Sosei Heptares

Sosei Heptares presentation delivered at the 37th Annual J.P. Morgan Healthcare Conference on Monday, January 07, 2019 at 9:30 AM

Krishna: Good morning, everyone. My name is Krishna. I'm from the J.P. Morgan Healthcare Investment Banking team. It is my great pleasure today to introduce you to Chris Cargill, the Chief Financial Officer of Sosei Heptares, the world leader in GPCR drug design and development.

Chris, over to you.

Chris Cargill: Thank you, Krishna. Good morning, everyone. Welcome to the Sosei Heptares presentation at the 37th annual J.P. Morgan Healthcare Conference. It's great to be here today.

It's the second time running that we've presented here in the main track at J.P. Morgan, the world's premier healthcare conference. We thank our friends at J.P. Morgan who are in the audience today for their support and for inviting us.

This morning, I'll give you a brief overview of our technology, our corporate philosophy, our business model, but most importantly, our exciting pipeline of drug candidates.

Slide 4

For those of you who don't know who we are, we were founded in 1990 in Tokyo and then made a transformative acquisition in 2015 of a UK biotech called Heptares Therapeutics. Thus, we became a truly global science-led organization, but we remain anchored in Japan today.

We've got almost 30 programs in development, 7 in clinical studies, 4 in pre-clinical development, and a burgeoning pipeline of 15 discovery assets. We're adding more and more to this every year.

We've built a pipeline primarily through partnerships with large-cap pharma, small biotech, and academia. We love executing partnerships. They clearly validate the application and value of our technology and our approach to drug design. We can expect to do more of these in 2019 as well.

We also have an emerging in-house pipeline, which I'll touch on later. It's primarily focused on the

rare and specialty setting.

Slide 5

How do we structure ourselves, globally? As I mentioned, we're Japan-anchored, but we're a fully integrated, global discovery and development business, with the research arm in Cambridge, in the United Kingdom. We've got approximately 150 employees, globally.

On the UK side, as you can see here on the left-hand side, we have 120 full-time scientists located at our new state-of-the-art facility in Cambridge, United Kingdom. We relocated here late last year, and the value of this relocation cannot be underestimated. It's been highly motivational to our scientific teams to work in an integrated, purpose-built facility.

We've got everyone from platform technology, research, drug discovery, translational science, and clinical development all under one roof. Cambridge is certainly one of the world's leading biotech innovation hubs, and we're already seeing improved productivity, enhanced collaboration, and better partnership opportunities because of the move.

On the right-hand side, the Japan side of the group, we run our head office operations here. Importantly, it's where we maintain our public listing. We have fantastic access to low-cost capital over there.

In Japan, to complement our research and development capabilities in the UK, we have late-stage clinical development expertise. That team has had great success over the years navigating the Japanese regulatory landscape to bring drugs, not only to be approved but also to market. In conjunction with partners such as FujiFilm, we've had recent success.

Slide 6

Many people ask what's our secret sauce? It's called StaR®. It's our exclusive technology. It enables much smarter, GPCR-targeted drug design. We focus on GPCRs because we know they widely influence human disease.

We believe StaR®, which stands for ‘stabilized receptor’, is the only scale commercial technology available in the world that enables GPCRs to be stabilized in their natural states, retain function, and opened up for detailed structural analysis.

This technology opens up a world of rich mechanistic and structural information that our scientists can use to develop better drugs such as those with improved physiochemical properties, better

safety and efficacy profiles, and, ultimately, reduced clinical attrition rates.

StaR® is not just for small molecule development. It's also useful for peptide and antibody discovery. While in theory we could go after the entire landscape of 400 GPCRs which are known to impact human disease, we have historically tended to focus on those targets which have a good level of clinical or otherwise targeted validation.

It's this potent mix of our exclusive technology and focusing on targets with validation which has driven our success and productivity over the years. Going forward, we will be looking to work increasingly on novel, first-in-class targets as well.

Slide 7

I wanted to touch on our corporate philosophy because it's important, and I believe it's what separates us from our traditional peer companies, particularly in Japan.

First and foremost, we're a technology company. We're technology-driven.

We have a fantastic technology in the StaR® technology, which was first patented over a decade ago. It revolutionized GPCR structure-based drug design at the time, and it remains highly relevant to drug discovery today.

We can't stand still as a company. Technology evolves, and we must evolve with it. That's why we're constantly pursuing technology deals to improve our discovery capabilities. Examples of this include our deal a few years ago to acquire the CHESS and SaBRE technologies in Zurich, and our integration of Cryo-EM into our discovery platform.

We've also got a collaboration ongoing with University of Cambridge to roll out AI across our platform.

Secondly, we believe in keeping it small. Our organization needs to be small and nimble. Over the last few years, since we acquired Heptares, we have had to scale up somewhat to overcome attrition, but we've done so ensuring that we didn't sacrifice our culture of quality, innovation, and trust.

We don't want a bloated, bureaucratic structure. We believe less than 150 R&D employees is the optimal size for this business. That's how we're going to foster innovation going forward.

