Kevin Pan – CEO, Asieris, China



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Kevin Pan, CEO of Asieris, shares the origins behind the company's distinctive name and how it reflects their ambition to bridge scientific discoveries and innovative medicines; their focus on genitourinary (GU) tumours and related disease because of the significant and oft-overlooked medical needs there; and the importance of building and maintaining strong KOL and other stakeholder networks to position themselves as an innovation leader in their therapeutic area.

Kevin, could you start by sharing the story of how Asieris was founded in 2010?

Our company's English name, 'Asieris', is actually a portmanteau of the Greek words for 'rainbow' and 'Asia', just as our Chinese name '□□ ' means 'rainbow from Asia' as well. This reflects our ambition for the company to be a bridge between exciting scientific discoveries and medicines for patients. This ambition derived from the recognition that between basic research and pharmaceutical therapies lies a huge gap, sometimes referred to as the 'Death Valley', which have resulted in so few scientific discoveries being translated into life-saving medicines.

Both my co-founder John Zhuang and I are so-called 'sea turtles', or overseas returnees, who started their education in China, went to the US for PhDs and started industry careers, and then returned to China for new careers. Both China and the US have their own advantages when it comes to pharmaceutical innovation. China is a fast-growing country with a very dynamic market that is in need of innovative companies and medicines. The government and the capital markets

are also increasingly supportive. On the other hand, the US has significant technological advantages and a great talent pool of experienced industry professionals. From this perspective, we hope Asieris can also bridge both countries and synergize all their advantages to build an outstanding company with great products.

Our core focus is in genitourinary (GU) tumours and related diseases. This originated from a serendipitous discovery: our first product, APL-1202, is a potential treatment for non-muscle-invasive bladder cancer (NMIBC). During the nine years we spent developing this product, we built strong connections with hospitals and KOLs and accumulated a significant amount of expertise in this therapeutic area. Along the way, we also realized that urology and women's health are rather overlooked areas with genuine unmet medical needs. For instance, while many biotechs focus on cancer, they tend to focus on late-stage metastatic cancers. However, in the GU area, cancers are typically diagnosed at earlier stages, so patients need safer and friendlier drugs compared to the potent but highly toxic drugs used to treat late-stage cancers. Due to all these factors, we decided to continue specializing in GU diseases.

You currently have two products in the clinical pipeline. Could you introduce them?

Our first product, APL-1202, is being developed for the treatment of non-muscle-invasive bladder cancer. This is an area that has not seen new drug approvals globally for 20 years. The current standard of care is intravesically instilled chemotherapy or Bacillus Calmette-Guerin (BCG), which is an invasive, painful and inconvenient procedure, carrying risks of bleeding, pain and infection. Efficacy is also poor. No orally available drug has been developed for this indication, so we see a huge unmet medical need here.

APL-1202would be the first oral drug for this indication and it also has a novel mechanism of action. It is currently in Phase III trials in China and we have recently completed enrolment of over 350 patients, a very exciting milestone for the company. In the US, we have just started Phase Ib trials to evaluate the combination of our drug with the current standard of care in the US, BCG therapy.

Our second product, Cevira®, is a photodynamic therapy for women with HPV-induced pre-cancerous lesions on the surface of their cervix. We in-licensed this product from a Norwegian biotech company, Photocure. The current and only standard of care for this condition is surgical treatment but this has several issues. Firstly, it is the overtreatment issue, because the rate of spontaneous regression – where the patient's immune system kills the pre-cancerous cells – is quite high, nearly 30 percent, these patients would not actually need surgery. Other issues include

usual risks like infection and bleeding associated with surgery. Perhaps most importantly, for women of childbearing age, such a surgery has the potential to compromise their ability to bear children or affect the stability of pregnancy. This also presents a dilemma for patients of childbearing age because they have to make a decision on whether to have the surgery.

Our product is non-surgical. The Phase II data have shown that over two-thirds of patients can be cured with our product, thereby offering patients a non-surgical treatment option.

What other innovations can we expect from Asieris' own internal development pipeline?

We position ourselves first and foremost as an R&D company so internal R&D capability is critical to our long-term success. We currently have two technology platforms.

The first platform focuses on MetAP inhibitors, MetAP1 and MetAP2. MetAP2 is well-known for its activity in inhibiting angiogenesis. However, we discovered that MetAP2 inhibitors may also have strong synergies with checkpoint inhibitors, so we are now moving the research direction from anti-angiogenesis to immune-modulation. Checkpoint inhibitors are rapidly becoming the backbone of cancer therapies so if MetAP2 inhibitors can enhance their activities, it would give us a broad arena to play in.

For MetAP1 inhibitors, we discovered that they can hit an enzyme crucial for bacterial growth, which could form a very exciting target for multi-drug-resistant (MDR) infections. We have already discovered some novel compounds that have demonstrated promising activity in animals. We are collaborating with Fudan University in Shanghai on this project as they are quite excited about our research findings. We hope to advance at least one compound from this research into the clinic within the next two years.

Our second platform aims to improve the overall PK, safety and even efficacy profiles of certain approved drugs. Here we are looking to make clinically meaningful improvement to marketed drugs, which still has huge market potential but with lower risks compared to novel drug development. We have very competitive and competent drug discovery and formulation teams so we want to combine both strengths to target approved drugs that have limits when it comes to PK profile. I believe this can also bring significant value to patients.

In addition to your internal pipeline, Asieris also has an in-licensing strategy. What kind of products are you looking for here?

