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Taiwan's investment culture remains heavily oriented toward semiconductors and electronics, and few investors are yet convinced to commit capital to biotech

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Dr. Lin, Founder and Chief Scientific Officer of Tripartite Therapeutics, discusses the inspiration behind the company's ADC platform of OmniLink® and Polarpeutic® technologies, designed to overcome key limitations in linker chemistry, payload delivery and drug-to-antibody ratios. He outlines Tripartite's strategy to advance its lead candidate through Phase I/II before out-licensing, while highlighting its patent position, recent Emerging Stock Board listing and ambition to establish Taiwan as a source of globally competitive biotech innovation.

Dr. Lin, could you introduce yourself and your scientific background?

I hold a PhD from Harvard University, where I majored in biochemistry and molecular biology. After graduating, I returned to Taiwan because my mother was very ill at the time. I initially worked as a researcher at Academia Sinica, Taiwan's national academic institution, for about ten years. The impact of my mother's death profoundly influenced my career. I felt that, however capable a molecular biologist I might be, I had not been able to do anything for her, and that experience turned my attention toward developing anti-cancer therapies that could genuinely benefit patients and their families in similar situations. At the time, though, I did not find quite the right field to enter, until around the year 2000, when the first antibody drug conjugate (ADC) reached the market.

What drew you specifically to ADCs, and what problem is your OmniLink platform designed to solve?

I had long been drawn to the concept of targeted therapy. In 1907, a German Nobel laureate, Paul Ehrlich, proposed the idea of the “magic bullet” to treat disease, at a time when medicine relied almost entirely on non-specific drugs that acted on diseased and healthy tissue alike, which never struck me as the right approach. That idea stayed with me for years. When the first antibody drug came to market in 1986, it was indeed an improvement over existing drugs, and subsequent rise of monoclonal antibodies provided therapeutic benefits through specific targeting, but lacked the efficacy of small molecule drugs. With the approval of the first antibody-drug conjugate in 2000, I thought the moment had finally arrived, though that particular drug was later withdrawn. In 2011 and 2013 the second and third antibody-drug conjugates reached the market and proved considerably more reliable, and it was then that I felt the field was genuinely ready.

I went back through the history of ADC development and came to understand the state of the field closely. Much as the old “one gene, one protein” theory in genetics had proven to be a fallacy, I noticed that everyone in the ADC field was essentially searching for the right linker for their payload of interest, and I felt this was precisely where my expertise could contribute. Nonetheless, when I began raising funds to establish the company, I did not expect it would take seven years to solve the core technical problem. I assumed, rather naively, that it would be straightforward, though in hindsight this was not surprising: the history of ADC development shows that finding a genuinely effective linker for a given payload has taken the field decades, not years.

Manufacturing is comparatively straightforward, since you know your material requirements in advance and can order accordingly. Research and development is different; problems arise constantly and must be solved as they emerge. Taiwan’s market is small, and chemical suppliers do not maintain local warehousing here. When I was working in the United States, ordering a new reagent meant overnight delivery and having the compound the next day. Here, the shortest realistic wait is ten days to two weeks, and for more difficult materials it can stretch to two or three months. Working within that constrained environment, it took roughly seven years to develop our universal linker successfully. That linker can now be applied to over a dozen different payloads to construct ADCs, and it is built from an oligosaccharide structure. Sugar is biocompatible and genuinely hydrophilic, and hydrophilicity matters enormously because hydrophobicity remains one of the major challenges facing the ADC field.

This addresses one of the biggest issues with existing ADC technology where around 99.9 percent of an administered ADC is cleared by the immune system, with only about 0.1 percent actually reaching the tumour site, which is not only wasteful but somewhat absurd, since an ADC is meant to kill cancer cells, not immune cells. The underlying cause is that current ADCs are highly hydrophobic, contributed by both linker and payload, so addressing that hydrophobicity directly is essential. Even reducing immune clearance from 99.9 to 99.8 percent effectively increases drug delivered to the tumour from 0.1% to 0.2%, which means doubling its therapeutic potential. This is precisely the problem OmniLink® is designed to solve. Other groups have attempted this, generally using commercially available PEG-based linkers, which are somewhat hydrophilic in chemical terms, certainly more so than conventional hydrophobic linkers. But because PEG linkers are commercially available to anyone, they offer no genuine platform uniqueness.

