CLOSER LOOK

MEMORANDUM

Zealand 4Q25 – Topline phase 2 results for petrelintide expected in 1Q26; phase 3a petrelintide monotherapy to begin in 2H26; phase 2 petrelintide + CT-388 on track for 1H26 launch – February 19, 2026

Executive Highlights

- **Zealand presented its 4Q25 and full-year results today in a call led by CEO Dr. Adam Steensberg and CMO Dr. David Kendall** – see press release, presentation slides, workbook, annual report, and webcast.
- **Petrelintide (long-acting amylin analog)**, which is co-developed in a $1.65 billion partnership with Roche, continues to be evaluated in phase 2 trials for weight management, with phase 3 trials planned for 2H26. Notably, the phase 2 ZUPREME-1 trial (n=494) for adults with obesity and without diabetes has completed enrollment, with topline results expected in 1Q26. Management cautioned that ZUPREME-1 was not designed to optimize weight loss but instead inform phase 3 design.
  - **A phase 3a trial for petrelintide monotherapy** is expected to begin in 2H26, with outcomes-focused phase 3b programs to follow. Timeline and additional details on the trial design were not disclosed in today's call.
  - **Petrelintide will target tolerability** and a "significantly better treatment experience" to differentiate itself from incretin-based therapies. Management believes amylin-based therapies will ultimately become a larger category than GLP-1 RAs in the obesity market since improved tolerability could lead to greater steady-state prescription volumes.
- **Survodutide (a dual glucagon/GLP-1 RA),** which is developed in partnership with Boehringer Ingelheim, continues to be investigated for obesity and overweight in the phase 3 SYNCHRONIZE program and for MASH in the LIVERAGE program.
  - **The phase 3** SYNCHRONIZE-1 (n=727) and SYNCHRONIZE-2 trials (n=756) for people with overweight or obesity without or with T2D, respectively, are on track to complete in February and April 2026, with topline results expected in 1H26. The phase 3 SYNCHRONIZE-CVOT trial (n=5,531) evaluates long-term CV outcomes in participants with obesity and established CVD/CKD or risk factors for CVD. The study completed enrollment in 1Q25 and is expected to complete in June 2026.
  - **Zealand aims to report data from key phase 3 trials** for obesity in 2026 and expects findings to support survodutide's first regulatory submissions for 2027.
- **Zealand is reactivating the development of its in-house GIP analog (ZP6590)** as a future combination partner with petrelintide to enhance sensitivity and adipose tissue biology, rather than a standalone weight-loss therapy.

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Pipeline Highlights

1. Topline results of phase 2 obesity trial for petrelintide expected in 1Q26; phase 3 launch set for 2H26

Petrelintide, a long-acting amylin analog developed in partnership with Roche, continues to be evaluated in the phase 2 ZUPREME-1 and ZUPREME-2 trials for overweight or obesity with or without T2D, respectively. As background, petrelintide conferred a favorable tolerability profile and weight loss of up to 8.6% compared to 1.7% in the placebo group in phase 1b results (n=48) announced in 3Q24. Roche and Zealand entered a $1.65 billion partnership in March 2025 to co-develop and co-commercialize petrelintide.

- **Topline data for the 42-week ZUPREME-1 trial (n=494)** for people with overweight or obesity and without T2D is expected this quarter (1Q26), consistent with the previously communicated timeline. Full study completion remains expected for March 2026. Among its 2026 objectives, Zealand lists completing and reporting data from ZUPREME-1 as the primary goal of petrelintide.
    - **Ahead of its topline results,** management cautioned that Zealand did not design ZUPREME-1 to optimize the headline weight loss percentage. Instead, management shared that the ZUPREME-1 study design serves to generate a robust data set and inform the phase 3 design.
- **The 28-week ZUPREME-2 trial (n=221) in people with overweight or obesity and T2D** has completed enrollment as of November 2025. Topline data are expected in 2H26.
- **A phase 3a trial for petrelintide monotherapy is planned to start in 2H26,** with phase 3b outcomes-focused (obstructive sleep apnea, osteoarthritis and pain, muscle mass, functional status, women's health, CV outcomes, liver disease, and other metabolic comorbidities) studies expected to follow and expand petrelintide's position beyond weight loss. Given the nature of Roche and Zealand's partnership, management did not disclose further details on phase 3 design or timelines.

