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<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Thank you, everybody, for joining this session. My name is Steve Barker, pharmaceutical analyst with Jefferies in Tokyo, and it's my pleasure to host Sosei for this fireside chat. We have Chris Cargill, CEO. We have Matt Barnes, who is President of Heptares and Head of UK R&D. And also Hiron Nomura, who is the CFO of the Sosei Group. So Sosei is a Tokyo-based company. It's listed on the Tokyo Stock Exchange with the ticker 4565. It is a commercial stage biopharmaceutical company with operations in Japan, Korea, and the UK. The UK operation is mainly composed of a Cambridge-based Heptares. And so, Chris or maybe Matt, maybe you could tell us about the Heptares proprietary drug discovery platform.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Awesome. Thanks, Stephen. What I might start out with is just sort of outlining how the group is structured. You sort of mentioned it just now. All of our research in drug discovery and early clinical capabilities are actually based in the United Kingdom up in Cambridge with the unit that's led by Matt. As you alluded to at the beginning, we're also a commercial company, so we have a commercially available product that just launched recently in Japan. So, our late-stage development and commercial capabilities are across the pond in Japan. So, we do all of our research over here, research in early clinical, the late-stage development and commercial stuff. We focus on Japan and APAC, and the way that we access the United States and other markets is by way of partnerships with large-cap pharma and large-cap biotech predominantly.

Our mission pretty much is to invest in cutting-edge science and work on making medicines by structure-based drug design, and then push those medicines through our internal capabilities or onto partners. In terms of the frontend of everything we do, research in Heptares and the proprietary technology, I'll let Matt talk to that. Thanks.

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Okay, thanks, Chris. Yes. So yes, in the UK, so we have about 180 scientists there at Granta Park in Cambridge. And effectively, the company is, first thing we should say is it's focused on GPCR targets as a drug target class, so G protein-coupled receptors. So, we're very much the world leader in the drug discovery space for GPCRs. They're a very tractable drug target class, so more than 30% of FDA-approved drugs are GPCRs. So they're very tractable. But to actually do structure-based drug design with GPCRs is actually quite difficult, because they're a membrane protein. So, as soon as you take the protein out of the membrane and try to do any crystallography with the protein, it just disintegrates. So what we do is we introduce stabilizing mutations into the protein, and that really helps us use the protein outside of that cell membrane environment. And that allows us to do really cool things like structure-based drug design. So, really, that's very much a rational

drug design approach, so we're making less molecules in a shorter time frame. So we've been incredibly productive using that platform in anger over the years.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Yes. So yes, a very productive platform, and you've done a lot of partnerships with larger companies. Could you tell us about some of those partnerships?

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Sure, yes. So firstly, we should just say that probably 50% of our pipeline is actually in partnership, and 50% is in-house. So the partnered programs, so they kind of split into two forms, really. So, we do – this is how we bring revenue into the business, which helps fund our internal pipeline. So those partner programs take two forms. So, one is like a platform type of deal. So companies like Takeda or AbbVie or Lilly will come to us and say, we've got these GPCR targets that are quite difficult to work with. You're the experts. Can we use your platform and your people to prosecute, help prosecute those? So, we bring in revenue from upfront payments and downstream milestones and royalties as part of that.

We also do licensing of assets when we've developed them in-house. So I guess in the past, we've done more of that more at the preclinical stage. So, we did one with GSK a few years ago, but actually now we're actually starting to try to take those assets deeper into the early clinic to build more value and then partner with them to really try and increase that value inflection, like we did with Neurocrine in the muscarinic space, and that partnership is very productive clinical stage. We have a Phase 2 asset with Neurocrine in schizophrenia.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Yes. I really want to talk about some of those specific assets, but Chris, maybe you could talk a little bit more about the business model. I think people who cover healthcare look at biotech stocks. They have an image of what a proper biotech business model should be like, and it's a little bit different in Japan. Wouldn't you agree?

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Yes. No, I would. I mean, people do typically look at biotech as high cash burn, generate clinical data. Hopefully, the data is good and you can do an equity capital raise and fund yourself for a few more years. Japan is not what I'd consider a marketplace where there is a lot of biotechs. In fact, we are the only biotech company that's listed on the prime segment of the Tokyo Stock Exchange, and that is why we run the business model that we run that Matt's alluded to. We are always trying to use the productivity of our platform to enable us to execute partnerships that bring in non-dilutive sources of cash flow, so that we can fund the business for a longer period. That has been very successful for us, and we will continue to do that going forward.

