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With its dual business approach â?? commercializing acquired products while developing a novel respiratory disease pipeline â?? Nuance Pharma, after closing Series D funding and establishing a solid revenue stream, has set its sights on Asia Pacific. Founder and CEO Mark Lotter, discusses the regulatory and talent acquisition challenges in China, how market access has evolved, and the advantages of diversifying in Asia-Pacific and using Hong Kong as a launching pad.

What milestones has Nuance achieved since we last spoke in 2019?

Nuance has achieved several significant milestones since 2019, when we were about to successfully close our Series D funding round, raising USD 180 million. This funding was swiftly deployed into several strategic initiatives, including a small commercial acquisition of some legacy UCB products and multiple in-licensing agreements. Notably, we secured a deal with Verona for their novel first-in-class PDE3 /PDE4 inhibitor, Ensifentrine, which was approved recently in June 2024. Additionally, our partnership with Aerogen, a first ever surfactant which can be delivered intranasally via a nebulizer for neonatal respiratory distress syndrome conditions, has been progressing. We have had also entered agreements with Altamira for an allergy product and Bavarian Nordic for an RSV vaccine, although the latterâ??s phase III program was subsequently withdrawn.

In parallel with these strategic moves, Nuance has expanded its commercial footprint significantly. This year, we anticipate reaching approximately CNY 800 million (around USD 100 million) in revenue, supported by a robust team of over 500 employees, with a substantial portion dedicated to commercial operations. Moreover, our focus has been on building a dual business model encompassing both commercialization and the development of a novel pipeline with a core focus within the Respiratory Franchise, which is atypical for early-stage companies in China.

Nuance Pharma was set up in 2014 with the intention of differentiating the company on three different levels (1) establish a dual wheel model i.e., a commercial platform together with a

developing novel pipeline (2) target respiratory disease (3) establish a presence in China and Asia Pacific as a region.

Strategically, we have pivoted away from traditional oncology and immunology approaches to concentrate heavily on respiratory medicine. This expanded focus encompasses biologics, drug device combinations, and innovative therapies for conditions like asthma, COPD, and allergies. This strategic shift is rooted in the substantial patient populations with 100 million affected by chronic obstructive pulmonary disease (COPD), 50 million with asthma, and over 250 million suffering from allergies in China alone. The high unmet medical needs in these areas, combined with limited innovation from multinational pharmaceutical companies following the implementation of value-based pricing (VBP) regulations in China, present Nuance with a compelling opportunity.

I first recognized the potential in respiratory medicine during my tenure with AstraZeneca in China. Given the evident market demand and our capabilities, we believe that concentrating on respiratory medicine not only aligns with patient needs but also positions Nuance uniquely amid the industryâ??s evolving dynamics.

Given investorsâ?? general preference for oncology focused companies, was it challenging to convey the value proposition of Nuance related to respiratory when securing your Series D funding?

In 2019 and 2020, the market was quite robust, and differentiation was key. Traditionally, the focus had been on oncology and immunology, with numerous companies targeting Chapter 18A filings on the Hong Kong Stock Exchange and fetching strong valuations. However, as the market became saturated in these areas, forward-looking investors started looking for new narratives. Our approach, which focused on respiratory medicine and a dual business model, resonated well.

Many investors were grappling with the reality that profitability was elusive in many pharmaceutical ventures. This reality became more apparent as market challenges intensified, affecting fundraising globally and in China. Diversifying risk and demonstrating a clear path to sustainable growth and profitability became critical when seeking funding

Operating solely in China certainly poses unique challenges, particularly around market access and regulatory hurdles. Once a product is registered, the process of gaining a commercial foothold requires meticulous planning and is time-consuming, often involving sequential approvals across various administrative levels. This can significantly delay the availability of products in leading hospitals, despite receiving regulatory clearance.

For instance, it is not uncommon for products to be approved but not commercially accessible even after several years, due to complexities in market entry. This dynamic makes accurate long-term forecasting challenging, especially regarding reimbursement projections.

Moreover, in contrast to other parts of Asia-Pacific where regulatory pathways may be more streamlined, China often requires additional clinical studies, like Phase III trials, even for products with existing approvals elsewhere. Key to the Chinese regulators is the issue of safety and efficacy in the Chinese population. This regulatory divergence underscores the importance of diversifying our market presence across different regulatory environments.

How would you evaluate the operating environment for companies like Nuance in China today? What are the biggest challenges?

The single biggest challenge for young companies like ours remains acquiring and retaining talent. Moving individuals from established multinationals involves opportunity but also significant costs and risks. Multinationals offer well-structured support systems and infrastructure, which are not always present in early-stage companies. Moreover, transitioning from a multinational career to a start-up environment requires careful consideration, given that past experience does not always lead to success in a different setting like a start-up environment.