Consistent with previous quarters, management expressed confidence in the potential for petrelintide to be a foundational therapy for weight management with a strong efficacy, safety, and tolerability profile. Though petrelintide is expected to achieve a 15-20% body weight reduction in phase 3 studies (compared to up to 24% weight loss with Lilly's retatrutide), management emphasized that Zealand's goal is not to deliver the greatest possible weight loss. Rather, its goal is to target weight loss that a majority of people with overweight or obesity would prefer to enhance long-term adherence.

- **During Q&A,** Dr. Steensberg once again pushed back against what he termed the "Weight Loss Olympics," reiterating that up to ~60% of GLP-1 RA discontinuations in real-world use are driven by GI-related adverse events. He argued that current GLP-1 RA and oral incretin launches do not address this limitation. Transforming weight loss medications from short-term tools into chronic, persistent therapies would unlock greater value in the obesity market.

2. Phase 3 readouts for BI/Zealand's survodutide (dual glucagon/GLP-1 RA) expected in 1H26; first regulatory submissions planned for 2027

Boehringer Ingelheim (BI) and Zealand have partnered on the development of survodutide, a dual glucagon/ GLP-1 RA investigated for obesity and overweight in the phase 3 SYNCHRONIZE program and for MASH in the LIVERAGE program.

As background, in a phase 2 trial, survodutide demonstrated 19% weight loss in people with overweight or obesity after

46 weeks of treatment. Management reaffirmed that topline results of the phase 3 SYNCHRONIZE-1 (n=727) and SYNCHRONIZE-2 trials (n=756) for people with overweight or obesity without or with T2D, respectively, are expected in 1H26. The trials are on track to complete in February and April 2026. The SYNCHRONIZE-CVOT trial (n=5,531) is also active and will evaluate long-term CV outcomes in participants with obesity and established CVD/ CKD or risk factors for CVD. The study completed enrollment in 1Q25 and is expected to complete in June 2026.

- Zealand aims to report data from key phase 3 obesity trials in 2026 and file regulatory submissions in 2027.

Zealand is also evaluating survodutide in phase 3 trials for MASH, with initial readouts expected in 1H26. In a phase 2b trial (n=295) presented at EASL 2024, 65% of participants achieved improvement in fibrosis without the worsening of MASH, compared to 26% receiving placebo. Though different trials cannot be directly compared, management argued in 3Q25 that survodutide has the strongest clinical data compared to the two existing therapies for MASH, Rezdiffra (resmetirom) and Wegovy (semaglutide).

- Of note, survodutide received Fast Track designation by the FDA and PRIME designation by the European Medicines Agency (EMA). In October 2024, survodutide received FDA Breakthrough Therapy Designation for MASH with stages 2 or 3 fibrosis (moderate to advanced fibrosis without cirrhosis).

Survodutide is currently being evaluated in two phase 3 trials for MASH:

- The LIVERAGE (n=1,800) trial of survodutide in MASH with moderate or advanced fibrosis (stage 2 or 3), expected to complete in December 2031; and
- The LIVERAGE-Cirrhosis (n=1,590) trial of survodutide in MASH with compensated cirrhosis (stage 4 fibrosis), expected to complete in June 2029.

Recall that Zealand licensed survodutide to BI. BI holds responsibility for development and commercialization globally. From this partnership, Zealand is eligible to receive up to €315 million (~$367 million) and high-single to low-double-digit percentage royalties on global sales.

3. Zealand to re-activate development of ZP6590 (GIP analog) as a future combination partner for petrelintide

During Q&A, Dr. Kendall confirmed that Zealand is reactivating the development of GIP analog ZP6590 as a combination therapy, rather than a stand-alone weight-loss agent.

