Ian Laquian – CEO, Kariya Pharmaceuticals

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Ian Laquian's journey from Big Pharma strategy leadership to entrepreneurial venture creation exemplifies the innovative thinking required to address intractable neurological challenges. Having spearheaded CNS therapeutic area strategy at Takeda Pharmaceuticals, Laquian has pioneered a ground-breaking approach that leverages metabolic pathways to treat neurodegenerative diseases. Through the establishment of Kariya Pharmaceuticals, he has successfully translated academic research into clinical-stage assets, demonstrating how strategic vision combined with Denmark's robust biotech ecosystem can accelerate drug development for patients with unmet medical needs.

Could you provide an overview of your professional trajectory and explain how you came to establish Kariya Pharmaceuticals?

The genesis of Kariya Pharmaceuticals emerged from strategic portfolio analysis conducted during my tenure as head of CNS therapeutic area strategy at Takeda Pharmaceuticals. Our mandate involved identifying repurposing opportunities across the company's therapeutic portfolios, particularly mechanisms that could address central nervous system disorders through novel approaches.

The intellectual foundation for our current platform originated from our team's deliberate departure from the prevailing amyloid-beta hypothesis. Following Eli Lilly's substantial investment in anti-amyloid antibodies and subsequent Phase III failures, we adopted what we termed an "A-beta

agnostic” approach. Rather than pursuing the conventional approach of targeting “toxic” peptides and clearing amyloid from the brain, we focused on underlying pathophysiological mechanisms.

Our hypothesis centred on cellular energetics, glucose utilization, and mitochondrial health as fundamental drivers of neurodegeneration. This metabolic approach led us to investigate pioglitazone, one of Takeda’s diabetes therapeutics, which demonstrated neuroprotective properties in early studies. Although our Phase III trial ultimately failed, the basic research validated our conviction that metabolic interventions represented a promising therapeutic avenue.

What led you to focus specifically on GLP-1 receptor agonists for neurological applications?

Takeda’s robust diabetes portfolio provided us with access to GLP-1 receptor agonists at a time when Novo Nordisk had established market leadership with liraglutide. Critical preclinical evidence emerged demonstrating that GLP-1 receptor agonists, when administered to animals in models of neurodegeneration, significantly enhanced survival and functional outcomes.

Unfortunately, Takeda’s strategic decision to divest its diabetes portfolio created an unexpected obstacle of losing access to our primary development candidate just as the scientific rationale was solidifying.

For Kariya, the breakthrough came through the persistent research of Professor Christian Hölscher, whose work at the University of Ulster and later Lancaster University consistently demonstrated GLP-1 efficacy across multiple neurodegeneration models. Despite these institutions’ modest research backgrounds, Hölscher’s publications maintained remarkable consistency in demonstrating positive outcomes.

Clinically, the pivotal moment arrived with the publication of clinical data from the United Kingdom involving 40 Parkinson’s patients treated with exenatide, a twice-daily GLP-1 receptor agonist. Following twelve months of treatment, patients demonstrated superior motor symptom scores, with improvements persisting twelve months post-treatment cessation. This represented the first clinical evidence of disease modification in which the disease trajectory is altered rather than merely managing symptoms. Subsequent randomised, placebo-controlled studies conducted at University College London confirmed the effect, and patients demonstrated sustained motor improvements.

How did you differentiate your approach from existing GLP-1 therapeutics in the market?

Recognition that existing GLP-1 therapeutics would inevitably face generic competition necessitated a differentiation strategy. Our experience of European pricing models revealed that regulatory authorities would likely classify any conventional GLP-1 as a generic equivalent, severely limiting commercial viability.

Our solution involved developing a dual GLP-1/GIP receptor agonist at a time when no such compounds existed in the market. More critically, we identified brain penetration as the fundamental limitation of existing diabetes formulations. While pharmaceutical companies had optimized GLP-1 receptor agonists for systemic retention through fatty acid modifications, these alterations significantly impaired brain penetrance.

Professor Hölscher's innovation involved incorporating a cell-penetrating peptide that actively shuttles the compound across the blood-brain barrier. This approach maintained the peptide's natural characteristics while ensuring central nervous system bioavailability, which is a critical requirement for treating brain diseases. These concepts laid the foundation for what would later be Kariya Pharmaceuticals and our lead program KP405.

What role has Denmark's biotech ecosystem played in your company's development?

Following my departure from Takeda in 2017, I approached Novo Seeds with the conceptual framework, lacking only the actual compounds. As I was seeking promising development compounds, good fortune led me to connect with Professor Hölscher, who had already developed superior dual agonist compounds optimized for enhanced brain penetration.

Within two months, we had licensed the intellectual property from Lancaster University. Our initial strategy involved approaching Novo Seeds for funding, but the Bioinnovation Institute's timely emergence suddenly provided an alternative path. Their EUR 1.5 million convertible note program offered exceptionally favourable terms, converting only upon subsequent funding rounds while providing sufficient capital for initial development activities.

The availability of GLP-1 expertise in Denmark also proved invaluable. Having the founder of GLP-1 research on our advisory board, combined with the concentration of GLP-1 companies and technical expertise, created an unparalleled knowledge ecosystem. This became particularly evident when we recruited Mikael Thompson, former head of clinical pharmacology at Novo Nordisk

and a key contributor to liraglutide’s development, as our Chief Development Officer.

How have you achieved drug development progress without traditional venture capital funding?

Conventional wisdom suggests that drug development requires substantial venture capital investment. However, our experience shows that strategic capital allocation can achieve remarkable efficiency. With EUR 1.5 million and a nominated development candidate supported by robust preclinical data, we focused efforts on successfully completing CMC (chemistry, manufacturing, and controls) and GLP toxicology studies to achieve Phase I readiness.