You not only design linkers but also engineer payloads through your Polarpeutic® platform. Could you explain how it works, and how you differentiate and protect your IP in an increasingly crowded ADC landscape?

We modify the payload to address its inherent hydrophobicity by introducing hydrophilic functional groups, a process we call Polarpeutic®. This in turn allows us to establish our proprietary payload library. As for patent strength, I am not aware of any company working on precisely what Tripartite is doing, across both the linker and the payload modification. That is the basis of our competitive strength in this field.

Beyond the immune-clearance problem, conventional ADCs face a second major limitation: a low drug-to-antibody ratio, or DAR, with most marketed products sitting below four. This, too, stems from the hydrophobic nature of conventional linkers and payloads, and it feeds directly into a further problem in the field: with only a few exceptions, marketed ADCs achieve an overall response rate below 50 percent, meaning fewer than half of patients respond to treatment. This is a direct consequence of low DAR, since efficacy depends heavily on how much drug a single antibody can deliver. Without changing the linker and payload chemistry, this ratio simply cannot be improved, which is precisely why it took roughly seven years to mature the underlying technology.

Could you comment on your results in addressing that, particularly your improved drug-to-antibody ratio? I understand the industry standard sits below four, whereas you are

achieving around eight.

That connects to the third historical limitation in the field: the absence of a genuinely universal linker. We have not achieved universality across every conceivable payload, since there are roughly twenty payloads of interest across the field now, but we have successfully linked more than twelve of them to antibodies through our platform, covering the prominent payload classes of tubulin inhibitors, DNA damaging agents, topoisomerase inhibitors, inhibitors of critical metabolic pathways and immune stimulating agents.. I believe those three core issues, immune clearance, drug-to-antibody ratio, and linker universality, are precisely what Tripartite has gained remarkable improvement. As for the ratio itself, eight works out to be an optimal balance between efficacy and toxicological side effects, and excessive loading of the antibody with higher ratios risks unfavourable trade-offs with higher immune clearance of the ADCs. Looking at the history of the field, some companies have attempted ratios as high as more than twenty per antibody, and the outcome was a failure in clinical trial.

Your lead candidate is built on a trastuzumab-based ADC, currently at the preclinical stage. What are your plans for clinical development and eventual out-licensing?

Yes, though we have since expanded the technology to other antibodies as well. Trastuzumab was chosen largely for convenience, given that it is easily available and allows us to run the full range of experiments needed to validate the underlying concept. In the ADC field, once you have Phase I/II data, large pharmaceutical companies take your platform seriously for evaluation of potential asset acquisition. This alleviates the burden of small biotech companies like ours to have to progress the programme through late stage clinical trials and eventual marketing ourselves. Phase I/II will not be conducted exclusively in Taiwan and sites in the US or another Western jurisdiction are being planned to include different ethnic populations to ensure recruitment includes representative patient populations. So our primary focus is maturing the technology, advancing into Phase I/II, and then out-licensing.

Beyond trastuzumab, you mentioned other programmes are underway. Could you comment on those?

We deliberately benchmarked our early development against trastuzumab-based comparators, including two ADCs widely regarded as the leading products in the field, precisely because

outperforming those two would be the most convincing evidence of our technology’s strength. We are now confident we have achieved that goal. That said, the trastuzumab space itself has become extremely crowded, so from a business standpoint, it makes more sense going forward to apply our technology to a less crowded antibody target, which is generally easier to position for a large pharmaceutical partner.

Is your focus primarily on breast cancer, or are you also exploring other cancer types and indications, such as metabolic disease?

