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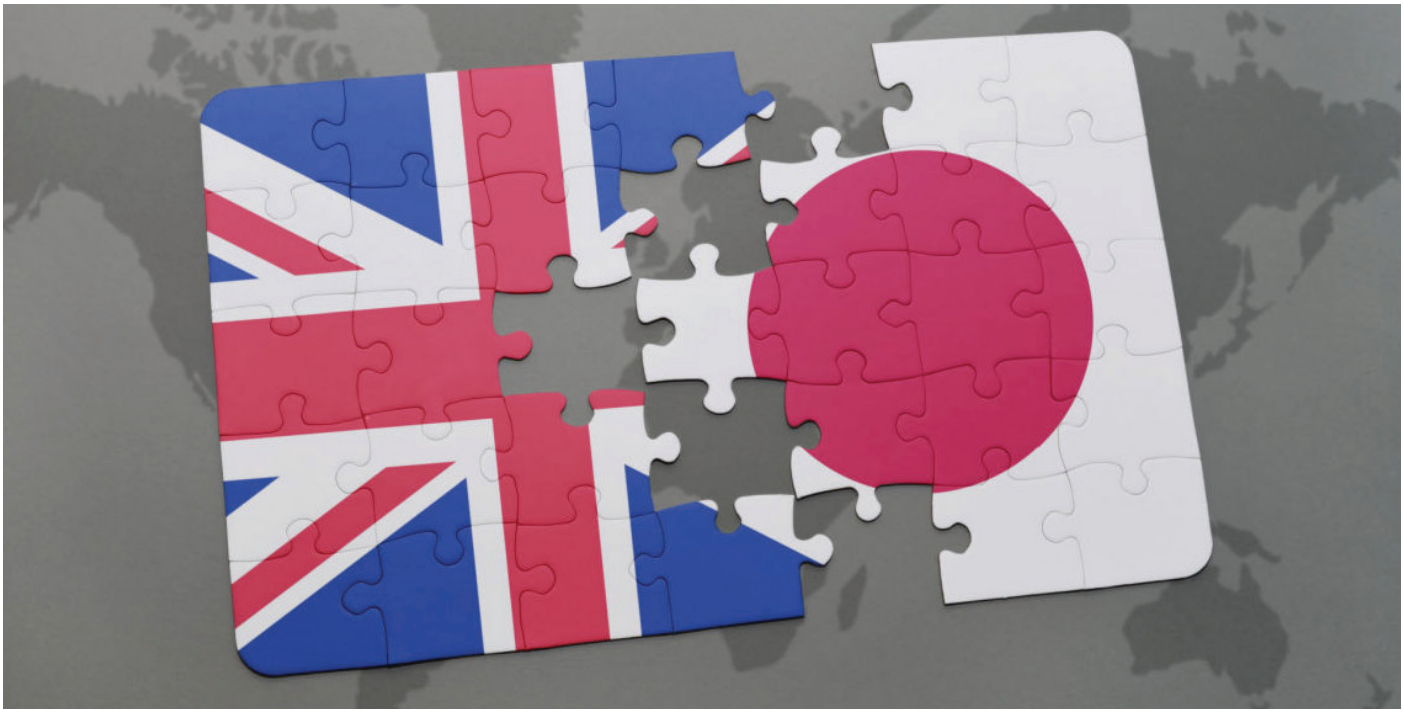

Sosei Heptares Eyes Asia Build-Out On Internal, External Assets

Parallel To Partnering

By Ian Haydock

Japan-UK firm is looking to build on a combination of internal and external assets to pursue a more independent business development path in Japan and beyond, in parallel with ongoing discovery and development collaborations.

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When Chris Cargill became president and CEO of Sosei Heptares in March 2022, high on his initial to-do list were a number of items around the transition of the Japan-UK company to the next stage of its journey.

There were four main strategic goals: make the company's R&D unit as effective as possible; put translational medicine at the forefront; merge the preclinical and early development teams in the UK under a new translational medicine function; and the further build out of a science-led organization.

Speaking to *Scrip* in an exclusive interview at the firm's Tokyo headquarters, Cargill said other key mid-term strategic goals include a greater emphasis on progressing in-house projects to the mid-clinical stage before deciding on partnering deals, and targeting Japan and other markets in Asia for both independent and alliance business development.