I think this year, I'm sure you'll touch on it a bit later, Stephen, but the way that we became a fully integrated commercial stage biotech was actually by way of acquisition. So we did an acquisition

earlier this year. Japan is, of course, our home market, but we see Japan as an increasingly attractive place to do business. I mean you might have seen overnight this. We made a bet earlier on the year that actually we think the Japanese market is going to reform. So, all of the historical issues that they've had around drug loss, drug lag, low pricing, we see ourselves as really well positioned to ride a kind of a new wave of investment in Japan.

The thing that makes us different is we're obviously almost like a foreign biotech listed in Japan. So we're really positioning ourselves going forward in Japan, not only to develop and commercialize our own products, but really to become the partner of choice for U.S. biotechs or farmers that want to license their assets and have them developed in Japan by an outfit that is ostensibly not that Japanese. We're Japanese, but we're not that Japanese.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

So, the business model is going to be generating revenues, cash flows, profits in Japan whilst concurrently investing in R&D in the United Kingdom, where equally through just the plethora of kind of collaborations that we have. There's a lot of non-dilutive sources of cash that come into the business. So it enables us to invest over a longer cycle and avoid that boom bust that you see with U.S. biotech.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right. So, it's a relatively low risk, but potentially very high return.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Yes. The way I look at it is downside is underwritten, so actually it's kind of all upside. It can't get that bad for us because there is always a continuous source of cash flow coming into the business. The upside potential through a lot of these partnerships that we have, some of them which are on clear blockbuster targets or drug opportunities, will eventually start to pay off significantly for us in the future.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right. Yes. So we get on those assets, save the best for last, but before we get there, what about the – you talked about two different types of relationships that you have with partners. Can you share anything about the financial details of those deals in broad terms?

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Well, yes. Okay, dual. I'll pick this one. The up-fronts are always disclosed, generally speaking, as are the buyer box. But the way – I mean the deals that we do, the one thing that we don't do is

we don't do fee-for-service, right. So, the revenue that's coming into the business is high-end premium revenue because we as an outfit have achieved a milestone for a partner and they're paying us a premium. We don't license out the platform for fee-for-service revenue. So that is probably what makes us a little bit different. It does, of course, make the cash flows lumpier, but we back ourselves in to very consistently, year upon year, deliver on milestones for our partners. And as with all collaborations, the deeper you go, the larger the milestone becomes.

So, we've now got a pipeline that is progressing and advancing through early clinical. So the most advanced asset is in Phase 2. We would expect that to complete next year. And if successful, those clinical assets that are being advanced by partners in the U.S. in large indications will start spitting off \$10 million, \$20 million, \$30 million, \$50 million milestones quite soon. So, that's actually quite exciting for us because we can do a lot with a \$50 million milestone.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Yes. Yes. Great. Tell us about your lead asset...

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Just on the partner side of things or...

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Well, honestly, on the partner side of things, what's the most advanced asset?

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Yes, sure. It's a muscarinic M4 receptor agonist. And it's very much following in the path of KarXT Karuna. It's indicated for schizophrenia. It's partnered with Neurocrine. It's going really, really well. They're chasing down CeraVe, and as I said, we're very, very hopeful that next year that will read out Phase 2, but I'll let Matt speak in a bit more detail given it was actually Matt's team that discovered the asset.

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Thanks. Yes. So, yes, it's now in the hands of Neurocrine, so they're running that – sponsoring and running that Phase 2 study in schizophrenia in the U.S., but as – Chris is right, so the origin very much was in the UK. So it's actually part of a suite of assets that were licensed in Neurocrine. So, that whole kind of muscarinic receptor space, as Chris mentioned, has become alive over the past few years. Most people will know there has been no new mechanisms in schizophrenia for decades. It's always an iteration. It's always another antipsychotic. This is a new mechanism. And I think Karuna with KarXT have done an amazing job actually how they've configured a drug product that probably will get approved this year, but actually our molecule is quite different. So theirs is a non-selective molecule, and they're kind of offsetting the non-selectivity with a peripheral

antagonist. So, they're using a non-selective agonist, and they're blocking parts of that selectivity with an antagonist.

We don't need to do that with ours because we've used that structure-based drug design approach to build a selective M4 agonist molecule, so that's the difference between the two. We haven't got to worry about the same side effects that Karuna have. So I really think there's a potential for best-in-class there with that particular molecule. The other thing we should point out earlier this year, as part of that same agreement, Neurocrine also initiated a Phase 1 study with what they call a dual, an M1/M4 agonist. And the reason the M1 is important is that it might bring in some effects on cognition, which actually is significant symptomology in schizophrenia. It's a real unmet need at the moment, antipsychotics, I don't touch that.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right. So, that's an example. You deal with Neurocrine where you discovered the asset and licensed it out. You've got other types of relationships where you give partners access to the platform. Could you talk about an example of a partnership like that?

