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China Biotech Interview: BeiGene Co-Founder Wang Eyes Next Big Things

China's Role In Going Global Strategy, PD-1 to AI

by Brian Yang

BeiGene co-founder and chair of the major global biotech's Scientific Advisory Board, Dr. Xiaodong Wang, sits down with *Scrip* in an exclusive audio interview to shed light on the rapid rise of China's biotech innovation, the country's role in BeiGene's global strategy and the next big things to watch.

One decade ago, when there was no viable innovative new drug R&D in China, a Chinese-American scientist and an American entrepreneur co-founded *BeiGene, Ltd.* .

Now, BeiGene has grown to become a leading cancer drug developer with administrative offices in Basel, Beijing and Cambridge, Mass. that is fast expanding in the US.

The scientist co-founder Xiaodong Wang, fresh from the J.P. Morgan Annual Healthcare Conference in San Francisco, sat down with *Scrip* in this exclusive audio interview to discuss his views on China biotech innovation, the path forward for BeiGene, where he is chairman of the scientific advisory board, and the next big thing.

The wide-ranging chat with the well-known researcher and biotech entrepreneur took place on 26 January at his office at the National Institute of Biological Sciences (NIBS) in Beijing, which he has been leading as director. Wang is also a member of the American Academy of Sciences and a foreign member of the Chinese Academy of Science.

Timing Was Everything

When asked where the next BeiGene may come from, Wang predicted “it probably won’t happen

again.” That’s because perfect timing is everything, which in China means an alignment of time, place and people.

Wang said that both he and the other BeiGene co-founder, chairman and CEO John Oyler, were outsiders, not in the core of drug development. "I used to joke about it, that both John and I didn't know what we were doing," Wang fondly recalled.

While Wang was the primary investigator at NIBS, Oyler was the president and CEO of contract research organization BioDura, later acquired by *PPD, Inc.* The two were not afraid to seize the timing that could not have been better in 2010 to start pioneering new drug research and development in China, Wang said.

The first driving factor was talent. By then, generations of overseas scientists had built a foundation for the birth of innovative research in the country, Wang explained. This included returnees to China, who continued their work in universities and academic and other research institutions.

Regulatory reforms in China also contributed to the good timing. In 2008, the US Food and Drug Administration opened one of its first overseas offices in China, and soon bilateral collaboration stimulated changes in China's previously isolated regulatory systems, leading to harmonization and global connections.

By 2015, harmonization has become a core task for the Chinese regulatory agency, which took drastic measures to eradicate fraudulent clinical data, reduce poor quality and redundant filings and speed up new drug approvals.

Wang said the third driving force was China's capital market. A large influx of money to new drug R&D recognized the talent and regulatory policy changes, but also stimulated a boom in the sector from 2019 to mid-2022.

Despite the economic downturn and ongoing chilly sentiment towards biotech investment since then, Wang said cycles are always moving up and down but that a core of innovation had now been established in China. He predicted this would also be only the first wave of biotech innovation in the country.

PD-1s, ADCs To AI

When asked about the next big wave of innovations on his radar, Wang said that novel modalities ranging from immuno-oncology anti-PD-1 antibodies to antibody-drug conjugates had already changed cancer treatment.

"Gradually, you can see that some of the [previously]

untreatable diseases have became treatable," noted Wang, adding that both PD-1s and ADCs have modest efficacy. Both are also being developed and used in combination use with conventional oncology therapies such as chemotherapy.

Wang is also excited about artificial intelligence-assisted drug development such as AlphaFold, a biology research tool developed by Google's DeepMind.

While AlphaFold 2 is already able to predict a protein's three-dimensional structure, the newly released AlphaFold 3 can predict the structures of most molecules in the US Research Collaboratory for Structural Bioinformatics' Protein Data Bank and ligand, nucleic acid and post-translational modification structures.

But despite the open-source AI platform outperforming its predecessor in protein structure prediction, challenges remain in predicting RNA structures, Wang noted.

Rising Domestic Innovation

China's rapidly rising biotech innovation has caught worldwide attention over the past year through multi-million dollar deals between local firms and major multinational drug makers.

Wang pointed to the rising force of innovation from two main kinds of domestic developers. Established firms such as *Sichuan Kelun Pharmaceutical Co Ltd.*, *Shanghai Fosun Pharmaceutical (Group) Co., Ltd.* and *Jiangsu Hengrui Medicine Co., Ltd.* are armed with large cash coffers and recruited talent.

