# Xueming Qian – CEO & Co-Founder, Transcenta

***China has become a vibrant hub for innovation, yielding numerous first-in-class molecules. We are proud to possess such molecules ourselves and are actively engaging with multinational partners***

17.07.2024

Tags: China, Biotech, Oncology, Transcenta

*We last spoke with Xueming Qian, CEO and co-founder of the biotech Transcenta in 2019. Since then, the company has seen some important milestones: listing on the Hong Kong Stock Exchange and advancing its first-line gastric cancer treatment into phase III trials. Qian outlines Transcenta's progress, including its global multi-centre clinical trials and the continuous manufacturing capability it has developed, and weighs in on varying investor response as well as the Chinese biotech ecosystem.*

**Since our last interview in 2019, apart from the impact of COVID-19, what significant developments have occurred at Transcenta?**

I am pleased to say we have made substantial progress over the last five years. During the COVID-19 pandemic, we initiated the clinical trial for our lead compound, a second-generation antibody targeting Claudin 18.2, which began in the summer of 2020.

We advanced this program rapidly, and we are now entering phase III trials. This trial focuses on first-line gastric cancer, a condition affecting approximately 1.1 million people globally. Notably, China accounts for about 40 percent of the global gastric cancer population. The five-year survival rate for gastric cancer patients remains relatively low at around 30 percent. We aim to revolutionize treatment for patients with the Claudin 18.2 expression by integrating our antibody with the standard care regimen.

Our treatment approach involves combining the standard of care, which currently includes immuno checkpoint inhibitors and chemotherapy, with our antibody. This combination aims to provide broader coverage for patients with HER2-negative gastric cancer. Our antibody, Osemitamab (TST001), is added to a PD-1 plus chemotherapy regimen.

Recently, we presented our phase two trial data at the American Society of Clinical Oncology (ASCO). This trial included 82 patients and demonstrated significant improvements. For patients without the Claudin 18.2 expression, the progression-free survival (PFS) was about seven months with a response rate of 50 percent. However, for those with a high or medium Claudin 18.2 expression, adding our antibody increased the overall response rate to 68 percent and the PFS to 12.6 months.

**How does your molecule under development differ from current standards of care?**

We have brought together top global leaders in the gastric cancer field to join our global phase III trial for which we have seen quite promising results. Currently, we are the only company, apart from one competitor, to combine Claudin 18.2 with chemotherapy in a global regulatory setting. However, our competitor is only combining with the older standard of care chemotherapy. In contrast, we are combining Claudin 18.2 with the current standard of care, creating a triple combination therapy that leverages the synergistic effects of targeted therapy, immunotherapy, and a chemotherapy backbone.

Treatment methods will always require chemotherapy to eliminate resistant tumour cells. We found that adding Claudin 18.2 targeted therapy to these patients upregulates PD-L1. Initially, most patients with Claudin 18.2 do not benefit significantly from checkpoint inhibitors combined with chemotherapy. By adding a Claudin 18.2 antibody, we can upregulate PD-L1, making these tumours responsive to checkpoint inhibitors.

**Were your clinical trials conducted solely in China, or were they multi-centre trials with data that could be interoperable for other markets?**

Over the last three to four years, we have worked diligently to make global multi-centre controlled clinical trials a reality. Several key steps were involved in this process, first of which was to generate Phase II data both in China and the US. Then, our drug production quality had to meet the standards of the FDA, EMA, China NMPA, and other regulatory agencies. Finally, we had to develop a precision tool to select patients, known as a companion diagnostic, which is essential for conducting a global Phase III trial.

This trial is indeed a global multi-centre controlled trial, involving sites in the US, Europe, China, Japan, South Korea, and potentially other countries. This is an exciting time for Transcenta because we are the only company conducting such a trial on this scale.

Compared to our competitor, we are targeting a much larger population. Our trial builds on the existing standard of care and targets a broader patient group. Additionally, their antibodies are first-generation, with lower potency compared to ours. They use a chimeric antibody developed 15 years ago, while we have developed humanized antibodies with increased affinity and enhanced components of the immune system. This allows our antibody to engage natural killer (NK) cells, a critical mechanism for this type of targeted therapy to kill tumour cells.