It comes back to our vision. We want to be a fully-fledged China-based biopharma company and a leader in our therapeutic areas of focus. If we only relied on our in-house drug candidates, this vision would take a long time to realize. To accelerate our growth, we can in-license carefully chosen drugs that target specific and significant unmet medical needs in Chinese patients. China still lags behind mature markets when it comes to healthcare. Therefore, through in-licensing, we can firstly bridge that gap, and secondly, develop our commercial presence and capabilities quickly.

However, we are highly selective. We only focus on late-stage (i.e. Phase III) or commercial assets in our core therapeutic areas of urology and women's health. With the booming Chinese biotech industry, competition for in-licensing assets is fierce. This is why we have selected niche areas where we have deep expertise to avoid competing with companies crowding into hot areas like PD-1/PD-L1 checkpoint inhibitors or CAR-T, just to name a few.

We also benefit from our extensive KOL networks. We are currently in discussions with two European companies to in-license two products from them. One of the products was actually recommended by a KOL in China that we knew well, and he told us that his patients were actually going to Hong Kong to access this product, as it has already been approved there. Our close relationships with the KOLs in these therapeutic areas often give us access to key insights into the local market.

Asieris has fingers in many pies, it seems! With biotech innovation being such an inherently risky endeavor, how do you manage your resources and priorities?

Once again, we are driven by our vision to be a China-based biotech with global impact. Looking across the entire biotech environment, we may not be the biggest or the fastest-growing but we are extremely dedicated and focused on our core therapeutic areas. For our internal R&D, we only work on novel compounds that are well-positioned to generate substantial value within global markets. We will not work on 'me-too' or 'me-better' programs.

This is indeed a risky approach, so at the same time, we try to mitigate the risks of developing novel compounds. For instance, the compound being developed for treating NMIBC had previously been used to treat urinary tract infections (UTIs). This means we have substantial safety and PK

data in humans, and we could be reasonably confident that this drug would work on some part of the urinary tract system.

For our in-licensed photodynamic product, Cevira®, it is actually a second-generation product. The first-generation product entered Phase II trials but was discontinued because it was not efficacious enough. The second-generation product has made improvement in design to increase its absorption, which should theoretically increase the sensitivity of the drug to photo-activation. In addition, the phototherapy device has been miniaturized so it can be implanted on the cervix. Patients can leave the hospital and remove the device easily by themselves once the treatment is completed. Importantly, the product has shown positive Phase II results, which finally gave us the confidence to invest.

These are some of the ways we try to offset the risks of novel drug discovery and development. We want to be unique, selective and differentiated – and we also want to balance some of the risks by looking at ways to make more reasonable and rational investment decisions.

Ultimately, we are driven by unmet medical needs. For example, we know that companies working in the area of antimicrobial resistance (AMR) have recently struggled with their market valuations. However, this is a critical research area for humanity, so we want to invest in this area. We have been supported by the Chinese government, who recently awarded our parent company in Jiangsu CNY 3.65 million (USD 510,000) for our AMR research program.

With two products in Phase III already, what are your plans for commercialization?

We are currently preparing to build our commercialization capabilities, including manufacturing, sales and marketing, and so on. The transition from an R&D company to a fully-fledged biopharma company is a challenging task, and we will rely on trusted partners to help us. For instance, we have partnered with three local CMOs on the manufacturing aspect. We are also speaking to a few local pharma companies with strong presence in urology to discuss co-promotion and co-marketing opportunities. Through these external partnerships, we hope to quickly bring our products to patients as well as develop our own commercialization capabilities.

For global markets, we plan to out-license our compounds so that our global partners can help us with the commercialization. We are open to working with different companies as long as they have a strong presence in our target therapeutic areas.

Having worked in the US and China, how do you compare the biotech ecosystem and models in both countries?

Biotech research needs diversity. There is no single ‘correct’ biotech model. Diseases are so diversified, technologies are so diversified – so company strategies should be diversified too. We have seen very successful models in China; for instance, some companies focus on ‘me-too’ or ‘me-better’ products and build nice antibody technology platforms to generate drugs for Chinese patients at lower costs. This is going to benefit Chinese patients and payers. However, we have a different strategy focused on developing highly-innovative and proprietary novel compounds in GU diseases.

The US and China ecosystems are also different. For instance, US investors are quite risk-tolerant, so if the technology is very exciting, they are willing to keep investing. Capital markets are also more friendly, so it is easier for early-stage investors to exit, which in turn lowers the risks of investing in highly-innovative technologies. China is different. Investors are less experienced, they have lower risk-tolerance levels, and while exit opportunities are increasing (e.g. with HKEX and Shanghai STAR markets), these exchanges still have much higher requirements compared to the NASDAQ in the US, for instance. That creates a different ecosystem for Chinese biotechs, where we cannot afford to invest in one or two extremely innovative technologies alone, as that would unnerve investors.

We have to undertake a more balanced approach, which is why Asieris has implemented a relatively balanced development strategy by: working on first-in-class targets with de-risking opportunities, in-licensing late-stage or marketed assets, and developing improved versions of marketed products with significant market potential. We believe this balanced will allow us to grow stably and sustainably in China for the long run.

What else do you think is critical for a sustainable business in China?

Definitely the talents the company possesses! Besides our science and pipelines, we strive to create a unique culture where every employee feels respected & fulfilled working in the organization, through discovering and developing new drugs that will improve and dignify many lives.

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