Therefore, attracting individuals with both the skills/expertise and the adaptability to fit into this unique environment is crucial for success. Joining our company means thriving in a distinctive environment where competence is immediately evident, adding value whilst emphasizing the need for caution when transitioning from multinational corporations to start-ups in China.

How has Nuanceâ??s â??dual wheelâ?? approach evolved with your recent emphasis on respiratory and allergies?

The dual-wheel strategy we employ refers to maintaining both a robust commercial performance, measured by commercial earnings before interest and taxes (EBIT), and ongoing pipeline development (measured by company EBIT). Regarding our focus on the respiratory franchise our licensing model remains quite attractive, allowing us to build a critical mass and a leading presence in the RE space. On the licensing metrics during the peak years, there was a significant shift towards US-style economics, with payments covering upfront fees to clinical and commercial milestones. We anticipate some adjustment in these dynamics as competition for assets has driven costs higher. Nonetheless, our goal remains to solidify our position in respiratory medicine, which affords us flexibility across device, drug-device combinations, biologics, and small molecules in the short to medium term. The build will allow for commercial synergies and an increased opportunity to leverage new launches off the established platform.

What does Nuanceâ??s shift towards respiratory and related fields mean for its existing products in other areas?

We are taking a very pragmatic approach. Our existing products in other areas provide a solid commercial and financial performance contributing to both revenue and profitability in the short to medium term. These products continue to support our P&L, attract commercial talent and build our reputation as we advance our focus on respiratory and related innovations. Importantly, when considering a potential public listing, having a diversified revenue base as well as novel pipeline of assets in late-stage development enhances our attractiveness to investors. For instance, in HK meeting revenue thresholds enables us to pursue listings on the main board, offering greater liquidity and additional strategic options. Currently, we believe investor interest in companies will heavily favour companies with established revenue streams, thereby making a robust revenue model essential for securing funding,

It seems like there is a shifting landscape where companies are re-evaluating their strategies towards China. How do you perceive the future of the healthcare market here? Are we looking at perpetual price compression or is there room for innovation?

I think the current market dynamics in China are quite unique and evolving rapidly. When we launched Iressa at AZ, an advanced targeted therapy, there was scepticism about its marketability due to its high cost without reimbursement at the time of launching. Surprisingly, we achieved USD 60 million in sales in the first year despite these challenges, something never seen until this time. This highlights that in China, if there is a perceived value in a treatment, patients and providers will find ways to afford it, unlike in some Western countries where insurance coverage dictates usage almost entirely This does not mean that the market is not price sensitive and reimbursement driven, but only that the funding and adoption of novel therapeutics in China remains high.

The ability to pay and market access remain key commercial drivers across China â?? the model versus that in the West is distinct in China. Even amidst current economic challenges and post-COVID-19 recovery, urban centres like Shanghai and Beijing boast a robust upper-middle class that can seek and afford high-quality healthcare. This demographic stability and willingness to invest in healthcare contrasts with more cautious reimbursement models seen in other countries. The adoption pattern will of course vary and be contingent on the product profile and uniqueness.

You have mentioned the importance of leveraging both the China and Asia-Pacific markets. Could you tell us about your interest in Asia-Pacific, given that these countries vary widely in terms of regulation and income levels?

Diversification is key for us, especially to mitigate risks associated with being solely based in China. If you look at the Asia-Pacific region excluding Japan, it is collectively as significant as China in terms of market size. This collective market should not be underestimated. Moreover, many multinational companies have seen substantial growth in Asia-Pacific, surpassing that of the US and Europe. Economically, it is a compelling region.

From a demographic and disease profile perspective, Asia-Pacific shares more similarities with China than with Western markets. This alignment makes expanding into Asia-Pacific a logical step. Rather than focusing solely on emerging markets like the BRICS countries (Brazil, Russia, India, China, South Africa), Asia-Pacific offers a blend of regulatory friendliness once you have registration in key markets. For instance, once you are registered in two major markets, additional entries become administrative filings, simplifying the regulatory burden compared to mainland China.

Economically, setting up operations in Asia-Pacific is comparable to China, making it feasible to establish teams and commercial infrastructure with relative ease. Multiple models have been trialled and adopted and deployed across the region. There is also a robust demand for innovative intellectual property in these markets, which presents opportunities for partnerships with regional distributors or establishing local teams selectively across different countries.

Overall, expanding into Asia-Pacific not only reduces operational risk but also enhances economic viability through streamlined regulatory processes and diverse market access models.

How is Nuance looking to capitalize on some of the recent policies being rolled out in Hong Kong, not least the big investments in innovation and technology as well as increased integration across the Greater Bay Area (GBA)?