Getting published, the third point. We love to see our scientists get recognized for challenging the frontiers of science. We've got 120 R&D team members and over 80 PhDs in the company, and this a testament to the quality of our scientists.

Since 2010, we've solved 259 x-ray structures from 23 receptors and published many of them. This has driven our work and our in-house research and discovery efforts. Importantly, it's led to over 175 top-quality publications in journals such as ‘Nature.’ This drives interest from the scientific community. More importantly, it drives our partnerships as well.

We're focused on creating value. With a discovery platform that’s as productive as ours, it's only natural that, from time to time, we're going to generate targets that sit outside our core areas of expertise. For this reason, we aggressively pursue partnerships and co-development deals to keep the pipeline moving and the value creation opportunities fluid.

At the same time, we like to retain for ourselves the niche opportunities in disease areas where we can cost-effectively develop them. As I mentioned, later I'll touch on our emerging pipeline in the rare and specialty setting.

The last point here about our corporate philosophy is being productive. We believe we're one of the most productive technology platforms in Cambridge and the UK, if not the world.

Slide 8

On the next slide, I wanted to highlight some of that productivity. We've identified 22 agents in total against 18 targets, 12 of which have been identified since the Sosei acquisition of Heptares in 2015. Projects had been taking, on average, two and a half years to reach pre-clinical candidate stage. We've got that down to two, and we've got more improvements to come.

Furthermore, pre-clinical candidates are now generally being synthesized in less than 500 compounds. We believe this all adds up to impressive rates of productivity, and it stacks up well against industry averages.

Slide 9

Moving on to our business model, as I touched on earlier, it's designed to create and capture optimal value at various points. Pharma and biotech are expensive businesses. It's widely known that R&D costs are becoming increasingly unsustainable.

Depending on whose numbers you believe, it can cost between one and two billion dollars to

bring a product to market. This is going to result in an ongoing decline in return on investment going forward. Our model is very much focused on creating and capturing the value at various stages of development.

As I mentioned earlier, we've got far more programs than we can possibly prosecute ourselves. Therefore, we aggressively manage our portfolio and look to actively partner and co-develop in areas where we can crystallize value at the right time.

When we do choose to partner or co-develop an asset, it's for good reason. We're generally trying to leverage someone else's expertise. We always seek to retain the most value possible when we partner or co-develop, as well as contributing to the growth of those assets going forward. We do so by participating in funded research collaborations on those assets or participation in joint steering committees going forward. This is how we learn, and this is how we grow.

Lastly, there are assets that I mentioned that we like to keep. They're typically in the rare and specialty setting. They have a manageable translational and clinical pathway, and trial costs which are digestible for a company of our size.

Slide 10

Next I wanted to touch on our strategy for this year. We're very excited. We think we've created the next wave of novel candidates, which are poised to create value for the company. We've had a lot of success partnering on assets to date. As a result, we've had to reinvest heavily to replenish the pipeline and generate new candidates of interest.

At the same time, we've balanced that with the need to fund our growing in-house pipeline, which is shown here on the slide in orange. We've achieved this, and we're well-positioned for 2019.

To build on this a little bit more, the four in-house assets that are mentioned there in the orange on the right-hand side, they're all planned to go into Phase I clinical studies this year, but our investment across the platform has generated 15 new discovery candidates across high-value therapeutic areas, such as immuno-oncology, GI, inflammation, and neurology.

For the first time today, I'm happy to announce and disclose some of the targets that we're working on in this space. We've got GPR35 and EP4 in the GI space, Apelin, H4, and PAR2 in the inflammation space, and OX2 in the neurology space.

I'm very confident these assets are going to drive a new wave of partnerships and/or selective in-house progression for the company. As you can see, we've got a strong and balanced pipeline, and we're well-positioned for future value creation.

Slide 11

This is very exciting for us, moving on to the partnered pipeline that we have. I'm very, very happy to announce today that we've got a new milestone of $15 million from AstraZeneca. This relates to the progress of our next-generation immuno-oncology program, which we partnered with them some years ago.

As you can see on the left-hand side of the slide, this is the fourth milestone we've received since exclusively licensing this candidate to AstraZeneca. We're certainly thrilled at the progress. The compound is a potential next-generation I/O therapy. It was designed by us using our propriety StaR® technology. It was optimized using our structure-based drug design platform.

We're very, very excited. The results of first-generation I/O therapies were certainly very remarkable. As many of you know, not all tumors respond to current I/O therapy, and some tumors that do initially respond, lose that response.

This next generation of I/O therapy, such as this program that we have with AstraZeneca, focuses on identifying additional immune inhibitory pathways that can be blocked to boost immune response.

Today's news highlights the adenosine 2A receptor pathway is rapidly emerging as a very, very promising target. We're super-excited to be partnered with AstraZeneca on this one, who are a clear world leader in this space.

Slide 12

Picking up on that, I wanted to highlight how thoroughly AstraZeneca is testing this compound in Phase Ib/II studies. The first study is designed as a monotherapy or in combination with their checkpoint inhibitor durvalumab.