ZP6590 was described to improve tolerability and adipose insulin sensitivity, reduce ectopic fat accumulation, and enhance metabolic flexibility at WCIRDC 2025. In today's call, Dr. Kendall highlighted emerging evidence that GIP pharmacology can enhance insulin sensitivity and the effects of amylin and incretin combinations in complex metabolic disease. A first-in-human phase 1 trial is planned for 2026.

Close Concerns' Questions

1. Does Zealand plan to develop ZP6590 as an in-house combination therapy specifically for petrelintide?
2. For petrelintide's phase 3a study design, does Zealand consider its endpoint of weight loss at six months to be sufficient for regulatory approval?
3. Which comorbidities does Zealand aim to explore first in phase 3 trials of petrelintide?

Analyst Q&A

On petrelintide

Q (Mr. Håkon Hemme Bro Jorgensen, Danske Bank): In regard to the upcoming phase 2 readout on petrelintide phase 2, the ZUPREME-1, what level of detail are you able to share with us on the day of the announcement? Apart from the weight loss, would you include the data on petrelintide's tolerability profile in the announcement?

A (Dr. Adam Sinding Steensberg, President & CEO): We can confirm that the data are anticipated this quarter, which

of course means also in the coming weeks. We highly anticipate being able to share the data broadly. We will, as we always do, share topline results that provide a balanced presentation of the data while also reserving data that can be presented at scientific conferences later in the year. You should expect a balanced view which will discuss both topline efficacy and safety tolerability.

Q (Mr. Rajan Sharma, Goldman Sachs International): I wanted to get your latest perspectives on competitive dynamics in the obesity market following the first oral GLP-1 RA launch. You've always been clear on the view that injectables will be the largest segment of the market. Has anything changed given the launch trajectory of Wegovy? And then to add on that, where do you expect the net price to be in obesity by the time petrelintide launches?

A (Dr. Steensberg, President & CEO): Our minds around the orals versus injectable therapies have not changed due to the recent launches. It's very important, and we remain focused on the fact that all GLP-1 RAs that are launching right now do not address what we can see as the biggest issue with the GLP-1 RAs, which is tolerability. As we discussed in the prepared remarks, we have 50% of the patients who stopped taking these medicines are due to adverse events related to their gastrointestinal tract. While we do expect that all options to expand the GLP-1 RA market, we do not think it's actually addressing the main issue around the current therapies that are around. That's why we are so excited about being able to lead in another category, which we think has the potential to provide patients, as David discussed, the weight loss they are looking for with a more pleasant weight loss experience. It's really back to the thing which we have also advocated for a long time. Instead of having such a keen focus on prices, as an industry, we need to move the focus into how we help patients stay on therapy. The key to unlock the value of the obesity market is to make sure that obesity medications are used as chronic therapies rather than event-based weight loss agents. That's why we think petrelintide and the amylin category have the potential to unlock the market value for obesity. When it comes to prices, and which of course has a lot of focus right now in the current competitive environment also with having had compounders around, it's again the same dynamics that we have talked about for a long time and the uniqueness about the obesity market is we have the more classical market where we have payers and insurance companies and then we have the self-paid market and we need to address both. Of course, when you launch with a new category which may provide a much more pleasant weight loss experience, there will be novel dynamics also with regard to pricing. So, while the GLP-1 RA dynamics will affect entrants into that market, we do anticipate that novel themes will play out when you launch novel categories just as we have seen in other therapeutic areas. It's too early to provide any specifics on the net pricing when we launch petrelintide.

Q (Ms. Kirsty Ross-Stewart, BNP Paribas SA): Can you just expand a little bit on the types of opportunities you're hoping to unlock with the broader clinical trial program and how much of the total opportunity do you believe is represented by the monotherapy? Is that kind of the majority part? Is that what we should be thinking as the main part? Or just are you seeing this as a small portion and just the tip of the iceberg? And just related to that, can you remind us on the financial obligations from you and Roche regarding the future Phase 3b development?

