James Xue – Founder, Chairman & CEO, CANbridge Pharmaceuticals

James Xue – Founder, Chairman & CEO, CANbridge Pharmaceuticals

> [The “In China for Global”] approach not only ensures that we can provide effective treatments to Chinese patients but also unlocks the full potential of our drugs for a global audience

13.08.2024

Tags:

China, Biotech, CANbridge, Rare Diseases

Dr James Xue, founder, chairman and CEO of CANbridge Pharmaceuticals shares the career journey that led him to China’s first rare disease-focused company and the role CANbridge is playing in shaping policies relating to rare diseases, such as the National Rare Disease List. Xue also outlines the company’s robust pipeline and its “In China for Global” approach to R&D in partnership with Wuxi Biologics.

Can you explain why CANbridge has such a strong focus on rare diseases, and how your background influenced this direction?

Interestingly, I never envisioned working in rare diseases until I joined Genzyme right after business school. It was there that I met Henri Termeer [former Genzyme CEO – ed.] who became my mentor for 16 years and is often regarded as the godfather of the biotech and orphan drug industry. Genzyme was pioneering in this field, launching the first treatment for rare diseases in the 1980s, which set a template for others to follow.

Early in my career, I was entrusted by Genzyme to establish a presence in China, not just building a company, but also creating a rare disease-oriented ecosystem. China has around 20 million rare disease patients, yet very few had access to treatments back then. When I started with Genzyme in 2002, treatments were primarily available through charitable efforts, like Project Hope.

Over the years, we have seen significant progress. Tens of thousands of Chinese patients now receive effective treatments, largely due to the efforts of multinational companies setting up infrastructure in China. When I set up Genzyme China, it was the first and only organization focused on rare diseases in the country.

With CANbridge, we have continued this mission. We were the first domestic pharmaceutical company in China to develop and commercialize rare disease products, handling everything from preclinical to post-market development and manufacturing. Our aim is to establish a comprehensive

infrastructure and reimbursement system for rare diseases in China, which is crucial for sustainable progress in this field.

Since our establishment in 2012 and going public in December 2021 on the Hong Kong Stock Exchange, CANbridge has been at the forefront of this journey. We were the first public company in Asia to be squarely focused on rare diseases at the time of our IPO.

Being the first homegrown company in China to focus on rare diseases must be challenging. Can you share some insights into these challenges and the impact CANbridge has had?

Being the first is indeed much harder. There are no precedents to follow, which means we have had to pave the way in many aspects. This involves a tremendous amount of education for all stakeholders—investors, government policymakers, the media, and non-profit organizations. However, the reward is that we have significant influence in shaping the policies and regulations related to rare diseases.

For example, we played an active role in drafting and editing the first textbook on rare disease diagnosis and treatment, and we were involved in formulating the National Rare Disease List. I also co-founded the China Alliance for Rare Disease, a highly influential non-government organization (NGO), where I currently serve as Deputy Director General. Additionally, we have partnered with Peking Union Medical College Hospital to establish the first rare disease-focused translational development centre, which we announced on Rare Disease Day this February.

We have already launched two rare disease products in mainland China, Taiwan, and Hong Kong. In mainland China, we collaborate with the medical community to publish national treatment guidelines. For instance, we released a treatment guideline for MPS II shortly after launching our drug Hunterase two years ago. Recently, we launched our second drug, Livmarli for Alagille syndrome, and its treatment guideline was published on August 2nd.

Despite being a small company with fewer than 100 employees worldwide, we have made remarkable achievements. Our work led to the publication of two new national treatment guidelines. This is quite an incredible accomplishment for us.

Could you clarify the varying definitions of rare diseases across greater China and how these definitions impact your operations?

The designation of rare diseases can vary significantly between regions. For instance, the US Orphan Drug Act, passed by Congress in 1983, defines an orphan disease as one affecting a population of 200,000 or fewer individuals. In China, however, there is not yet a formal definition. Given the country’s vast population and the acknowledgment of around 7,000 rare diseases globally, China needs to develop its own criteria.

This is an ongoing discussion among legal scholars and policymakers in China. The focus has been on diseases that are widely recognized and have established diagnostic and treatment protocols in the international community. A significant milestone for China was the publication of the first national rare disease list in 2018, which includes 121 diseases. This list was a collaborative effort of five different ministries, which is quite unprecedented.

Without a legal definition, any disease on this list qualifies as a rare disease. Consequently,

developing or commercializing treatments for these diseases, or even importing drugs, can entitle companies to preferential treatment. This approach is designed to accelerate the introduction of existing treatments to Chinese patients and physicians. The Chinese National Medical Products Administration (NMPA) has also issued guidelines to expedite the approval of rare disease products listed in the national rare disease list, often without the need for additional bridging studies in China.