It's being tested in a cohort of patients with specific types of tumors. For some cohorts, these patients have not received I/O therapy before. In others, the patient's tumor has not responded to I/O therapy. The recruitment for the study is going very well, and we expect to see a readout of data in 2020.

The second study of this compound is in combination with oleclumab, which is AstraZeneca's anti-CD73 investigational drug. It's for patients with advanced non-small-cell lung cancer with mutations in the epidermal growth factor receptor. Again, this study's progressing well. Results are not expected until 2021.

In summary, we're very excited about this program. There's strong pre-clinical evidence that high adenosine concentrations in the tumor microenvironment are immunosuppressive. Pre-clinical data in tumor models supports this compound alone and in combination with other immuno-oncology therapies.

We're very pleased to see the progress of this drug, going forward. We also expect AstraZeneca will present interim Phase I clinical data at some stage during 2019.

Slide 13

I wanted to touch on the rest of our partnered pipeline. There are a few programs that I wanted to highlight, ones we haven't spoken about for some time, but which are progressing nicely.

With Daiichi-Sankyo, we have a compound that is advancing towards pre-clinical candidate stage in the pain space. This will entitle us to some small sub-$5 million progress milestones over the course of the year.

With Pfizer, we have a couple of undisclosed compounds that are progressing well from the multi-target deal that we announced with them a few years ago. Again, this will entitle us to a few small, less than $5-million progress-related milestones this year.

We've also got two monoclonal antibodies which are marching towards candidate selection. We've got a PAR2 antibody, which was developed with the help of MorphoSys in the inflammation space. We've also got an antibody co-developed with Kymab in the highly sought-after immuno-oncology space. As you can see, the partnered pipeline is moving forward very nicely.

Slide 14

Now to our in-house pipeline. We've got a rapidly emerging in-house pipeline. We've got four agents planned to go into Phase I clinical development this year. We were very proud to announce in December last year, our first dedicated in-house asset into Phase I development, an mGlu5 negative allosteric modulator for neurological disorders such as ALS or dystonia.

Our next clinical start is expected to be an SSTR peptide agonist for endocrine disorders. We've received UK regulatory authority and ethics committee approval late last year to progress this compound. We hope the first subject dosing will occur in the first quarter of this year.

The three other programs highlighted there, they're all expected to progress, probably in the second half of 2019.

Slide 15

Before I finish, I wanted to touch on a couple of frequently asked questions that we get from our investors and our shareholders, particularly over the last couple of months.

We had a change of CEO announced in December. The chairman and founder of the company has stepped back in to become Chief Executive Officer. The question that we receive a lot is, "Has the strategy changed since the CEO announcement in December?" The answer is no.

There has been no change in the strategy that we outlined at our interim results briefing in November 2018. In fact, it was the current CEO who delivered that strategy on the conference call, so you can be highly confident that the goals and objectives that he set for each division remain of critical importance to us as a company, and to our progress.

The next question we get a lot, "Are there any updates on the M1 tox issue?" which relates to our partnered Alzheimer's disease program with Allergan, and our proprietary dementia with Lewy bodies program in Japan. We don't have any updates today, but I can say the investigative work is proceeding very nicely with Allergan. We can expect to review the status during 2019 when the work is completed.

What we can say today is, since the issue, we've had the benefit of seeing some interim Phase Ib human clinical data from the study that was taking place in the EU. We think it continues to support the hypothesis for selective M1 agonism in this setting.

The next question we get is, "Is the advent of Cryo-EM going to impact our competitive advantage as a company?" Again, the answer is no. Cryo-EM is certainly revolutionary, but it's not going to dent our competitive advantage.

We, as a company, think Cryo-EM is going to be very helpful in getting to a first view of a structure quickly, but x-ray crystallography will still be required to get the plethora of complex structures that we've found to be beneficial in drug discovery. It's this latter point where we excel

as a company.

Many people in the Cryo-EM space are working exclusively on previously published structures. Our competitive advantage is that we have a deep and vast knowledge of unpublished, in-house crystallized structures of unique GPCR ligand complexes. That provides our competitive advantage, and this is not available to others.

Lastly, is there a role for AI or machine learning for GPCRs? The answer is yes. Definitely, we think that there is. In fact, we have an active collaboration with University of Cambridge to deploy artificial intelligence and machine learning across our entire platform for multi-parametric GPCR-related drug discovery.

Specifically, we're collaborating with a gentleman called Andreas Bender at the University of Cambridge. He is a chemo-informatics and AI expert and a co-founder of a company called Healx. We know AstraZeneca and Lilly have been quite successful in getting traction in AI in drug discovery method development via collaborations with Andreas, so we're certainly very happy to be aligned with him.

Slide 16

On this next slide, it's a summary snapshot of how we are rolling out AI across our drug discovery platform. We're looking to improve target selection, stabilized receptor design, ligand design, and synthesis planning, and ADMET prediction in our translational sciences business.

That concludes our presentation today. Thank you, everyone, for coming. If you'd like to join Dr. Miles Congreve and myself in the Sussex Room for Q&A, we'd welcome your questions. Thank you.