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Sure, yes. So maybe the most recent one actually, which is Lilly. So, we did an agreement with Lilly back in December last year, so not quite at the year anniversary. So, we've been doing this quite a long time, and we've sort of gained a reputation actually in this space. So we've had a lot of these collaborations with AbbVie, and Takeda and Genentech. So, Lilly actually approached us and said, oh, we are really interested in these GPCRs in the metabolic space, maybe that's not surprising. Lilly have had great success with peptides, but of course, they are very interested in small molecules, right, as a next generation.

And so they came to us to talk about developing some GPCR small molecule agonists in the metabolic space. So that's a very productive collaboration. It's a discovery collaboration, so it's very much about us developing a structural biology position and really enabling Lilly to actually then further do drug discovery. So, we are going to take that to an early part and then enable them to do the work that they would do.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right. Well, you mentioned Lilly and metabolism, so very hot topic. Yes. Could you tell us about, because you have other relationships with other companies that are also focusing on this area. I think in a sense, Sosei is perhaps the best play in this GLP-1 space in Japan.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Yes, thanks Stephen. I'll start with an intro on sort of how we are positioned as a company and Matt can dive into a little bit more of the specifics. We can't talk too much because they are obviously partnered programs and so those programs are owned by our partners. But in 2015 we

had another one of these collaborations with Pfizer and that collaboration has been particularly productive. It resulted in four clinical starts over the journey. There is currently three active programs that are in the clinic, one of which is, of course, an oral, small molecule targeting the GLP-1 receptor. And there has been amazing interest in that and everyone understands that Nova and Lilly are clearly ahead, but there is a lot of companies chasing them down with an oral small molecule approach.

And we as a company are very fortunate to be having a program that was discovered by Pfizer using our technology and therefore we have an economic position on what could potentially be obviously a very huge opportunity for us.

Matt has mentioned we then have inter-partnership more recently with Lilly which is very much focused on the next generation of oral small molecule targets in that same sort of area. And of course we couldn't be more chuffed than to be partnered with Lilly in that space because they clearly are the front runners.

And then beyond that we obviously have programs that we are working on upstream of those receptors that are in-house programs which could eventually find their way to some of the leaders in the metabolic space or we may hang onto them a little bit longer ourselves, but basically we have a position all across the spectrum in Type 2 diabetes, obesity and you know what surely will follow will be additional indications.

But Matt maybe you want to talk a little bit?

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

I don't think there is anything you can add.

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Yes, I mean actually Chris mentioned this at the – we had an R&D Day last week just to plug that so it's available on our website. And actually he mentioned that actually we shouldn't really forget, so us as a company we were the first to publish the GLP-1 receptor structure.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Wow!

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

And it was published in Nature a few years ago. And so we would like to think that we were very much at the forefront of all of that small molecule concepts around that target. So, that's important to not forget that. And I think Chris did a nice job of doing that last week.

We are going back to sort of Pfizer and that specific target. So as Chris mentioned, that particular collaboration has been very productive not only GLP-1 but a couple of other targets as well. But Pfizer very much was almost a bit spoiled for choice right. So, they had two molecules that they were trying to run alongside each other and they did announce the discontinuation of one that we had that value attached to. That was earlier this year in June.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Lotiglipton, right?

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Lotiglipton, **yes**, in June, that was very obviously very disappointing for us. But fortunately as an output of that same collaboration they have been able to identify quite quickly a backup compound that they again have discovered and developed by using our technology. And that entered Phase 1 that they announced in their quarter three results one week ago, I think.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right. Matt given your long background in this area could you give us your perspective on what's happening with these GLP-1 agonists because everyone seems to want to have one and they seem to be segmenting, what's your view?

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

It's fascinating, so yes I think, everybody, I mean I think, everybody knows about GLP-1 now right, everybody. And it's been used and the products are approved for diabetes and obesity. And there are a number of peptide products on the market, of course, but they are injectable, there are some adverse events associated with some of these GLP-1s so it's a little bit harder to manage when you've got an injectable sustained exposure product. So the desire for small molecule replacement, I think, has commercial strength. I think it's just the start though right.

So, I think that even if Lilly or Pfizer whoever gets the market first with their small molecule, I think, they've really aimed at trying to hit weight loss and blood glucose control as hard as possible. I think now we are starting to hear more terminology around weight management and more longer term thinking around weight management.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Weight management as opposed to obesity?