This expedited process is particularly important for genetic diseases and other conditions where existing treatments developed in other countries can be quickly made available to patients in China, even if the original clinical trials did not include diverse cohorts reflective of the Chinese population.

Genetic diseases, despite their varied impact, seem to have commonalities across different populations. Could you explain how this effects the development and testing of treatments, especially considering that many drugs were not originally tested with diverse cohorts?

Genetic diseases present unique challenges and opportunities. Most rare diseases, about 80 percent, have a genetic origin, meaning patients are often affected from birth. Unlike acquired diseases, such as those influenced by lifestyle or environment, genetic diseases are caused by inherited or spontaneous DNA mutations. While some rare cancers can be classified as rare diseases, the majority are genetic.

Despite regional and ethnic differences in the incidence of certain genetic mutations, the underlying causes of rare diseases are remarkably consistent worldwide. For example, Gaucher disease has a much higher incidence among Ashkenazi Jews, and Pompe disease is more prevalent in Southeast Chinese populations, such as in Taiwan and Fujian province. However, the genetic mutations responsible for these diseases are very similar across different ethnicities and geographies.

The genetic sequencing of diseases like Duchenne muscular dystrophy (DMD) shows consistent mutations regardless of location. In China, there are over 5,500 registered DMD patients, but estimates suggest there could be over 70,000 affected. This makes China one of the largest rare disease markets globally for this particular indication. Consequently, many companies are developing gene therapies for DMD, and significant breakthroughs may come from China due to the higher incidence and prevalence in the population.

What is the business model you are currently pursuing and what does your portfolio look like?

Our initial approach involved licensing drugs that were in the near-commercial stage and fully de-risked. We aimed to quickly make these treatments available in China, register them, and launch them ourselves. This not only provided treatments to Chinese patients but also helped train physicians in diagnosis and long-term patient care.

However, we realized that for a long-term solution, we needed to build our own R&D pipeline. We were fortunate to partner with Wuxi Biologics, who are also investors in CANbridge. Together, we developed a model we call “In China for Global.” This involves starting clinical development in China, progressing from phase I to pivotal trials, and potentially including global patients in phase two.

This model allows us to address the Chinese market quickly, while also developing treatments that can serve global patients. By conducting clinical trials that include both Chinese and international

patients, we can validate our drug candidates and amplify their value in other markets. This approach not only ensures that we can provide effective treatments to Chinese patients but also unlocks the full potential of our drugs for a global audience. We definitely can also allow partners to come in to license out our asset or to co-develop those drugs.

We have three products on the market. Two of these are for rare diseases, and the third is a breast cancer drug we acquired in the early days. Additionally, we have ten pipeline products at various stages of development, from preclinical IND enabling to phase I and phase II. This gives us one of the most robust rare disease pipelines being developed in China. Our modalities range from small molecules to recombinant enzymes, monoclonal antibodies, and AAV gene therapies.

We are strategic in choosing which projects to develop in-house. For biologics, we typically rely on academic institutions for discovery, then take over for development. With AAV gene therapies, we adopt a hybrid approach, collaborating with academic institutions while also maintaining a small but efficient discovery team in the US. Gene therapy is particularly exciting because it is a relatively new field with few successful commercialized products. We have made significant progress, especially with our next-generation SMA (Spinal Muscular Atrophy) and DMD (Duchenne Muscular Dystrophy) gene therapies, which have shown promising results in animal models.

Both our next-generation SMA and DMD gene therapies are still in the pre-IND stages, but the potential is significant. We believe that genetic diseases are best addressed with curative solutions rather than chronic treatments. Nobody wants lifelong infusions every two weeks. With advancements in genetic engineering, gene editing, and mRNA technologies, we are optimistic that we will see more diseases cured rather than just treated in the next decade.

You mentioned earlier that China offers unique advantages in terms of regulatory flexibility and patient population. How do these factors contribute to potentially shortening development timelines and reducing costs compared to Western developed countries?

China’s regulatory environment and the vast population of treatment-naive rare disease patients provide distinct advantages. Regulatory frameworks like Investigator-Initiated Trials (IITs) allow for more streamlined clinical development pathways. This flexibility, coupled with a large patient pool, can significantly accelerate timelines and lower costs associated with drug development, which is quite unique to China compared to developed Western markets.

Now that you are in the stage of commercializing products, are you aiming to become a fully integrated company with R&D and commercial capabilities, or is this driven more by the need for increased cash flow, especially given your listing?

Our journey into commercialization is not solely driven by financial considerations. Having led the commercialization of the Genzyme product Cerezyme in China over 15 years ago, I understand the importance of building local expertise and infrastructure beyond revenue generation. Establishing centres of excellence for diagnosis and treatment is crucial for any rare disease company’s growth. While we currently handle both R&D and commercialization, the future path of whether we manage everything internally remains open for discussion. It is essential to experience the entire process first-hand to fully appreciate the value creation and delivery in rare disease treatments, which has been our focus over the past five years.