A (Dr. Steensberg, President & CEO): I'll start with a few remarks and then hand it over to David. As you know, the focus for the team right now is to accelerate timelines to a potential launch of petrelintide, and in parallel, to invest deeply in making sure that petrelintide will become a foundational and first choice therapy and thus also having the data foundation to support that positioning. And we'll share all costs with our partner, Roche, in those efforts. It's clearly the monotherapy that has our key focus right now. But as David also discussed, the combinations, now starting with CT-388, are also carrying investments as we progress these programs and we would hope to see more combinations really utilizing petrelintide potentially as the foundational therapy. But perhaps David you can comment a little bit more on the Phase 3 considerations and why we have strong belief that it can become a foundational therapy?

A (Dr. David Kendall, EVP & CMO): As noted, the Phase 3b program beyond a rapid acceleration of the phase 3a program to ensure the earliest possible submission and potential approval. You can imagine that the outcomes that matter most to patients and their providers that will be the focus not only of the weight loss studies in phase 3a but focusing on those complications which we know are readily tied to weight reduction such as obstructive sleep apnea, osteoarthritis and osteoarthritis pain. Noting that amylin agonists may have the unique potential to favorably alter bone metabolism and impact pain markers as has already been shown for the GLP-1 agonist reduced weight has its benefits, I mean going beyond that.

Beyond those, I think attention to preserving muscle mass, maintaining functional status, focusing on the population that seeks weight reducing therapies most specifically women and women's health implications. And, finally, a very important impact of those coexistent comorbid conditions are cardiovascular outcomes being primary. Looking at the impact on liver disease and other metabolic dysfunction-associated comorbidities. As Adam noted, the focus initially is on monotherapy, establishing amylin-based therapies and petrelintide in particular as a foundational therapy. But understanding that in complex metabolic diseases such as lipid disorders, hypertension and type 2 diabetes, we have learned that the complexity of these diseases often requires multifaceted approaches to therapy.

Combinations with incretin-based therapies and other modalities are being investigated by us and others, we believe will become the cornerstone of the optimal treatment for obesity and its related conditions. To reemphasize what Adam stated, we plan to promote petrelintide as monotherapy, which we firmly believe can be foundational, but also substantially improve the patient experience will be the focus of phase 3a, with the extension in phase 3b to unlock the full potential of this asset.

A (Ms. Henriette Wennicke, EVP & CFO): And just a comment from me, Kirsty, as well on the financial obligation. Yes, we both share our costs, both on phase 3a but also phase 3b is 50/50 with Roche. As I mentioned in my remarks, we will receive $575 million in connection with the phase 3 indication, and we will also receive $575 million in connection with phase 3b indication from Roche.

Q (Mr. Andy Hsieh, William Blair & Co.): Adam, I appreciate that you're moving the field away from the weight loss Olympics as you coined the phrase. To gauge expectations for ZUPREME-1, semaglutide and tirzepatide showed an additional 2% and 3% weight loss from 42 weeks to study end. Objectively, should we subtract that 2% to 3% from your TPP goal just to account for the timing difference and gender mix for the imminent readout?

And also, a macro question on what Lilly has done recently. They wanted to recategorize retatrutide as a biologic. If they are successful, do you think that that may set a precedent for all the peptides out there, including petrelintide?

A (Dr. Steensberg, President & CEO): When we have designed our ZUPREME-1 study, we have had one key focus and that is to generate the most robust data set to allow us for the most robust decision-making to move into Phase 3. We have not enhanced the study with a disproportional high amount of women or high BMI. We've also decided to look at the data point of being 42 instead of week 48 as others would do and also have the most robust data set for Phase 3 decisions. So, when we then think about what are the weight loss that we anticipate to see and we would expect in that study, these study conditions translate into a 15% to 20% weight loss in a Phase 3 study setup. That's how we will look at the data. And I would say, historically, when you look into male-to-female ratio, if you take a study that is enriched with only females versus males, you could probably expect 5% more weight loss in the female-only cohort.