Following Sosei Group Corp.'s $400m acquisition of the private UK-based, G protein-coupled receptor (GPCR)-focused drug discovery firm Heptares Therapeutics Ltd.

in 2015, the combined operation firm now straddles Japan and the UK, home to its Cambridge research site. While the joint entity continues the legacy listing of Sosei on the Tokyo Stock Exchange's (TSE) Mothers Growth Market, "we do not currently have a big business in Japan," he noted.

CHRIS CARGILL, CEO, SOSEI HEPTARES

Australia-born Cargill - voted Executive of the Year at this year's inaugural Pharma Intelligence Awards in Japan – has been with the company since 2017 and was previously chief financial officer, succeeding as CEO Shinichi Tamura, who became chairman. He has healthcare-focused investment banking experience at J.P. Morgan (which did work with Sosei) and also worked in corporate finance at KPMG, giving him a strong financial background.

At the time he joined (initially as head of IR and Strategy), he saw the firm as a "hidden gem" with both strong existing partnerships and research capabilities.

At the same time as the CEO change, Matt Barnes (ex-Takeda) was named head of UK R&D and president of Heptares Therapeutics. "The transition was a recognition that the company was planning to grow into its next phase" from a purely science-focused operation to more of a fully-fledged business, the CEO explained.

The majority of its 220 staff are UK-based, of whom 170 are scientists. While the intention is not to add too many more full-time employees in Japan – where there are around 15 now - "enhancing group structure and virtualising R&D will help us to scale flexibly," Cargill explained.

Besides discovery alliances, royalty revenue also comes from a portfolio of commercialized chronic obstructive pulmonary disease and asthma therapies, including Ultibro (indacaterol and glycopyrronium bromide) licensed to Novartis AG, and totalled around $40m last year.

Over-Arching R&D Strategy

While the company has so far been more focused on what the executive termed a fast-follower strategy, the aim now is to validate programs and seek more novelty, using the proprietary GPCR discovery platform to de-risk targets.

Given its productivity in generating small molecules, peptides and therapeutic antibodies, productivity is not an issue and the platform is an R&D engine that can essentially "reload the pipeline all the time." As such, "we can afford to be a little bit ruthless with the pipeline" and the firm will not hesitate to "kill off any early if needed."

"We have moved from a single product in 2005 to having world-leading technology now" and currently there are 41 programs in R&D, with three potential clinical starts slated for 2023. But this has brought with it the need for more active technology management.

Cargill described Sosei Heptares as now having a business model that has the "pipeline diversification of big pharma but the upside potential of biotech." It is also tapping external development service providers such as UK-based Weatherden for flexible "resources on demand."

In early-stage development, artificial intelligence alliances have also come into play as part of a TIV (target identification and validation) initiative to access new technology and speed up elucidation of disease/target links. This January, the company linked with Verily, a division of the Alphabet Inc. group created by Google, for what was the US firm's first drug discovery pact, focused on immune-mediated diseases to identify novel targets.

Verily is applying immune profiling technology to combine with the structure-based drug design and GPCR expertise of Sosei Heptares, which also has an AI-powered target discovery alliance with InveniAI LLC.

"We want to do more collaborations like these in future, including to identify a CNS target," Cargill told *Scrip*, as part of an evolving R&D approach that balances riskier, highly novel targets genetic associations that should be attractive to partners. "They will help fuel the next wave of novelty in the pipeline."

Looking To License Out - And In

Sosei Heptares already has multiple big pharma licensing partners for clinical-stage assets, and partnering of diversified types will continue to be "a big part of our business model" going forward, Cargill stressed. These out-licensed assets include inflammatory bowel disease programs with Pfizer Inc. and GSK plc and others including with AstraZeneca PLC, Takeda Pharmaceutical Co. Ltd., Neurocrine Biosciences, Inc. and Biohaven Pharmaceutical Holding Company Ltd.

There have been multiple positive developments for several of these programs over the past few months, notably strong Phase I data for the Pfizer-partnered GLP-1 agonist PF-07081532 for type 2 diabetes and obesity, a Phase II start at Neurocrine for the muscarinic M4 agonist NBI-11175678 for schizophrenia and other neuropsychiatric disorders.