Overall, I am very proud of our progress. It has been a long journey, with extensive planning. Without the simultaneous development of companion diagnostics, a Phase III trial would not be possible, as the FDA and EMA require it. Although China does not yet require companion diagnostics as stringently as the FDA, they are moving in that direction. Companion diagnostics are crucial as they help ensure that patients who are most likely to benefit from our antibody therapy are accurately identified, leading to better outcomes.

**How are you financing your future clinical trials in the current market environment? Given the current challenging market conditions, is securing funding a concern, or do you have sufficient resources to proceed independently?**

We have been very clear from the beginning that taking on this process alone is insufficient. We do not have a large clinical team in the US to manage this undertaking by ourselves. Our goal has always been to find a global partner, especially for commercialization. While we might handle the clinical development independently, thanks to our world class CMO, Dr Caroline Germa—who has extensive experience from her time at Novartis, AstraZeneca, and BMS—we still need a commercial partner to truly bring this therapeutic agent to patients.

Having a commercial partner is crucial as they can bring additional clinical resources to help accelerate patient enrolment and share the costs even if we had the funds to proceed on our own.

We have not publicly disclosed this partnership yet, but we are in the final stages of securing a partner with a strong strategic interest in gastrointestinal cancer and the capacity to manage and deploy the product effectively. This partnership will be key to our success moving forward.

**Can you share more about the additional indications and areas of expansion you are exploring?**

Our molecule not only holds promise for first-line gastric cancer but also for perioperative gastric cancer, whether it is before or after surgery. This accounts for another 30 to 40 percent of gastric cancer patients who initially undergo surgery but eventually experience progression. By adding Claudin 18.2 antibody along with chemo or checkpoint inhibitors, we can potentially shrink tumours pre-surgery and eliminate residual tumour cells post-surgery, leading to longer disease-free survival. Additionally, there is significant potential in pancreatic cancer, where about 50 percent of tumours express Claudin 18.2, which represents a very promising area for further investigation and

expansion.

Another major indication we are excited about is lung cancer. Our competitor, who has developed CDx assays with another company, cannot distinguish between Claudin 18.2 and 18.1 due to their antibody binding to a shared intracellular domain. However, our antibodies target an epitope near the therapeutic antibody binding site specific to Claudin 18.2. This specificity allows us to accurately screen for Claudin 18.2 positive lung cancer, which constitutes about 10 percent of lung cancer cases. This capability opens up a substantial new avenue for us.

**Introducing new medicines to the market requires system readiness and affordability. How do you envision your product being integrated in the standard of care, and in what ways will it be differentiated?**

Focusing on gastric cancer, many patients with Claudin 18.2 do not express high levels of PD-L1. Although they are treated with PD-L1 plus chemo, their PFS averages around 7 to 7.5 months, which is not long enough. Our goal is to see at least a 30 percent improvement. In our current phase II trial, we have observed an increase in PFS from 6.7 to 12.6 months, representing a 70 percent improvement. We are aiming for at least a 50 percent improvement in PFS, which typically correlates well with overall survival. We are targeting a significant extension of life, aiming for six to seven months longer survival compared to the current standard.

As I mentioned, our current trials focus on first-line treatment. The combination of our therapeutic agent, immunotherapy, and chemo is more tolerable due to non-overlapping toxicities. Mechanistically, they are very synergistic. Chemotherapy kills tumour cells and releases neoantigens, activating NK cells and T cells. Our antibody further engages NK cells, killing tumours and releasing cytokines that regulate PD-L1, making tumours more responsive to checkpoint inhibitors.

The synergistic effect of adding targeted therapy like Claudin 18.2 is crucial to our added value. Our engineered antibody has stronger NK cell engagement capabilities and higher affinity for tumour cells with varying levels of Claudin 18.2. This allows us to expand the benefit to patients with lower Claudin 18.2 expression – significantly broadening our target population.

**As you transition from early development to commercialization, how are you approaching manufacturing and pricing strategies? Will your commercial strategy differ**

**between China and international markets?**

As we transition from early development to commercialization, our approach to manufacturing and pricing strategies is pivotal. The pricing dynamics can vary significantly between markets like the US and China, potentially differing by 20 to 30-fold. While this phenomenon might also affect Claudin 18.2, the extent of price erosion depends on market competition. Unlike PD-L1 therapies with numerous players, Claudin 18.2 has fewer competitors in first line setting—currently around four globally and only Astellas in the US—reducing immediate pricing pressures.