If you then also enhance the BMI and the study duration, then you will see even higher differences. We are looking for a data set that when we do our internal modeling will allow us to get this 15% to 20% weight loss. The reasons that we approached to end the weight loss Olympics is just the plain fact that patients are not interested. Most patients are not interested in a weight loss above 20%. So why is it that we as an industry and a community keeps talking about those numbers as if they were so important? You can do these surveys among patients, and you will get the same answer across any survey that we have seen thus far and that's why I called for the end. As I also said and as we've discussed also in one of the prior questions, the key to unlock the value in this market is to develop therapies that provides patients with the weight loss they are looking for, and as importantly, therapies that they can stay on instead of therapies where they only take them for three to six months and then stop taking them.

The big dilemma we have with people don't stay on therapy is that most will likely regain the weight and thus never get to the health benefits. Both from a patient and society perspective but also from a company value perspective, the focus has to be on treatments that deliver the weight loss that most patients are looking for, 15% to 20%, and then importantly, medicines they can stay on. That's why I'm calling to end the weight loss Olympics, focus on medicines that deliver what the patients want and you will unlock the value in this market. On your other question, with regard to Lilly's efforts to move from a small molecule designation to a biologic, I'm sure that industry is looking into different ways to enhance you can say the positioning of their drugs. And I will not share our specific efforts to protect the value of our programs. But rest assure that we also have those efforts as key focus.

Q (Mr. Xian Deng, UBS AG): Looking to ZUPREME-1, I'm wondering what sort of profiles would you actually consider as really your target profile in terms of tolerability? Do you think it's actually possible to achieve placebo level similar to placebo level of vomiting and constipation? Any color on that will be great.

Also, a few days ago, Eli Lilly showed some quite interesting data combining tirzepatide and Taltz in psoriasis which actually showed better skin clearance in and Taltz alone. Of course, that's in psoriasis patients that are also obese but I'm wondering if you have any thoughts on that? And would you consider, for example, collaborating with some other autoimmune players on something similar as well in the future?

A (Dr. Steensberg, President & CEO): I'll start by putting some thoughts on your second question and then hand it over to David to follow up and also address your first question. I think maybe you also saw it yesterday, we also announced the Phase 1 data readout with our Kv1.3 ion channel blocker, which is a broad autoimmune anti-inflammatory target which has potential across a number of inflammatory conditions. And thus, we see that as a potential pipeline and a product. There's another notion out there that in relation to the obesity pandemic, you actually see quite significant increases in the prevalence of some chronic autoimmune and inflammatory conditions which had otherwise been seen as being rather stable. So, we see a strong link between the obesity pandemic and the rising prevalence of some of these conditions. And it's clear that – if you may name things like psoriasis or even IBD, there are some strong links with the obesity pandemic. We are highly energized by our own Kv1.3 data and the opportunity to perhaps link metabolism and inflammation in the future. But David, maybe you want to elaborate?

A (Dr. Kendall, EVP & CMO): On the issue of tolerability, noting that tolerability is really a collection of factors, we focus obviously a great deal on the GI adverse events that have been made so central, particularly to incretin-based therapies. While our Phase 1 data to-date have suggested the potential for significantly lower rates of nausea, vomiting and certainly lower rates of the more chronic GI adverse events associated with GLP-1 based therapies, namely diarrhea and constipation. In ZUPREME-1 and subsequent trials, tolerability and the acceptability of the entire experience will be the focus of our evaluation. Looking obviously at GI adverse events but in combination with the injection experience, the experience around dosing and dose escalation. And back to the question that was posed to Adam on orals versus injectable. If one thinks about the currently available therapies and the target product profile for petrelintide, we anticipate that the weekly injection will consume about 10 to 20 seconds of an individual patient's time, which clearly can be associated with the acceptability of a treatment, assuming that injection experience is without reactions, pain and discomfort, which we have seen in our Phase 1 trials to-date. I encourage you and others, as we will be doing, to look at tolerability and acceptability as a collection of these factors; GI adverse events and more. And to Adam's ultimate point, if that experience is highly acceptable to patients, that will further encourage long-term persistence on therapies and particularly therapies that give patients the weight loss they desire.

