China Biotech Scene, U.S. Collaborations Grow

Amgen–BeiGene deal reflects a broader shift toward increased partnerships on drug development

Late last year, Amgen made a $2.7 billion deal with the Chinese biotech BeiGene to expedite oncology drug development and expand into the Chinese market. The deal, while impressive in size and scope, also reflects a broader shift: Increasing collaboration between U.S. and Chinese pharmaceutical companies as China's biotech scene has rapidly grown—expansion driven largely by policy and regulatory changes.

It's "a complete sea change in what is happening in China in terms of drug development," says Joshua Berlin of BioCentury Inc.

China is a substantial market for oncology, with some 4.3 million new cancer cases per year, compared with about 1.8 million in the United States. Moreover, "there is a vast unmet medical need in oncology in China," says Frank Jiang, MD, PhD, chairman and CEO of CStone Pharmaceuticals, noting that the 5-year survival rate is about half that for U.S. patients. Yet prior to 2010, China's biotech industry was almost nonexistent, with drug development focusing on generic agents rather than innovative therapies.

In recent years, however, "the government became really invested in encouraging innovation," enacting several policy and regulatory changes, says Li Yan, MD, PhD, chief medical officer of Brii Biosciences. China's National Medical Products Administration (NMPA) initiated a hiring spree, drastically increasing the number of reviewers in its Centre for Drug Evaluation. In 2018, the agency shortened the review process for clinical trial applications from an unlimited amount of time to 60 days—on par with the 30-day process in the United States.

"Previously, it was almost impossible to do simultaneous development in both the U.S. and China because the China cohort was going to be so far behind," Berlin explains, but now concurrent trials are feasible. NMPA has also begun conducting more stringent reviews of clinical trials.

As of 2016, the government no longer requires Chinese biotech companies to manufacture their own drugs—now they can outsource to contract manufacturers rather than building facilities. In 2017, the government began updating its National Reimbursement Drug List annually instead of every 5 years—and has since added many innovative drugs. The NMPA was also invited to join the International Council for Harmonisation, which has helped China align its drug-development regulations with international standards. In addition, the Hong Kong Stock Exchange began listing companies before they generate revenue, thus giving them earlier access to public funding.

"These reforms have really changed the landscape for both Chinese biotechs, as well as Western biopharma companies operating in China," Berlin says.

The changes are paying off. There are now hundreds of Chinese biotechs—many clustered in BioBay, an industrial park in Suzhou. One is CStone, which is developing immunotherapies and targeted agents for cancer, focusing on malignancies such as gastric and liver cancers that are more common in China than in other countries. The company has 10 agents in 28 clinical trials, including five late-stage candidates. Notably, CStone, founded in 2015, is developing several therapies in collaboration with two U.S. companies—Blueprint Medicines and Agios. Such partnerships are becoming increasingly common as China's biotech scene grows. "These reforms have actually provided for a lot more opportunity for Western companies to partner with Chinese biotechs on drug development as well as commercialization," Berlin says.

The Amgen/BeiGene deal is one of the most significant—Amgen gains a 20.5% stake in BeiGene, and BeiGene will commercialize two of Amgen's FDA-approved oncology agents in China. The companies will co-develop 20 other oncology drugs. "That is an eye-opening strategic collaboration," Berlin says. "It's a pretty big statement from Amgen that China biotech is coming of age."

These partnerships make sense, Yan adds, because they leverage the strengths of each company. U.S. businesses tend to have expertise in drug discovery and designing and running clinical trials, whereas Chinese firms have access to a large patient population and understand China's regulatory landscape, including how to get drugs approved and to market.

Therapies are also starting to move in the other direction. In 2019, the FDA approved BeiGene's Bruton tyrosine kinase inhibitor zanubrutinib (Brukinsa) for patients with mantle cell lymphoma—the first U.S. approval of a drug developed in China. The agency also designated Chi-Med's angio-immuno kinase inhibitor surufatinib (HMPL-012) as an orphan drug for pancreatic neuroendocrine tumors. More U.S. corporations are making deals to license Chinese drugs, too. For example, Lilly partnered with Innovent Biologics in 2015 to develop Innovent's PD-1 inhibitor sintilimab (Tyvyt).

To be sure, obstacles remain. Many researchers are returning to Chinese biotechs after gaining education and experience elsewhere, yet companies need to continue expanding talent at the highest levels, especially in running clinical trials. "The competition for talent in China is very acute now," Berlin notes. Recent investigations into intellectual property theft by Chinese researchers in the United States have bred some mistrust between the countries. Additionally, the U.S. government recently expanded the scope of the Committee on Foreign Investment in the United States, potentially hindering Chinese investment in U.S. biotechs.

Despite these challenges, Jiang is hopeful that collaboration will continue. The United States and China are the two largest oncology markets, he notes, "and there's every incentive for the countries to get together and have complementary contributions."

"The more deals the better," Yan adds. "Cancer is not a disease that one country can conquer single-handedly."

–*Catherine Caruso* ■

For more news on cancer research, visit *Cancer Discovery* online at http://cancerdiscovery.aacrjournals.org/CDNews.