Additional support from the Danish Innovation Fund’s InnoBooster program provided crucial funding at critical junctures. The key insight is that every euro raised has been deployed directly into development activities, with the founding team maintaining day jobs to minimize operational overhead.

This approach demands significant personal sacrifice but enables unprecedented capital efficiency. Our ability to bootstrap development while still maintaining scientific rigor has been validated through multiple partnership discussions and acquisition offers.

What challenges have you encountered regarding scale-up funding, and what strategies do you see going forward?

The venture capital landscape has evolved toward platform companies and substantial capital deployments. When discussing funding requirements of EUR 5-10 million, many tier-one venture capitalists indicated minimum deployment thresholds of EUR 20 million or more. This creates a fundamental mismatch for single-asset companies like Kariya.

The challenge extends beyond simple capital requirements. Raising EUR 45-50 million necessitates building a traditional biotech infrastructure with expensive executive teams and operational overhead. This transformation from our current lean, virtual model to a conventional biotech structure may not necessarily optimize patient outcomes or capital efficiency.

Additionally, our pragmatic approach recognizes that for CNS assets, the optimal return on investment typically occurs immediately following Phase I completion. This milestone generally requires minimal amounts of capital to achieve, while at the same time can be extremely value

generating in order to attract pharmaceutical partners.

When traditional venture funding proved elusive, we developed alternative approaches. Our Chief Development Officer’s relationships with contract research organizations led to an equity-based partnership for Phase I execution, significantly reducing cash requirements.

A fortuitous connection with a Korean pharmaceutical company transitioning from cosmeceuticals to longevity therapeutics provided USD 1.5 million in funding. Combined with a second InnoBooster grant of EUR 750,000, we secured sufficient capital to complete Phase I studies.

Given the historical challenges in CNS drug development, what is the current perception of GLP-1 approaches in neurodegeneration?

The pharmaceutical industry is fairly conservative and remains sceptical of novel CNS approaches given the myriad of previous failures. If we consider that my interests in the metabolic hypothesis started in 2012 based on research from Professor Hölscher which dates back to 2008, it has taken over a decade to get us to where we are now. We are thrilled to see that this emerging hypothesis for neurodegenerative diseases has gradually gained recognition, going from relegated congress symposiums, to now keynote presentations at major CNS conferences.

That said, the industry continues to await results from Novo Nordisk’s large-scale Alzheimer’s disease study, which will significantly influence sector sentiment. Currently, only Novo Nordisk and Eli Lilly have committed substantial resources to CNS applications of GLP-1 therapeutics, with Lilly also exploring substance abuse disorders and other neuropsychiatric conditions based on real-world evidence.

Our competitive advantage lies in head-to-head preclinical data demonstrating superior efficacy of our drugs against all marketed GLP-1 receptor agonists, including tirzepatide, liraglutide, and dulaglutide. The fundamental principle remains that treating brain diseases optimally requires brain-penetrant therapeutics.

Have you tested KP405 in Alzheimer’s disease models as well as Parkinson’s?

We have conducted comprehensive testing across three different Parkinson’s disease models and two Alzheimer’s disease models. In every instance, our compound has demonstrated positive outcomes and superior performance compared to existing diabetes medications. These results

provide confidence in our development candidate’s therapeutic potential.

The challenge lies in convincing pharmaceutical partners to make a significant leap of faith in our novel mechanism of action, despite the mounting clinical evidence supporting GLP-1 efficacy in neurological applications.

What are your anticipated milestones for the coming year, and what is your strategic vision moving forward?

We are three months from completing Phase I studies, which historically represents an optimal exit point for CNS assets. Precedent transactions include Syndesi Therapeutics’ acquisition by AbbVie for USD 130 million upfront in a billion-dollar transaction, and Prexton Therapeutics’ acquisition by Lundbeck for USD 120 million upfront with similar total deal value.

We received a number of offers following this year’s J.P. Morgan Healthcare Conference but subsequently declined due to concerns around organizational fit and compounded risk with the acquirers’ pipelines. We remain optimistic as many pharmaceutical companies have indicated interest post-Phase I completion, seeking safety, tolerability, and preliminary efficacy data before committing to a partnership.

Knowing that it takes time to find the right partner, we are also pursuing an alternative clinical path that leverages the pro-cognitive effects of GLP-1 analogues. Multiple investigator initiated studies have shown that GLP-1 drugs administered to patients with cognitive impairment produce measurable cognitive improvement in significantly shorter timeframes than traditional neurodegeneration trials. In this context, cognitive impairment associated with schizophrenia represents a particularly compelling indication, as no approved therapeutics exist to address this substantial unmet medical need, and Kariya is in a unique position to initiate a Phase II almost immediately following our Phase I.

What final thoughts would you like to share about your journey and the broader implications for the industry?

I remain profoundly grateful for our achievements and especially for the Danish biotech ecosystem that has enabled our progress. The combination of pioneering science, serendipity, and timely financial support from institutions like the Bioinnovation Institute has been instrumental, and I

firmly believe this success could not have been replicated in any other geographic or institutional context.

Denmark’s biotech ecosystem has proven uniquely advantageous for our specific development needs, providing access to GLP-1 expertise, favourable funding mechanisms, and collaborative networks that have accelerated our development.

That said, with more capital being deployed to larger platform ventures, single-asset companies like Kariya will continue to struggle to compete for funds. Personally, I would love to see the pendulum swing back our way, with greater recognition and support for the little guys.

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