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By Eleanor Malone

FROM CLINICAL PRACTICE TO ACADEMIA

TO biotech to big pharma: Paul Peter Tak has covered most of the bases when it comes to medicine. Last year he left his role as senior vice president of R&D pipeline, chief immunology officer, development leader and co-chair of the scientific review board at **GlaxoSmithKline PLC** to embrace yet another pillar of the industry: venture investment. He caught up with *Scrip* to talk about his latest endeavor.

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In October 2018, after seven years at GSK, Tak joined Cambridge, Massachusetts-based Flagship Pioneering as a venture partner. He readily acknowledges that at GSK he "achieved more than I could have dreamed of and was very lucky that I was so strongly supported to do the right things." So what prompted him to make the leap from big pharma to biotech generator?

Part of it was his interest in combining his varied experience and network across the entire ecosystem "to lead programs in oncology and immunology but also in other therapy areas." Also, he was attracted to the opportunity to do this "at a faster pace than I could do it at a big pharmaceutical company because the process is simpler and it's a very strong organization behind me."

Flagship's Allure

At Flagship he has already been placed as CEO of an undisclosed biotech start-up operating in stealth mode, and he is starting to take on board positions. He is also helping to identify other senior leaders for Flagship's portfolio companies.

Flagship Pioneering changed its name from Flagship


PAUL PETER TAK

Ventures a couple of years ago to signal its distance from the typical venture capital model of selecting and investing in firms that seek to progress step-wise from existing products, technologies and know-how. Rather, it creates think tanks to build companies from scratch around important unmet challenges, something that is very appealing to Tak. "Flagship's people ask big scientific questions that nobody has answered yet," he explained. "Otherwise, they don't do it." Rather than focusing on specific therapeutic or technological areas, the firm is "completely unbiased," following only the biggest areas of need for society and patients and where there is "really exciting very early science."

Tak added: "They are not interested in doing anything other people are doing already: they are looking for what is not only unprecedented, but what is unreasonable, almost. Thinking in a completely new way. They aim to invest in big things in a very novel and extremely smart way."

This chimes with his own approach, which favors following the science rather than committing to a particular condition or commercial opportunity. "That is a very traditional way of thinking that does not necessarily create a lot of value over time, because very often the big opportunities are somewhere other than where

you would have predicted." Rather, "you need to start with the pathogenetic mechanisms, the platforms to interfere with human biology in a truly innovative way, and then find out where it is that you can truly make a difference that leads to a beneficial effect on patients' lives. Not the other way round."

Flagship forms prototype companies to address the big questions it has identified and brings together small teams of "super bright people" working both with external laboratories and with Flagship's own laboratories to address the initial hypotheses. "When it looks good Flagship makes a decision on whether to fund a series A. It's all done in stealth mode and these companies are not announced," said Tak.

The firms are initially headed by a senior leader from Flagship. Should things progress positively, the decision will be made to transition the firm into a "growthco", with an external CEO appointed who further builds the leadership team and seeks additional funding through a series B round in which Flagship will co-invest.

"Flagship builds discovery platform companies and invests broadly in multiple programs. This is a fantastic way to de-risk the organization," said Tak. "And you can increase the probability of success of every medicine by being extremely thoughtful about the therapeutic target. You need to design relatively small clinical trials that will yield a high density of data to find out early on whether hitting the mechanism will lead to you hitting pathways downstream that are known to be associated with clinical effect."

Flagship's successes include messenger RNA therapeutics and vaccine developer Moderna, which became the largest biotech IPO in December 2018, raising $604m with a valuation of $8.1bn, and cellular therapy developer Rubius Therapeutics, which raised $277m and had a total valuation of $2bn in its July 2018 IPO. *(Also see "Finance Watch: Moderna Launches Biggest Biopharma IPO Ever As US Market Resets Expectations" - Scrip, 10 Dec, 2018.)*

Mutual Benefits

Tak pointed out that with $2.5bn in committed capital in 2018, more than 15 IPOs over the past five years, more than 40 therapeutics in development and around $1.2bn being spent on discovery each year, the Flagship ecosystem "could compete with any pharmaceutical company in terms of discovery investment." He sees his new role as a chance to "accelerate what I tried to achieve, which is basically getting into the clinic to make medicines that could be transformational for patients."

