Drug discovery in China: A snapshot of recent progress

Intensive policy reforms in China’s pharmaceutical industry have provided strong support for the shift from generic to innovative drug R&D, and the influx of huge amounts of capitals has provided ample momentum for the development of the pharmaceutical industry. Since this year, the international situation has been severe and complicated, with the recurrence of the pandemic, and the development of China’s pharmaceutical industry has inevitably been affected.

1. Policy reforms lead new drug R&D

China’s pharmaceutical policies continue to reform and drug regulation quickly aligned with international standards. The Center for Drug Evaluation has issued 204 guidelines since 2020, providing comprehensive guidance for new drug R&D, especially for the priority diseases and drugs. The dynamic adjustment mechanism for the National Reimbursement Drug List (NRDL) has been established, and the Adjustment Plan of 2022 NRDL has set up the inclusion and exclusion criteria, which can promote the applications of pediatric and orphan drugs, and balance the clinical needs of patients and the medical insurance coverage. It is expected that by the end of this year, the NRDL will be unified nationwide.

2. The first capital chill is underway

In H1 2022, the global pharmaceutical companies had suffered financing difficulties. In both the primary and secondary markets, the number of financing events and the amount of financing (only the disclosed amount was counted) for China’s pharmaceutical companies were remarkably decreased, with 177 financing events in the primary market (year-over-year growth, YOY ~47%), and $3.9 billion in financing (YOY ~47%); 15 financing events in the secondary market (YOY ~55%), including 10 initial public offerings, and $2.6 billion in financing (YOY ~73%) (Fig. 1). There were only 62 overall financing events in Q2 2022, the worst performance in the last five years, but it is reassuring to note that the financing situation appears to improve in Q3 2022.

Since 2021, the focus of capital market attention has gradually shifted to next-generation therapies, such as cell and gene therapy. In H1 2022, the number of financing events for gene therapy R&D companies was increasing against the negative trend, with 32 companies completing financing, accounting for 19% of all financing events, and 41 cell therapy R&D companies, accounting for 25%.

In fact, since H2 2021, most of China’s listed biopharmaceutical companies have experienced a pullback of more than 50%, the first large-scale capital cold wave in China’s pharmaceutical industry, and the primary market has not been spared as well, as investment institutions are more cautious and corporate financing is more difficult due to increased uncertainty of investment returns. There are several reasons for this situation. The complicated international situation, recurring pandemic, and stricter review of the sci-tech innovation board are only causative factors, the essential reason is that China’s pharmaceutical industry has accumulated too many bubbles in the process of rapid development and needs a round of adjustment.

The current international situation and the pandemic have relatively little impact on China’s pharmaceutical industry. There is still abundant capital in the market. After a short adjustment, China’s pharmaceutical industry will enter a stage of high-quality development.

3. New drug R&D trends

Globally, there are 9609 new molecular entities and new combinations in Investigational New Drug (IND) to New Drug Application (NDA) stage with active R&D status, and 3075 (32%) in the pipeline developed by or licensed to China’s companies.

3.1. Investigational new drug applications

Due to the impact of the pandemic, the growth of INDs in China slowed down significantly in H1 2022, with 302 new drugs (new molecular entities and new combinations, excluding traditional...
Chinese medicines, the same below) submitted IND applications for the first time in China (merely YOY +3%). In specific, there were only 35 INDs in April. Among 302 new drugs, chemical drugs and biologics were evenly divided, and domestic drugs increased to 235 (YOY +10%), accounting for 78%. Remarkably, the growth rate of domestic biologics was 25%, reflecting the booming R&D of China’s biopharma, while imported drugs decreased by 16% (Fig. 2 A). It is expected that there will be around 700 INDs in 2022.

The number of domestic emerging therapies has been rapidly increasing. There are 19 cell therapies, 8 gene therapies, and 4 proteolysis-targeting chimera (PROTAC) or molecular gels submitted IND applications in China in H1 2022 (Fig. 2B), and almost all of these products were developed by domestic companies. PD1/PDL1, HER2, GLP-1R, EGFRC797S, etc. are still the popular targets. TIGIT is an emerging oncoimmune target. Although its effectiveness has recently been questioned, related products are still advancing to the clinical stage. Candidates associated with other targets, such as CD276, CCR8, PRMT5, LILRB2, B7–H4, and IL–15, are in the early stage and with considerable development potential.