There was also a major AbbVie Inc. deal for neurology GPCRs earlier this year worth $40m upfront (Also see "Sosei Bolsters GPCR Focus With AbbVie Neurology Deal" - Scrip, 3 Aug, 2022.), while the Neurocrine alliance – struck at the Phase Ib stage - was worth $100m upfront.

Looking ahead, the general intention is to take more projects coming out of UK preclinical research into the Phase I/IIa clinical stage before out-licencing, given the bigger returns than for early-stage assets, the CEO said. This would again be supported by utilizing outside contract clinical development experts where necessary.

In addition, a new prong will be to use some of the capital from the alliances to bring in external assets for development in Japan and other Asian markets. Cargill declared at a recent company R&D Day that "In the near term, we expect to secure complementary world-class translational medicine capabilities to 'turbo charge' our discovery and early development strategy."

To this end, "we've done an enormous amount of work with a consultant" on identifying unique, clinically de-risked (i.e., Phase III or launched) assets in the US/EU, he said in the interview, with the hope being to secure projects here - "most likely from overseas" - in the next one to two years.

The studies suggest that firms such as mid-sized US biotechs may be less focused on retaining Japan/APAC rights, although it will be partner- and asset-specific.

Japan As APAC Linchpin

While "we recognise we are a Japanese company," one of Cargill's regrets is that Sosei Heptares is not yet delivering medicines to Japanese patients.

Driven by a combination of internal assets to which Japan/APAC rights will be retained and the in-licensed drugs, the goal is to rectify this through the development and potential first launch of a product in the country in the 2026-27 period.

"There are many, many reasons to invest in Japan, including an ageing population, robust reimbursement and regulatory system and amazing medical quality" and the company's local presence and license, he said. Despite some multinationals pointing to a multitude of pricing and other challenges, Cargill's view is that "the fundamentals remain strong," while it also "makes natural sense" to look at other APAC markets.

The hope is to progress up to five UK-originated internal programs across multiple modalities and indications in Japan using a virtualized development network of contract partners, for which the selection process is now in the early stages. These are likely to need local pharmacokinetic studies, then bridging and possibly repeat pivotal clinical trials.

The target therapeutic areas for Japan include rare and orphan disorders, CNS and immunology, where Sosei Heptares has identified high-potential, late- or commercial-stage assets with available Japanese rights.

One program was already highlighted at the R&D Day, a preclinical oral small molecule EP4 agonist for inflammatory bowel disease for which a clinical start is envisaged by end-2023. Cargill noted four or five other undisclosed internal programs for ulcerative colitis or Crohn's.

Overall, there may be three other clinical starts for in-house assets over the next year or so (in atopic dermatitis, schizophrenia/psychosis and immuno-oncology), which "solidifies our status as a maturing biotech company."

As for the rest of Asia, in-licensed assets are seen as being able to move ahead relatively quickly (maybe ahead of Japan) in Southeast Asian markets such as Singapore, and potentially Australia, that accept US approvals without the need for extensive local studies.

Again here, external pan-Asia distribution specialists (such as Zuellig Pharma and DKSH) are available and the early revenues would help support the lengthier development process in Japan.

China, however, is viewed as "too complex" for a small company, although the partnering option remains for internal assets to which big pharma partners may be interested in rights in what is a big market for them where they already have a presence.

Tokyo Prime Listing Plan

While Sosei's Tokyo Mothers listing has run for 17 years, it has attracted mostly retail investors, with no large Japanese institutional investors at present, Cargill observed. However, a planned shift to TSE's Prime bourse should attract more of these investors and build the investor base - which in turn could be tapped for future financing and "secure our financial future."

Progress of internal assets towards clinic "solidifies our status as a maturing biotech company."

Chris Cargill, president & CEO, Sosei Heptares

A regulatory decision on the Prime listing is expected around Q1 of next year, after which the company could move quickly. "We would be the only biotech on Prime and becoming a 'local hero' is our goal," Cargill said, adding it would be easier to "maintain a good share of eyes" versus the roughly 950 firms listed on Nasdaq in the US.

Cargill and current CFO Hironoshin Nomura - appointed to the position following Cargill's promotion and who also has a finance sector background - are confident they will be able to meet and manage the heightened compliance requirements.

In the meantime, if the current weakness of the yen (now at a 32-year low against the US dollar) continues, this might allow more work to be conducted in Japan, given that Sosei Heptares' main deals are dollar-denominated. "But any time benefit would be a consideration," Cargill said.

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