Can you elaborate on who drives and pays for healthcare in China, especially concerning rare diseases, and how this impacts your operations?

In China, healthcare financing is primarily driven by the government through tax revenues allocated to healthcare spending. A small portion, about ten percent of this funding is dedicated to innovative drugs, including those for rare diseases. Outside of government funding, there is a commercial insurance system sponsored by the government but operated by private companies. These insurers collaborate with the government and are guaranteed against losses initially, with potential profitability if managed well. However, coverage can be limited, particularly for pre-existing conditions, posing challenges for patients with genetic diseases.

Navigating China's healthcare financing landscape requires us to innovate not only in drug development but also in access strategies. We work closely with both government channels and commercial insurers to ensure our treatments reach patients effectively. Given the diverse economic and demographic landscape in China—ranging from urban to rural areas, and varying economic statuses—this necessitates a tailored approach.

Many of your counterparts that also listed via HKEX's Chapter 18A for pre-revenue biotechs are now somewhat disillusioned seeing the poor valuations and lack of liquidity. Do you feel the same way?

I believe it was a prudent decision by the Hong Kong Exchange to introduce a biotech board catering to non-profit or early-stage companies. However, this move coincided with a significant withdrawal of Western capital from Hong Kong's financial markets, which has had far-reaching consequences. One notable repercussion is the departure of specialized investors, essential for companies like ours. Most of the founders of the Chapter 18A companies have Western backgrounds and possess extensive education in their fields. Analysts who grasp the intricacies of our scientific approach, treatment algorithms, and competitive landscape are pivotal in understanding our company's trajectory.

Hong Kong's financial industry, primarily retail-oriented, excels in conventional metrics like revenue and profit, but often lacks expertise in niche scientific fields. Beyond political considerations, enhancing training and marketing efforts could elevate companies beyond traditional financial evaluations. There is a prevalent misconception regarding rare diseases in China, where government reimbursement rates are low, dissuading interest despite potential viability.

Over my two decades in this field, I remain optimistic that perceptions will evolve. Rare diseases could lead the way in biotech advancements, offering economically viable models beneficial to both patients and investors.

In terms of regulatory reform, the rare disease space is currently the most active. For instance, the Centre for Drug Evaluation (CDE) recently issued patient-centric development guidelines specifically for rare disease drugs, with several of our programs could be selected as pilot initiatives.

Rare diseases are a pivotal area globally. My analysis indicates that 17 out of the top 20 blockbuster drugs have received orphan designations, often preceding approvals for more common conditions. This regulatory focus is just beginning. Rare diseases present a level playing field where Chinese companies can compete effectively. With tools spanning biological proteins, recombinant

technologies, and even RNA and DNA levels, Chinese firms are well-equipped. It is now about their determination to pursue these significant opportunities. I believe China's biotech sector cannot indefinitely rely on subsidies from global markets. Entrepreneurs evaluating whether to establish companies in the US versus China face significant disparities in investment returns. Achieving equilibrium in these dynamics is crucial for sustained industry growth.

Looking ahead for CANbridge, what do you foresee as the next inflection points over the next three to five years?

In the near term, our commercial goal is to achieve break-even, contingent on significant pricing reforms in China. This hinges on what we term optimized pricing, although this remains beyond our direct control. However, even without these reforms, we anticipate organic growth driven by increased patient diagnosis and drug usage, alongside overall market expansion.

Another critical milestone involves gaining global recognition, whether through acceptance of our data by international regulatory bodies or through strategic partnerships with Western companies. We are actively pursuing these objectives to solidify our position as a global biopharmaceutical player.

The landscape in rare diseases has seen notable acquisitions, reflecting the sector's potential attractiveness despite financial challenges. We anticipate further consolidation in the market, offering opportunities for growth and recognition on a broader scale.

And what kind of values would a partner discover in CANbridge?

Over the past 12 years, CANbridge has meticulously built an impeccable reputation, drawing talent from esteemed rare disease companies like Genzyme, and Ultragenyx. Our willingness to take calculated risks and pioneer initiatives has been recognized both within China and internationally. In the US, for instance, we actively engage with organizations like UMass Chan Medical School, leveraging our base in Massachusetts to foster local collaborations. Our influence extends to shaping rare disease drug development policies through partnerships with PhIRDA, where I serve on the R&D committee. For potential partners, especially in biotech, focusing on rare diseases often comes with a personal commitment, driven by first-hand experience, or a deep connection to the cause. At CANbridge, we see this as a lifelong journey, supporting partners not only in their home countries but also globally, aligning our mission to ultimately benefit patients worldwide. Our aim is to forge mutually beneficial relationships, creating enduring value and advancing patient care.

See more interviews