3.2. Clinical trials

In H1 2022, China’s pharmaceutical companies initiated 96 pivotal clinical trials, a slight drop compared to last year, with 42 (44%) clinical trials in oncology. Some clinical trials conducted by China’s companies have achieved positive results. For example, the FGFR inhibitor gunagratinib and BTK inhibitor orelabrutinib developed by InnoCare have been revealed with high efficacy against head and neck cancer and systemic lupus erythematosus, respectively. These results are instructive for the development of new drugs in the pipeline.

3.3. New drug approval

In H1 2022, 32 new drugs have been approved in China (YOY – 35%), including 24 imported drugs and 8 (25%) domestic drugs (Fig. 3A). It is likely that these approved drugs will be included in the negotiation program in this year for NRDL. Probably due to the impact of the pandemic, there were only 2 and 4 new drugs approved in May and June 2022, respectively. From NDA to approval, the median time is 14.5 months, but the speed is significantly enhanced by the breakthrough therapy designation (BTD), with a median time of 8.6 months. Approximately 70 new drugs are expected to be approved in China this year.

The 32 approvals include 18 small molecules, 5 monoclonal antibodies, 3 combinations (Fig. 3B). The indications are mainly in oncology (16), infection (10), and hematological diseases (9). The marketing of the high-profile products will greatly meet the clinical needs of patients in China, e.g., ivosidenib (isocitrate dehydrogenase inhibitor) and lorlatinib (anaplastic lymphoma kinase inhibitor) for the treatment of acute myeloid leukemia and NSCLC, respectively; cadonilimab is the first domestic bispecific antibody, as well as the first anti-PD1/CTLA4 bispecific antibody approved in the world.

Furthermore, more high-profile products are expected to be approved in China in H2 2022, such as trastuzumab deruxtecan (anti-HER2 antibody–drug conjugate) for HER2-positive breast cancer, and pitolisant and ataluren for rare diseases (Table 1).

4. Shifting transaction types

In H1 2022, China’s pharmaceutical companies concluded 101 deals (YOY –28.4%), divided into three categories: license-in (35),
domestic deals (39) and license-out (27), with a total deal amount of $10.2 billion (only the disclosed amount is counted) (Fig. 4). The source of transaction has gradually shifted from mainly overseas projects to both overseas and domestic projects. License-out is an important way for China’s original innovative drugs to open up overseas markets, currently accounting for 27% of all transactions. As the R&D capacity in China improves, and license-out will become routine. For example, in May 2022, Kelun licensed the overseas rights of SKB264 (anti-TROP2 antibody—drug conjugate) to Merck & Co. for a total deal amount of $1.41 billion.

5. Internationalization

There are huge opportunities in the developed markets in Europe and the US and the emerging markets in the developing countries. In H1 2022, China’s pharmaceutical companies have made some breakthroughs in their internationalization progress, but have also suffered some setbacks. It is expected that 10–20 China-originated new drugs will be reviewed by FDA in the coming three years.
Ciltacaptagene autoleucel, co-developed by Legend and Johnson & Johnson, is the second China’s original new drug approved in the U.S. after zanubrutinib, and the second BCMA-targeted CAR-T cell therapy approved worldwide. However, in March 2022, the FDA denied the marketing application for sintilimab co-developed by Innovent and Eli Lilly for the first-line treatment of non-squamous NSCLC. In H1 2022, the NDA of surufatinib developed by HUTCHMED was rejected by FDA and toripalimab developed by Coherus and Junshi, was rejected, too. Junshi has resubmitted Biologic License Application (BLA) in July 2022.

The downturn in the capital market makes emerging biotech faces an existential crisis, which has little impact on big pharmaceutical companies but is instead a good opportunity for expansion. In H1 2022, China’s top pharmaceutical companies accelerated their internationalization by setting up subsidiaries abroad or acquiring overseas biotech. For example, Hengrui has established a wholly-owned subsidiary Luzsana Biotechnology to develop the company’s core products overseas; Sino Biopharmaceutical has acquired F-star Therapeutics, a British pharmaceutical company, to improve product layout and accelerate its overseas business.

China’s pharmaceutical industry will face internal or external challenges during the transformation process. Guided by ever-improving policies, China’s pharmaceutical industry is on the right path and is expected to maintain an upward trend in 2022.