Q (Ms. Jennifer Jia, Cantor Fitzgerald): I was wondering for the upcoming phase 2b obesity readout for petrelintide. In what way can it differentiate on safety, tolerability versus Lilly's amylin, eloralintide and also for the combo with petrelintide with CT-388? Could you give more context on dosing across the two products, titration schedule as well as how you want to mitigate the GI tox previously seen with CT-388?

A (Dr. Steensberg, President & CEO): We have tried to convey on this call, the most important aspect for us when we review these data is to confirm that we have a product that lives up to the target product profile, which we have discussed a number of times, which is delivering a 15% to 20% weight loss and a more pleasant weight loss experience. If we have that, we will have a leading category and a leading molecule within a new category. I think it's really, really important to also look back at the data that have been generated thus far with petrelintide, which gives us the confidence when we look across the different amylin assets, we have what looks to be the best-in-class amylin analog in development. And that's why we moved towards the Phase 2 data with a higher level of confidence, both with regard to weight loss and tolerability data. But the most important part for us is to get confirmation in this Phase 2 data with what we have seen in the Phase 1 and thus that we are fully on the path to deliver on our target product profile. And thereby, as we have also communicated several times, we think petrelintide and amylin in general has the potential to be a larger category for weight management than the GLP-1s. Because if we allow patients to stay on therapy and you don't have to go out and capture new patients all the time, you will rapidly see the volume of such a category outgrow the volumes of a category where people stop taking medicines early on. So, this is the key focus for us when we look at the data and we move forward based on the prior data experience, which I think we have released to the market. So, you all have the opportunity to look at those data that petrelintide has the potential to be the best-in-class amylin analog of those that are

in the clinic today. The combination product, of course, is also a unique opportunity. And with CT-388, when we did the diligence and the partnership with Roche, our conclusion was that CT-388 looked to be potentially also a best-in-class GLP1/GIP molecule, and we look very much forward to seeing further data from that program. But the combination, when we think about the combination with that molecule, our gut feeling, if you will, will be to max out on the potential of petrelintide and then add a teaspoon of the GLP-1 component to enhance the weight loss experience for those patients that need the highest weight loss. And so we look forward to share more on the study designs. And of course, ultimately the data that comes out of the Phase 2b study for the combination that we will start later this year.

Q (Ms. Kerry Holford, Berenberg): A question from me please just on the planned phase 3a study design. I wonder if you can share any more detail on that? It's clear that the message there is to expect you to accelerate the launch and deal with the CVOT data later. But can you discuss the endpoint, the study time period that you are looking at for the phase 2a study? I mean, for example, could we see a scenario where a six-month weight loss is sufficient to get a first approval for petrelintide?

A (Dr. Steensberg, President & CEO): I think what we can reassure you is that, together with Roche, we are doing everything possible to accelerate and we have identified some very good levers and have a lot of confidence that we can accelerate and push this program as fast as possible forward. We cannot share the details, also the exact details on submission timelines due to the fact that this is a partnership that we need to agree on when to discuss these things. But we are all-on in both organizations to make sure that things are being accelerated towards submission and ultimately announced. What is also important here to note and one of the main reasons that we decided to partner this program at the time we did was of course investments into manufacturing capacity. And we have been extremely pleased to see the announcements that Roche has come out with, with regard to investments into high-volume, high-throughput manufacturing capacity, which of course is needed if you want to secure a successful launch when these products hit the market. And I think that's again, coming back to the uniqueness of the partnership we have here. And the uniqueness of Zealand today is that we are, as I conveyed at our Capital Markets Day, we continue to operate as a biotech company but we will bring in the best from that world. But in the collaboration with Roche, we will also leverage the strength of a pharma company as we approach the market with petrelintide. And I don't think you have seen many of these partnerships, but that is why we keep coming back to the strategic value and of course the profit share we have in this partnership is unique and it's one which we are extremely pleased with to see also how it progresses. We will hopefully soon be able to share more on the exact timelines as we move the program into phase 3. But it's just perhaps one quarterly call too early.