Moreover, we have strategies in place to maintain robust profit margins even if price adjustments are necessary. Regarding manufacturing, the scale is substantial, particularly in China where 70 percent of newly diagnosed gastric cancer patients express Claudin 18.2—approximately 280,000 individuals. Our antibody can potentially benefit 80 percent of these patients, equating to a significant demand for our drug. Despite this, our efficient manufacturing process, based in Hangzhou, is equipped to handle this volume.

Our manufacturing capability is supported by an innovative continuous manufacturing process, approved by the FDA and China's NMPA for both Phase III trials and commercial production. Unlike traditional Fed-batch methods, which have a fixed production cycle, our process allows for continuous harvesting starting from day 11 up to day 30, adapting production to demand seamlessly. This flexibility ensures we can meet market needs without requiring additional regulatory approvals.

We began investing in these capabilities back in 2019, converting our manufacturing from Fed-batch to perfusion-based processes. This strategic move allows us to expand production efficiently without the upfront capital expenditure typically associated with large-scale manufacturing facilities. While we are pioneers in China with this approach, it is gaining traction globally among multinational firms for its cost-effectiveness and scalability.

Additionally, we will continue investing in our own R&D projects. Unlike commercial manufacturing, which requires continuous production, R&D projects typically involve fewer batches. This approach optimizes our facility's potential by dedicating specific spaces for different needs, thereby enhancing overall facility utilization.

Our facility in Hangzhou is designed to meet stringent Chinese regulatory requirements, which mandate that drug substance and drug product manufacturing occur in the same facility. This setup supports our ability to serve both Chinese and international commercialization needs effectively. While regulations outside China allow for outsourcing drug product manufacturing, in

China, integration of both processes within one facility is mandatory, and we are fully compliant with these regulations. This positions us well to support commercial manufacturing requirements both domestically and internationally.

**As a publicly listed company what has been investor´s response to Transcenta´s inflection points?**

Investor response varies largely by region. In Asia, investors tend to prioritize revenue generation over potential, unlike their counterparts in the US who focus more on a company's growth prospects and clinical data. This difference means that our company's profile might be better appreciated as a US-based entity, where our innovative pipeline and clinical progress are more closely aligned with investor expectations.

Therefore, we are considering a dual-listing strategy for the long-term benefit. This approach allows us to appeal to both Asian and US investors, leveraging our robust pipeline. For instance, we have licensed a promising osteoporosis treatment from Eli Lilly, tailored for the Asian population. Osteoporosis poses a significant health burden here, with high mortality rates following fractures. Our clinical trials have shown promising results, but the Chinese market, focusing on near-term profitability, has not fully recognized its potential yet.

On the other hand, in the US, investors typically recognize and appreciate the potential of innovative drugs like ours, which addresses critical healthcare needs. In China alone, there are 3.3 million patients who have experienced one fracture, presenting a substantial market opportunity even with a modest market penetration.

Previously, Western investors showed strong interest in high-potential companies like Transcenta, but geopolitical uncertainties have led them withdrawal from certain markets. Although we anticipate their return eventually, we must also act proactively. We aim to align ourselves where our value is best understood, advancing our pipeline towards commercialization to resonate better with investors in Hong Kong and beyond.

**What final message would you like to share on behalf of Transcenta and the Chinese biotechnology ecosystem?**

I would first like to emphasize Transcenta’s dedication to science. By focusing on scientific innovation and developing differentiated products that meet patient needs, we are paving a clear path forward. Whether through independent development, partnerships with multinationals, or acquisition, this commitment remains essential.

China has become a vibrant hub for innovation, yielding numerous first-in-class molecules. We are proud to possess such molecules ourselves and are actively engaging with multinational partners. With time, these innovations will undoubtedly take centre stage, showcasing China’s prowess in biotechnology.

Creating a conducive investment and funding environment, along with supportive government reimbursement mechanisms, is crucial. We appreciate the government’s efforts to empower companies in setting fair drug prices based on their value. This approach not only benefits companies but also ensures that innovative drugs reach patients who truly need them.

Looking ahead, we foresee a future where innovative treatments meet the needs of many patients. This alignment will enable us to attract further investments, continue reinvesting in the development of novel therapies, and ultimately deliver essential treatments to patients who need them most.

**See more interviews**