treatment of depression. Dorzagliatin, a glucokinase activator in-licensed by Hua Medicine from Bayer, is China's first domestic first-in-class new drug for the treatment of type 2 diabetes to have met the primary efficacy endpoint.

A total of 12 drugs were included in the NRDL within the year of approval, namely rezvilutamide, tegoprazan, lorlatinib, luspatercept, upadacitinib, abrocitinib, brigatinib, finerenone, inebilizumab, letermovir, romiplostim and beclometasone glycopyrrolate. Developed by Hengrui Medicine, rezvilutamide is China's first domestically produced AR inhibitor. It is a second-generation AR inhibitor and was approved in June 2022. In 2022, two new drugs produced by Hengrui obtained marketing approval, the other being linperlisib co-developed with Yingli Pharmaceutical, which is the second PI3K inhibitor in China.

As a leader in the transformation and innovation of Chinese pharmaceutical companies, Hengrui Medicine has been dedicated to independent R&D, drug collaboration and licensing, and investment activities. On the other hand, it also has accelerated its entry into the overseas market. In May 2022, Luzsana Biotechnology, a global, wholly-owned subsidiary of Hengrui, made its official debut, and is mainly responsible for drug development and commercialization in overseas markets. Currently, an international multi-center clinical trial of rezvilutamide is ongoing. In addition, earlier this year, Hengrui granted the worldwide exclusive rights of its EZH2 inhibitor, SHR-2554, to Treeline Biosciences in a deal worth more than USD 700 million. The other is CSPC Group, which has sufficient cash flow reserves and unique business development capabilities. It not only allows their early asset transactions to go overseas through transactions, avoiding domestic competition, but also conducts transactions of cost-effective assets during the industry adjustment period. In general, the R&D mode in China at present is mostly "follow-on" innovation, which is accompanied by serious homogeneous competition. Despite the active exploration of overseas markets by pharmaceutical companies, including the establishment of subsidiaries, acquisitions, cooperation, etc., the issue should be addressed fundamentally.

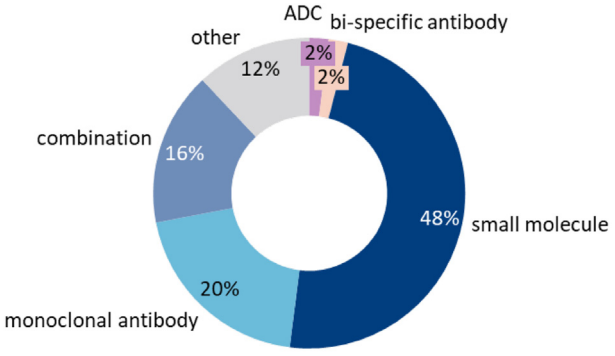

Figure 2 NMPA approvals by drug classification in 2022. Source: PharmaGO™ database, NextPharma® database.

From IND, clinical trial registration, NDA to drug approval, the number in 2022 has decreased compared with 2021. However, factors such as a backlog clinical trials due to the pandemic which leads to the rise of clinical trial registrations in 2021 and the drop in the number of INDs and clinical trials in 2022 should not be neglected. At present, the pharmaceutical industry is under adjustment. Pharmaceutical companies are considering expanding into larger overseas markets. However, after the out-licensing agreement, clinical trial evidence of differential value is necessary which requires the company to have reasonable clinical development strategies and rapid advancement capabilities. Domestic pharmaceutical companies with sufficient cash flow and innovative capabilities need to prioritize their pipelines to ensure their dominant position. Biotech with valuable assets may consider seeking partners to reduce expenses. In the future, with the continuous improvement of innovation capabilities of domestic pharmaceutical companies, favorable policies and the CDE's accelerated channel for new drugs, China's pharmaceutical market is to exhibit a pattern of active innovation and competition.

Appendix A. Supporting information

Supporting data to this article can be found online at https://doi.org/10.1016/j.apsb.2023.04.004.

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Received 22 March 2022
Accepted 10 April 2023