Wang Yinxiang â?? Chairman & CEO, Jacobio

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Chinese biotech Jacobio has made remarkable strides in pioneering first-in-class drug research, with their SHP2 inhibitor project only the second globally to initiate a clinical trial for a novel target and eventually licensed to AbbVie for approximately USD one billion in 2020. Chairman and CEO Dr Wang Yinxiang outlines Jacobioâ??sstrategic approach to conducting multicenter trials globally from the outset, and the companyâ??s positioning as a valuable partner within the global pharmaceutical industry, especially in the development of allosteric inhibitors for â??undruggableâ?• targets in oncology.

Can you reflect on the progress Jacobio has made since our last Pharmaboardroom interview back in 2018, highlighting some of the key milestones along the way?

Since our companyâ??s early days, weâ??ve remained steadfast in our strategy of pioneering first-in-class drug research. Over the past five to six years, weâ??ve achieved significant milestones. For instance, our first major project focused on a SHP2 inhibitor, where we became the second company globally to initiate a clinical trial for this novel target back in 2018. Subsequently, in 2020, we successfully licensed this project to AbbVie for approximately USD one billion, marking a pivotal moment for Chinese biotech firms as it was the first major licensing deal for small molecule drugs in the country. Additionally, weâ??ve made strides in other areas, such as developing small molecule drugs like BET inhibitor, which are relatively rare in the field dominated by PD-1 antibodies. I believe

this represents a turning point for the Chinese biotech company. Transitioning from researching generic drugs to developing first-in-class medications opens up opportunities for collaboration with Big Pharma companies from Europe or the US.

This progress has been supported by successful fundraising efforts, including a USD 200 million IPO in Hong Kong, though there was potential to secure even more capital based on market sentiment. Overall, these achievements reflect our commitment to innovation and collaboration within the global pharmaceutical landscape.

How has the companyâ??s engagement with the capital market influenced its governance and management approach?

The impact on governance and management stemming from our engagement with the capital market has been relatively minimal. The Hong Kong Stock Exchangeâ??s regulatory framework is not as stringent compared to other jurisdictions, which has translated into limited changes in our management practices. However, our interaction with the capital market has facilitated the development of our second product, a KRAS G12C inhibitor, which has undergone pivotal trials in China. With plans to file for China NDA approval in Q2 2024, this marks a significant milestone for us as it represents our first NDA submission.

Could you explain the rationale behind initiating multicenter trials globally from the outset, particularly for your first-in-class product, versus focusing on local trials at perhaps a lower cost?

Our strategy involves initiating multicenter trials globally right from the start, including sites in France, Spain and the US alongside China. This approach is driven by the need to gather diverse patient data, especially from regions like the US and Europe, which is crucial for potential collaborations with major pharmaceutical companies. Additionally, as we plan to pursue FDA approval, having data from US patients becomes essential. Variations in patient demographics and responses to treatment underscore the importance of collecting data from multiple geographic regions. Despite the associated costs, this strategy is essential for ensuring comprehensive clinical evidence and positioning our product for success in the global market.

Over the past few years, we have made significant progress. We currently have nine already approved for clinical trial commencement. This represents a substantial workload. Additionally, we are steadfast in maintaining five to six of our products among the top contenders globally.

Just reflecting on the complexity and virtues of your R&D, can you provide an overview of your technology platform?

Traditional drug targets bind to the proteinâ??s active site by competing with the natural substrate (like kinaseâ??s GTP binding pocket). Jacobioâ??s Induced Allosteric Drug Discovery Platform (IADDP) mainly focuses on developing drugs that target the allosteric site of the protein, which can induce the conformation change of the protein and finally modulate the function and the downstream signalling. The allosteric siteâ??s existence is not always obvious, which makes this approach challenging compared to traditional ones. Jacobio has generated a lot of deep in-house understanding of how to find these pockets. By using this IADDP we have successfully found

inhibitors like SHP2 and KRAS.

This approach presents significant advantages for collaboration with global companies, as it offers efficiency and in-house research capabilities that may not be available elsewhere. While many companies have similar platforms, our focus on in-house synthesis and comprehensive research sets us apart, ensuring a more robust and effective drug discovery process.

Can you elaborate on the therapeutic areas that this platform can help to accelerate?