We are certainly looking at other cancers as well; Her2 tends to be a common marker for many cancers, so breast cancer remains one target of many rather than the only one. On metabolic disease, our technology could in principle extend to areas such as GLP-1 and dual-incretin agents, since that field similarly depends on linker technology, in a manner conceptually similar to ADC linker chemistry. I do think our platform could be applied there, though given our current resource constraints, that remains a longer-term consideration rather than an immediate priority.

Ahead of your Emerging Stock Board listing, you suggested a licensing agreement could be announced in the near future. What validation do venture capital investors and pharmaceutical partners look for, and what captures their interest most?

Looking at current trends in the ADC field, two directions stand out as particularly attractive to potential partners. The first is the dual-payload ADC. With a conventional linker, achieving genuine dual-payload synergy is difficult, since different linkers carry different release kinetics and the two payloads cannot be released simultaneously within the tumour. In our case, because we use the same linker chemistry across different payloads, we can achieve near-simultaneous release, which is an advantage other platforms simply cannot replicate, and I believe this is a compelling basis for pharmaceutical collaboration.

The second, and in many ways more ambitious, direction is using an ADC to activate a patient’s own immune system against the tumour, which would remove the drug-resistance problem entirely, since, unlike a tumour, the immune system does not constantly mutate, and it retains memory: once it recognises a tumour as harmful, that recognition tends to prevent recurrence. The historical difficulty has been that conventional ADC technology, when applied to this immune-activation approach in the clinic, has consistently caused patient deaths, without exception, again

due to the foreign-substance problem, compounded by the immune-stimulating nature of the ADC itself, which over-activates the immune system to the point of harming the patient. Prior immune-ADC research was typically conducted in immunocompromised mouse models, where the immune response is muted and side effects appear manageable, but in fully immunocompetent models, conventional technology causes visible distress within the animal almost immediately. Using our platform under the same immunocompetent conditions, the animals show only mild, transient reduction of activity for about fifteen to thirty minutes, before returning fully to normal. We believe this makes the immune-related toxicity of our platform genuinely acceptable, and this represents another strong point of interest for potential pharmaceutical partners.

Turning to capital markets, you have recently listed on the Emerging Stock Board. What does that mean for the company’s next stage of development, and who has been backing you so far?

We now have a strong technology platform, validated through proof-of-concept studies in animal models, and our focus is on bringing this forward into Phase I clinical trials, to obtain human validation that these therapies genuinely work in the intended patient populations and indications. Part of the capital we are raising is intended to fund the necessary pharmaceutical development work: further preclinical studies, toxicology, scale-up to GMP manufacturing standards, and the clinical trials themselves. On financing, we have been backed by government funding alongside venture capital; Taiwan maintains specific government-backed funds dedicated to supporting this kind of development, and we have drawn on those alongside private VC investments.

Licensing at a global scale requires strong intellectual property protection. How have you structured your patent strategy across different regions?

Our patent portfolio is organised around two main categories: one covering the Polarpeutic® modification of the payloads themselves, and one covering the saccharide-based linker. Both have been filed with the USPTO in the United States, and from there we are pursuing global protection through the PCT pathway. We have currently filed with around twenty national patent authorities, including most major markets such as Europe, the UK, Canada, Brazil, China, Korea, and most of Asia.

On the core science, I would say the strength lies largely in the fact that, globally, no one else has proposed this particular molecular approach to linker design, and the same is true of the therapeutic application itself, so in both cases it is really a matter of securing the position over time.

Having served on a Taiwan Stock Exchange listing review committee, how do you assess the way Taiwanese investors value biotech companies today? What is working well, and what remains missing?

[Dr. Lin] Taiwan’s investment culture remains heavily oriented toward semiconductors and electronics, and relatively few investors are yet convinced to commit capital to biotech, which makes it something of an underdeveloped sector here by comparison. Looking outward, though, I am hopeful that international investors, and pharmaceutical companies in particular, will recognise that Tripartite’s technology genuinely leads the field, which I believe should make us a more compelling proposition to knowledgeable investors than much of the rest of Taiwan’s biotech landscape.

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