For its part, Flagship gains from Tak's understanding of "what a medicine looks like," his insight into patient needs – thanks to his decades of clinical practice (he has received an award from the minister of health in his native country the Netherlands for being the best rheumatologist in the country), his existing network in the UK and continental Europe, and his experience in experimental medicine and leadership.

Under Tak's steerage of GSK's immuno-inflammation therapy area unit, development programs included:

- GSK3196165, a granulocyte-macrophage colony-stimulating factor licensed from MorphoSys AG which has yielded positive Phase II results in rheumatoid arthritis;
- the interleukin-6 inhibitor sirukumab, which GSK handed back to partner Janssen Biotech Inc. in 2017 as part of an R&D cull shortly before the product's rejection by the FDA for rheumatoid arthritis;
- and a subcutaneous formulation of the lupus drug Benlysta (belimumab), which was approved by the FDA in 2017.

Silo Breaker

But it was arguably earlier in the pipeline that he really made his mark. Tak's passion for "breaking down silos" saw him foster the application of immunology research beyond autoimmune conditions to include other disease areas, most notably oncology.

For example, GSK's initial research into the RIP1 kinase, which regulates inflammatory cell death and inflammation, in autoimmune conditions like rheumatoid arthritis and inflammatory bowel disease was expanded to include pancreatic cancer after the researchers saw a scientific publication on a possible link between inflammatory cell death and pancreatic ductal adenocarcinoma. Similarly, the company expanded its systemic stimulator of interferon genes protein (STING) agonist development program into cancer.

Tak also established GSK's Immunology Network to bring together pharma, biotech and academic scientists, which led to the establishment of Sitryx Therapeutics to develop treatments based on the emerging area of immunometabolics. *(Also see "GSK-Backed Sitryx Launches With Six Immunometabolism Eggs In Its Basket " - Scrip, 8 Oct, 2018.)* Validating Tak's approach, GSK's chief scientific officer and president of R&D Hal Barron last year announced the company's new R&D strategy, which will focus heavily on the immune system and genetic science, as well as external collaboration and fostering a culture "of truth-seeking versus progression-seeking."

It is apparent that Tak has an enthusiasm for shaking up science as well as organizations that is underpinned by an impatience to advance medical science. His diverse career is indicative of a focus on the end – creating transformational treatments for patients – rather than any one means of getting there, whether that be academia, medical practice, big pharma or biotech. Right now, like quite a few other émigré executives from big pharma, he's attracted to the nimble, risk-taking, entrepreneurial spirit of biotech.

"I led a very significant part of the R&D at GSK over the past few years, including oncology, immuno-inflammation and infectious diseases, and after looking at other global head of R&D jobs in big pharma, as well as venture jobs and senior roles in academia, I came to the conclusion that I wanted to lead a biotech company, to develop medicines for patients and create value for the investors and for the company," he explained. In fact, it's not his first foray into biotech: in 2005 he founded gene therapy firm Arthrogen, to target rheumatic diseases, and for a few years he was CEO of the GSK spin-out Tempero Pharmaceuticals, which was re-acquired by its originator in 2015.

> **"This is the best time ever: it's a privilege to be able to work in this era in history on biomedical science." - Paul Peter Tak**

Tak has found the atmosphere in the US's East Coast biotech community inspiring. "It's very clear that Boston and Cambridge, Massachusetts is the world capital of biotech. It's very dense: there are many, many people in academia, biotech and venture in a relatively small area. In the streets, people talk about genes and molecules. Every time I went for a networking meeting and would wait for an elevator someone would tap on my shoulder and say 'Well, Paul Peter, what are you doing here?' So I realized how much is going on, how many people who are relevant in this field are there, and how fascinating it would be to be part of this community. And it is."

For Tak, it is very much a case of right place, right time. "I think this is the best time ever: it's a privilege to be able to work in this era in history on biomedical science, because we are seeing an explosion of knowledge at the moment, at the same time as enormous unmet need to address many diseases where we don't have therapeutic options that are good enough, and it all comes together with the whole tech revolution, including the digital revolution. Being at this interface is an incredibly exciting opportunity."

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