Q (Suzanna van Voorthuizen, Van Lanschot Kempen): Looking beyond the phase 2b readouts that we're all eagerly awaiting and I believe hope that you could provide an alternative to incretins and the product profile you're targeting is very clear. I wonder if you could elaborate for the longer run, based on the knowledge today and the data sets that have been reported for the various amylin assets out there, how do you expect petrelintide to be positioned within the amylin class? What would you expect in terms of differentiation versus the other amylin's later down the line? And maybe one clarification about the research site in Boston. What will this help focus on and how would that complement the capabilities in Copenhagen?

A (Dr. Steensberg, President & CEO): It is too early for us to share our thoughts about the ultimate differentiation between the different amylin analogs. We have been extremely pleased with the data that we have seen thus far when it comes to the balance between weight loss and tolerability and safety findings. Also, when we compare across the different modalities and the different amylin analogs in the clinic today. We see a clear opportunity to continue to develop that differentiation that we have already observed until today. Another key aspect, which I think is important to note as well is as we enter this market, this will be the number one, two and three focus for Zealand to build petrelintide into a leading molecule within the amylin class. Others will have to spend more time thinking about existing franchises and how to protect current molecules that are already on the market. And that's a strength and a force which I don't think people should underestimate. On the research side in Boston, as Utpal shared a little bit on our Capital Markets Day, but it's really going to be a site that will complement what we do in Denmark. In Denmark we are one of the strongest, if not the strongest research group within peptide chemistry. And also having worked in metabolic diseases and health for more than 25 years, have known unique expertise in those areas. In Boston, we will build complementary skills, including focus on high-throughput research labs, machines that are built and labs that are built specifically to tap into the automatization that we are seeing in research these days. And on top of that, we are also going to broaden out the modalities beyond peptides and part of that broadening out will be through partnerships. We just announced one in

December with OTR, which has to do with small molecules, but we expect to announce more partnerships, but we will also build some in-house capabilities so we can become best partners to these opportunities. It's broadening beyond peptide modalities and it's also with a high focus on automatization and high throughput really leading to our firm conviction that we can deliver industry-leading times from idea to the clinic as we build our infrastructure in the coming period.

Q (Ms. Susan Chor, Wells Fargo Securities): A quick question on the ZUPREME-1 dose titration cohorts. Can you speak a little bit more on the rationale behind the timing and the step-up doses that were chosen for the trial? And as a follow up, where do you expect to see the most improvement on the side effects?

A (Dr. Steensberg, President & CEO): The rationale for the dose titration or you could even say that even at titration because you can expect to also see weight loss even at the lower doses. But it's the ability to get to the higher doses. A dosing escalation every four weeks is a practical way to do it. Our phase 1b data suggest that we could do more frequent dose escalation and not compromise the tolerability from a GI side effect profile. It was clean, as you remember, except for one dosing arm where they started at a higher dosing what we do here. It's also about the practical timing for dose escalation. I don't think we have the same issues as you have with the GLP-1s where you need to titrate carefully. And remember, also a lot of patients, you will have to down-titrate when you have decided to titrate up and you have to back off for some weeks and then back off. That's why it becomes so complicated to get the patients to the higher doses of the GLP-1. But we have not seen that with the amylins. In all our titration tests, we have seen patients being able to tolerate the next dose with any significant new adverse events. So, for us, it's more a practical decision rather than something that has to decide on how you have to do it actually from a side effect profile.