Companies such as Kelun's biologs subsidiary Kelun Bio have signed large agreements with *Merck & Co., Inc.* to develop several ADCs for the US market, while Fosun and Hengrui are ranked among the top 50 R&D-based pharma firms in the world. However, they are still evolving, Wang said.

The other main driving force is a new crop of smaller biotech startups, which includes ADC developers such as BlissBio and *Duality Biologics* that have started stepping into the spotlight, indicating strong momentum and sustainability.

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'A Volume-Driven Market'

During the JPM conference, BeiGene's Oyler noted that roughly 90% of patients enrolled in the clinical development of the company's BTK inhibitor Brukinsa (zanubrutinib) were enrolled outside of China.

In addition, China's "biotech paradox" has also prompted the company to accelerate its globalization push. To be included in the National Reimbursement Drug List, drug prices are routinely discounted as much as 50%. Such deep cuts have made biotechs actively look for opportunities to expand overseas, Wang told *Scrip*.

"The Chinese domestic market is a volume-driven market and prices are being discounted."

Oyler cited in his JPM session the pricing of Brukinsa in China to illustrate the point. "When we started BeiGene, our estimate for China was an innovative medicine would be reimbursed at $1,000 to $3,000 and we thought the average would be $2,000. I think the average crossed below $2,000 but now it's bounced back up above that," he observed.

J.P. Morgan: China Inc. Being Hotly Pursued Amid Rising Innovation, Upbeat Sentiment

By Brian Yang

12 Jan 2024

After years of laying the foundations, China Biotech Inc. is being pursued by multinationals looking for innovative candidates to commercialize in both China and globally, executives and deals from the just concluded J.P Morgan Global Healthcare Conference show.

Read the full article here

However, "The Chinese government in the reimbursement process put in some guardrails so that you didn't have the risk of ruin, which led to more rational behavior.

"And if you can get that extra 10% or 15% revenue at the very high gross margins we have on a product like Brukinsa or Tevimbra (ti[leilizumab] even at the low Tevimbra pricing in China, you want to get it because it helps pay for the upfront cost, which makes you more profitable and more affordable everywhere else in the world."

'Very Concerned'

As one of the leading biologics researchers in China, Wang said he is "very concerned" about the ongoing competitive relationship with the US.

China has the advantage of quickly and cost-effectively expanding access to some new technologies, such as electric vehicles and solar panels, and the US should work together to address common health issues since they face similar threats, Wang suggested.

BeiGene's head of Biology Yu Shen and head of Research in Chemistry Zhiwei Wang all once worked in San Diego, reflecting the international nature of the biotech firm.

Also, BeiGene's anti-PD-1 antibody tislelizumab is still pending approval in the US and the PDUFA date has been delayed. The agency approved the first PD-1 drug from China, *Shanghai Junshi Biosciences Co., Ltd.*'s toripalimab, in 2023.

China's tightening reigns related to national security and overseas data transfer have worried industry observers that US FDA inspectors and unannounced inspections could be hindered due to potentially being subject to strict national security regulations. (Also see "*China Regulatory Overreach Prompts Concerns For FDA Inspections, Innovation*" - Pink Sheet, 18 Jan, 2024.)

New Neurology Startup

Sironax, a new startup founded by Wang, is dedicated to the development of novel drugs for neurogenerative conditions, drawing on his research into cell death mechanisms.

Its research is focusing on regulated cell death driven by internal changes to cause ageing, shortened life span and life vitality and Wang is looking to apply new underlying mechanisms to drug discovery. So far, it has three candidates, all in oral form.

Interview time stamps:

0001 - 0005: Observations from JPM

0006 - 0010: "Timing was everything" to start BeiGene in 2010

0011 - 0015: China's positioning in BeiGene's global strategy

0016 - 0020: China commercial challenges for innovative new drugs

0021 - 0025: "Very concerning" US-China tensions, impact on bilateral collaboration

0026 - 0028: Rise of Chinese domestic innovation

0029 - 0035: Cell death mechanisms and new startup Sironax

0036 - 0040: Why US-trained Chinese scientists are returning to China

0040 - 0045: Advice for aspiring biology researchers

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