Hong Kong has recently seen a notable shift in its approach to healthcare, marked by a proactive involvement from the government with substantial investments, including an HKD 30 billion (USD 3.84 billion) fund. This fund is not solely directed at pharmaceuticals but also embraces high-tech

sectors, underscoring a broader commitment to innovation.

Moreover, the integration of the GBA into Hong Kongâ??s regional scope represents a significant enhancement. On the clinical development side, previously, Hong Kong was limited to conducting Phase I studies, necessitating moves to mainland China or across Asia for subsequent phases. This regional expansion now offers a more comprehensive platform for pharmaceutical companies where both phase 2 and 3 studies can be conducted across GBA

Furthermore, Hong Kong maintains its position as an open economic hub within the Asia-Pacific region, offering flexibility that has becoming increasingly scarce in other parts of Asia. Despite geopolitical challenges, it remains an attractive destination for global talent, bolstered by government initiatives and funding incentives aimed at supporting businesses. Singaporeâ??s recent prominence has inadvertently created a gap that Hong Kong is poised to fill. For Nuance Pharma, Hong Kong serves as an ideal launchpad for expanding across Asia-Pacific. We have already conducted several successful clinical trials through Hong Kong Universityâ??s Clinical Trial Centre, one of them has been recognized and accepted by Chinese authorities, streamlining regulatory processes.

Looking ahead, our focus extends beyond clinical trials to encompass manufacturing, commercial expansion, and regional office functions. The ongoing integration of hospitals in Guangdong into the Greater Bay Area network, while initially posing regulatory challenges, promises to align clinical development efforts more closely across Hong Kong and mainland China.

In essence, while regulatory harmonization remains a hurdle, the infrastructure and capabilities for clinical development in Hong Kong and the GBA presents a robust foundation for future growth in the Asia-Pacific region.

How do you mitigate concerns from potential investors who might perceive Hong Kong as declining?

I do not see concerns about Hong Kong or Chinaâ??s stability being a significant issue for our future investors. From our perspective, Hong Kong remains an extremely attractive destination, especially for potentially taking our company public. Additionally, while there may be fluctuations in sentiment from time to time, China retains its status as the worldâ??s second-largest market.

Certainly, geopolitical factors and market challenges are realities we must navigate, but these are challenges seen across many global markets today. The key is in adapting our business model to effectively operate within China. The outdated approach of simply prioritizing presence in China at any cost no longer holds. Instead, we focus on strategic positioning and leveraging Hong Kongâ??s strengths as part of our broader Asia-Pacific strategy.

What are your top priorities for the next two to three years?

I see three key priorities ahead for us. Firstly, it is crucial to strengthen and further build on our companyâ??s revenue and bottom line. This involves continuing to grow our commercial business, both locally as well as via expansion across Asia-Pacific. We have already begun commercializing some products in Hong Kong, and the plan is to extend this across the region. It also involves building our presence in our key TAâ??s and market segments i.e., hospitals, OTC and DTC

Secondly, we need to bolster our pipeline. Building on our success in respiratory treatments, we are exploring opportunities in allergy immune therapy and other areas to enhance our portfolio.

Lastly, gaining access to public funding is essential for driving innovation. Privately funding innovation poses significant financial challenges. Going public would allow us to secure funding more effectively and capitalize on market recognition of our achievements.

We have reached a point where we have demonstrated our business model effectively. We have established a robust commercial presence, developed a competitive pipeline, and laid the groundwork for expansion. Scaling this model further, however, would be challenging without accessing public markets. Hence, the logical next step for us is to transition to a public company.

We have already prepared extensively for an A1 filing, including due diligence and appointing bankers. Internally, the company is readyâ??we have invested in systems, reporting, and compliance to meet public market standards. Now, it is a matter of waiting for a conducive market environment to execute this transition effectively.

What would you like our readers to take away from this interview about the Chinese pharma market today?

The key message here is about clarity and focus in building the company whilst ensuring a strong and experienced team to execute the plan. Speed and flexibility are paramount to success as is sufficient funding to scale the company.

It is crucial to dispel any misconceptions re the China market. China is not a market where you can enter lightly or expect easy access or success. It is complex, expensive, and requires a highly focused approach. Just as you would not enter the US market without a solid plan and experienced team, the same level of preparation and commitment is necessary for China.

From my experience, China demands clarity of purpose and a pragmatic mindset. Emotional decisions rarely align well in such a market environment. Companies need to align their goals with the realities of Chinaâ??s scale and complexity, the competitive forces as well as very clear understanding of government policy. It is now a major global player, akin to entering the US market as a non-US company.

When I first arrived in China, it was a vastly different landscape. Today, it is a powerhouse with immense potential but equally high demands. You need to actively compete with both foreign and domestic players in what is a highly competitive arena. Companies must be prepared to invest wisely, understand regulatory nuances, and commit to long-term strategic goals.

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