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

As opposed to obesity, yes. So it may be we reach a position where in the future people want that rapid induction of weight loss but actually to sustain and keep that off they might want something that's a bit more gentle and a bit more physiological to kind of keep that weight off. That we think maybe, it could be a direction of travel there but there is a lot of biology and pharmacology to further understand that at the moment.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

And is that – that thinking, is that guiding your own discovery efforts?

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Yes it's a great question. Yes, so we last week at the R&D Day we also highlighted – we didn't disclose the target because we typically don't before we develop a preclinical candidate, but we do have a discovery based program that's very much based on this axis and in this metabolic space, but actually it's upstream of these incretin receptors that everybody is talking about GLP-1 is one of them, so GIP is another, and glucagon is another. We are very much thinking about this upstream. And we're thinking more around how can you target receptors that are upstream that more likely represents a physiological levels of some of these incretins rather than the sledgehammers that are coming with direct agonists.

Yes that's sort of where we're thinking now.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Right. So, could you tell us a little bit more about your in-house pipeline?

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Sure yes. Thank you for asking. Yes I mean it's 50% of what we do. And actually this year we are really, really proud to announce that we had two Phase 1 starts. One was an EP4 antagonist in immuno-oncology that's actually with Cancer Research UK. It's actually a Phase 1, Phase 2a study initiation, so it's straight into patients. So we are dosing patients with that compound now and we've got two clinical sites open, a third to come. So, Cancer Research are a fantastic partner in this space. Of course in the UK they are very linked into that network of clinical trials so they're a great partner.

The other one was GPR52 agonists which is a novel orphan GPCR and we think that this could develop into an amazing treatment for schizophrenia. So we are the first company to take a GPR52 agonist into clinical trials and we did that earlier this year. So, we are very proud to do that.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

First-in-class.

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

First-in-class, yes.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Does anybody have any questions? Well I'll ask another about your recent acquisition earlier this year Chris.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Yes, sure. So earlier in the year in July we announced the acquisition of Idorsia pharmaceuticals business in Japan and Korea. As a company that's been listed in Japan, domiciled in Japan is inherently Japanese it had been a bit of a shame that we had not developed significant business over the journey. The acquisition gave us a very, very unique opportunity one that doesn't come up a lot in Japan and that was to acquire a business with a very recently launched and now commercially available drug it's called cerebral vasospasm. It was launched in April last year.

So, it's very much it's very much kicking off, it's doing really well. The real world evidence from neurosurgeons that are using the drug in the ICU has been fantastic. So that drug is saving patient lives daily in Japan and we expect it to continue on a bit of an upward trajectory.

We have a quick follow-on product as well that will come through and that's a drug for chronic insomnia, it's a dual orexin antagonist. And we expect – we filed that actually a couple of weeks ago with the PMDA and we are expecting that to launch hopefully in Q4 next year. And where the Japanese market is a little bit different relative to the rest of the world is the orexin class is actually very, very well supported. It's absolutely growing its share of sleep disorder drugs, Eisai's Dayvigo is going very, very well. And we have a best-in-class position there. So, we expect to capture good market share with our co-promotion partner, Shionogi.

So, we got two we got two drugs that by early 2025 will be on the market and very much in their launch phase which is super exciting. But what was more important for us was the personnel. So, we get a team that is not only very experienced at late-stage development, but also in getting drugs registered, approved and launched. So, we have a modest commercial infrastructure which we will scale up by use of sort of contract sales and external partners.

And as I alluded to earlier in the presentation what we want to be is not only a team that can develop our own assets and take those through to patients in Japan, but be one of the most nimble and agile operators in Japan so that we can make sure we're delivering medicines to Japanese patients that are already available to patients in North America and other parts of the world. And we are already seeing the Japanese regulators loosening their restrictions that they can start to begin to solve drug lag and drug loss by removing things like bridging studies and additional study requirements so we can get drugs to patients faster in Japan. And we're going to be positioned really well to capitalise on that.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

And if you actually move with the regulator, I think, you'll be in a better position than a lot of the Japanese pharma companies that tend to be stuck in their old ways.

<<Chris Cargill, Representative Executive Officer, President and Chief Executive Officer>>

Yes, hopefully. I mean like I said, the benefits of acquiring this particular business that we acquired is it's in a growth phase, it's only 130 full-time employees, it doesn't come with the thousands of employees that you will usual kind of operators in that market would come with. So we very much have an opportunity to grow it, and develop it and scale it the way that we want to build it. And we are not going to be you know stuck with legacy.

<<Stephen Barker, Analyst, Jefferies Japan Limited>>

Great okay we're out of time so gentlemen thanks very much.

<<Matt Barnes, Executive Officer, Executive Vice President, President of Heptares Therapeutics Ltd., and Head of UK R&D>>

Alright, thanks Stephen.