On survodutide

Q (Mr. Yi Han Li, Barclays Capital Securities): I wanted to switch gears a little bit to survodutide and also MASH. For MASH, based on our recent KOL checks, the off-label use for MASH appears increasingly common. For example, our physicians will still use survodutide in MASH, even though it is not formally approved by regulators. I'm curious from your market research, are you observing something similar in terms of the physician's behavior? And more broadly, assuming survodutide will be launched in 2027 and you might be more open on this partnership, I'm wondering if there's anything you could share regarding its commercial strategy across obesity and MASH?

A (Dr. Steensberg, President & CEO): It's important to note that it is Boehringer Ingelheim who is solely responsible for the development and the commercialization of survodutide. We will just get the milestones and then high single to low double-digit royalties. The profile that we have seen thus far from the clinical data released by Boehringer of survodutide gives us a lot of confidence in the molecule, both with regard to weight loss but also in MASH. On the weight loss parameters, as we have discussed before we think the weight loss levels and the weight loss experience is going to be quite comparable to what we have seen with some of the market-leading GLP-1s on the market today.

We look forward seeing the phase 3 data. When it comes to the MASH data, the phase 2 MASH data that we have seen and it's also expressed by Boehringer at the time when the data was released, we see them as breakthrough data. These are unprecedented levels of improvement. And I think that's also reflected in the fact that Boehringer have decided to invest in the largest-ever phase 3 program for MASH, not only addressing F2 and F3, but also F4 patients which gives unique opportunities to broaden the potential label if approved beyond into the most severe cases of MASH but also with the scope of the program could provide very early indications of clinical and not just biomarker improvements.

With regard to what you mentioned as off-label use, if I heard you right, of the GLP-1s, I would say please remember that the majority of MASH patients are obese in the first place. And thus, of course, it's a logical choice to use the existing medicines to help patients achieve some weight loss. As many MASH patients suffer from both obesity and other complications than MASH, so that is only a natural consequence. What we believe is that once you have a product that can make a significant larger effect on the disease stages, we should expect to see a very attractive take-up, also exemplified by the enrollment into the phase 3 program and Phase 2 program for survodutide. So, we have a high confidence in the program. We have a high confidence in Boehringer's ability to execute. They are one of the strongest large pharma players in the cardiovascular metabolic space. And we look forward to seeing the data coming out this year, including the cardiovascular outcome data in obesity.

On ZP6590

Q (Mr. Rajan Sharma, Goldman Sachs International): Could you just discuss the rationale for restarting development of a GIP analog? Firstly, just to clarify, is this the same asset which you previously de-prioritized? And then just in terms of strategy here, do you expect to see monotherapy activity or is this really a combination asset for the future? And how should we think about that in the context of CT-388, which is a GLP-1/GIP co-agonist?

A (Dr. Kendall, EVP & CMO): This is the asset that has been part of our pipeline all along. And as you have likely noted, I mean the interest in leveraging GIP pharmacology, while it is still in its infancy, both with the development of tirzepatide and other GLP-1/GIP molecule, the recent announcement of Novo looking at combinations with an amylin analog. Our understanding, as we've stated all along, that combination therapies can ultimately be leveraged to target this complex metabolic set of disorders, obesity and beyond. And while GIP monotherapy has been reported by others, may not in and of itself have potent weight-reducing effects and the potential to further improve insulin action or insulin sensitivity, the ability to unlock even greater effect of other molecules, including amylin analogs, other incretin hormones and other peptide signals is becoming clearer. And for us this is yet another venture into potential for combination approaches to targeting these complex metabolic diseases. And again, our commitment to improving metabolic health overall goes beyond, as Adam said, simply reducing body weight, simply targeting MASH to improving things like insulin action, targeting specific aspects of fat cells or adipocyte behavior, and using this pharmacology to really target multiple tissues, multiple organs and further enhance the effect of other peptide and non-peptide signals. Starting with the first-in-human to ensure understanding of the PK and safety and tolerability, and then we hope to rapidly advance into assessment of unique combinations with amylin assets and other signals.

-- *by Elizabeth Rose, Kat Moon, Monica Oxenreiter, and Kelly Close*