Our primary focus is on oncology, with a particular emphasis on two key areas: targeted therapy and the next generation of immunotherapy. In targeted therapy, we concentrate on developing allosteric inhibitors to target previously â??undruggableâ?• targets. These targets have long been recognized for their relevance to cancer, but finding effective small molecule treatments has been historically challenging. Our goal is to address this gap by developing innovative allosteric inhibitors. Additionally, weâ??re exploring cancer immunotherapy, aiming to advance beyond the limitations of current approaches like PD-1 antibodies. While PD-1 antibodies have shown efficacy in some cancers (20-30 percent in solid tumours), they are ineffective as monotherapy in others, particularly those lacking sufficient lymphocyte infiltration. To address this, weâ??re developing strategies to attract lymphocytes into tumor tissues, potentially unlocking new avenues for immunotherapy. One example is our work with small molecule-stimulated immuno-stimulant conjugates, such as STING stimulator, which have shown promise in enhancing immune responses against tumours. Through these efforts, we aim to pioneer the next generation of cancer immunotherapy.

What are Jacobioâ??s plans for creating a stream of revenues, especially at a time when returning to the capital market may not be ideal? And if you can please clarify the pitfalls of the highly publicized deal the company had with Abbvie a few years ago.

We have two primary strategies for revenue generation. Firstly, we continue to raise funds from the capital market, primarily in Hong Kong, despite the current downturn. Last year, we successfully secured funding, and we anticipate further fundraising efforts this year. Additionally, we pursue licensing agreements, such as our deal with AbbVie, which brought in a significant sum of USD 110 million despite not having gone to the end of the milestones. With a substantial portion of this capital in reserve, equivalent to nearly three yearsâ?? worth of operational expenses, we are well-positioned financially. Moreover, as our first project, the KRAS G12C inhibitor, nears approval for marketing this year in China we anticipate generating income from sales in the near future.

Regarding commercialization, we remain open to various avenues. We are exploring licensing agreements and partnerships to leverage our strengths while considering collaboration with pharmaceutical companies for hospital promotions and sales. This collaborative approach allows us to focus on our core competencies while ensuring effective distribution of our products.

To what extent do you believe the Chinese NMPA (National Medical Products Administration) is fit for purpose to help accelerate the clinical development of homegrown biotechs compared to the FDAâ??s approach?

The NMPAâ??s role in new drug research in China has been quite significant, mirroring the FDAâ??s involvement in the United States. Upon filing the IND (Investigational New Drug)

application, the NMPA typically responds within 60 working days, which is approximately two months slower than the US FDAâ??s response time. Other than that, weâ??ve never encountered significant delays in the past several years while having nine products in clinical stages.

In important to note, that currently, our global research strategy has led us to establish a team and office in Boston. With around 10 employees in the US, we can conduct Phase One trials independently. Four years ago, we recruited a former oncologist, our CMO Dr Andrea Wang-Gillam, who specializes in pancreatic cancer. She primarily oversees clinical trials in the US and Europe from our Boston office. Our approach involves filing for Phase One trials in the US first due to quicker execution times. Subsequently, we gather data before proceeding with Phase Two or Three trials in China, where there is a significant patient population. Additionally, we explore partnerships for conducting global multicenter trials, utilizing data from previous trials conducted in both the US and China.

What are the key objectives you have set for Jacobio in 2024?

In 2024, we have three primary goals in focus. Firstly, we are dedicated to obtaining NDA approval for our first product in China. Concurrently, we have several projects progressing towards IND filings, including our P53 activator (IND approved in US already, applying for China IND now) and the highly anticipated KRAS ^{multi}, which holds immense potential in covering a substantial portion of cancer patients (20 percent). We are likely to become the second or third company to have a KRAS multi-inhibitor in the clinical stage. We are currently preparing the necessary documentation to file for Investigational New Drug (IND) approval, which we anticipate submitting around June or July in China and the US. We are also driving forward with our iADC programs, aiming to initiate clinical trials for our second-generation immunotherapy for cancer. With these endeavours, we are poised to make significant strides in advancing healthcare innovation and addressing critical unmet needs in the field.

As someone who has experienced the highs and lows of this industry over the years, what final message would you like to convey to our international audience about why they should consider partnering with Jacobio Pharmaceuticals?

Despite the challenges and uncertainties inherent in this field, I remain deeply passionate about the potential impact of our work. As a scientist, witnessing the translation of concepts from textbooks into clinical reality is immensely gratifying. Our dedication to advancing technology and making tangible differences in healthcare is unwavering. Partnering with Jacobio Pharmaceuticals offers a unique opportunity to collaborate on groundbreaking initiatives that have the potential to shape the future of medicine.

Reflecting on international relations, back in 1970, the US and China had no diplomatic relations. It is therefore evident that significant progress has been made since then. Everything is possible, we need to carry on with our work.

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