

Lundbeck A/S
First Half 2023 Report
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Transcript

Speakers:

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Welcome, everybody, to the First Half Report for Lundbeck. Thank you for dialling in. It's going to be a good conversation. May I have the next slide, please? You've seen our forward-looking statements many times before, so I won't go over them in detail, I'm sure you'll be glad to know.

The first half for Lundbeck has been an outstanding performance across all of our business. We have broken records in revenue, achieving the highest first half revenue for Lundbeck ever in its history, achieving approximately DKK 10 billion, with a reported growth rate of 13%, 10% in constant currencies.

I know there's a lot of focus on Vyepti, and I'm very proud of the growth rate of Vyepti at 91% in constant currency. And of course, that's on the back of the US and the global roll-out, and you'll hear more about that from Jacob and Tom, who are with us to talk to you about that. Also, the strategic brands generally, across the world, have performed extremely well and achieved DKK 6.6 billion, which are now 66% of the total revenue for Lundbeck. In aggregate, the strategic brands grew 18%.

We're also going to be talking to you about promising early uptake with the launches of Rexulti in agitation in Alzheimer's disease or agitation associated with dementia in Alzheimer's disease, I should say, given that is our FDA label, and, of course, Abilify Asimtufii, the two-monthly version of aripiprazole long-acting.

The profit has also grown commensurately with the EBIT margin reaching 33.4%. We do know that there is lower planned spending in the first half than the second half for a variety of reasons that we'll talk about.

The pipeline has delivered very strongly in the first half of this year. Of course, the approvals are the biggest milestones, and we were delighted to achieve the priority review approval of Rexulti in agitation in May on time and, of course, Abilify Asimtufii being approved at the end of April. Those launches went into effect late May and early June.

Johan will be taking you through the results of the DELIVER trial, the long-term follow-up of that trial, which confirms the efficacy of Vyepti over a longer period of time. And of course, we were very, very excited to announce the proof-of-concept achieved in the new mechanism of action in migraine prevention with our anti-PACAP. Next slide, please.

You'll see here that all regions are growing strongly, and the

strategic brands in all regions are growing strongly. And that's, of course, the engine that is going to be driving Lundbeck forward to steady growth in the coming years. On the right-hand side, you can see which regions are growing from which brands, because it is a mix. Next slide, please.

Let's talk more about Vyepti. We've got very strong momentum for Vyepti, with strong demand in the US. And we can see that demand on a continuing growth curve, with a 78% growth in constant exchange rates, first half of 23 versus first half of 22.

Now, there are a number of factors underlying that growth. We've fuelled it with new patient starts. And that's coming from those physicians who've prescribed Vyepti before and who are prescribing more of it, because it's working well for their patients, and adding new prescribers. So that's a very good construct to be able to see for the future growth prospects of Vyepti. The number of prescribers has increased significantly.

The DELIVER trial we'll talk about more. That was presented at the American Headache Society. And so we continue to expect strong growth in the second half of 23. The market share now has reached 7% in the first half, looking at the US migraine prevention market, or at least the branded market of the CGRPs and the gepants. Next slide, please.

Vyepti is becoming a global brand, and we're seeing more and more countries launching. So all told, Vyepti's global revenue is up 91%. When we look externally, of course, it's off a small base, but we've got incredible growth coming for Vyepti with the global roll-out extending. We've launched seven markets already in 2023, and nine more launches are expected in the second half, and we're seeing really good uptake.

If you look at the left-hand curve, we can see strong market penetration in a number of markets, UAE, over 14% market share in the prevention market, the branded prevention market in the 21st month, Switzerland close to 13% in its 13th month, and Canada in its seventh month at 11.6%. Germany is very early, but we're looking very favourably upon the growth in Germany.

So I'd like to remind you that this is the first global brand that Lundbeck has launched independently, so it's always exciting to see not only the US growing strongly but the global markets contributing to the growth of Vyepti. Next slide, please.

Brintellix/Trintellix is on a great growth trajectory. The principal contributors here are, of course, continued growth in Japan, a really great market share together with our partner, Takeda, but Europe has been a stand-out, with extremely strong growth as we've seen the market shift. There's more GP prescribing, but we've had a slightly increased footprint over the last few years as we've experimented with promoting to GPs. And that has paid off and has driven strong uptake within Europe.

In the US, Trintellix has grown a little slower. First of all, the market has fragmented more. There's a lot more nurse practitioners, physician assistants, GPs prescribing in the MDD segment than there were before COVID. We do have a well aligned sales force with Takeda, and we are working strongly together, focusing on the efficacy of Trintellix both through our sales force channel and the omnichannel approach to our customers. So we are seeing new-to-brand prescriptions growing in Q2 versus Q1 of 2023.

And I'd remind you that during 2022, we did experience some disruption in promotion on this brand as we, together with Takeda, resized the sales force. Takeda was experiencing a loss of exclusivity on Vyvanse, and so both of us reduced the total number of reps that are promoting, but increased the profitability of this brand. Next slide, please.

Rexulti has been a tremendous performer for us in the first half. The US obviously has been the biggest market for a long time, given the approval in both schizophrenia and MDD, which we also have in Canada. We've seen that MDD growth, and we've talked about it in prior quarters continuing in the US, in Canada and Brazil, but we are seeing some green shoots from the launch of Rexulti in agitation.

The first, let's say, green shoot coming up in the Spring is an increased utilisation that we're seeing in the 65-year-old and older patient group. And we don't get fully claims data until... There is a lag in us getting that data. So this is the data that we have on hand to date.

We're also getting significantly interested prescribers and some prescribers who've already used Rexulti reporting that they're seeing a tremendous change to the positive for their patients and the caregivers. So we're very encouraged about how this launch is progressing. The unbranded DTC was launched in the second quarter. The branded DTC campaign will launch in the Fall, once approved through the FDA. Next slide, please.

Abilify Asimtufii is launched in the US, and the overall

franchise for Abilify Maintena and Abilify Asimtufii has grown strongly, and it's grown in all regions. The LAI market growth has continued, but we are penetrating that market with Abilify Maintena. And you see a good growth in all our regions of the world.

Asimtufii was really put into the market in June of 23, so we're very early in the process of that launch. But we can already see that having that franchise together is lifting the overall aripiprazole long-acting business for us in the United States. I think, with that, I'm going to be handing over to the first of my colleagues that's here with me today, Johan Lutman, our Head of R&D. So you take it away, Johan.

Johan Lutman

Thank you very much, Deborah. So let's take a look at the further information on R&D. So during the first half of 23, in particular during the second quarter, we had a rich flow of important positive R&D events. So it has indeed been a very productive year so far.

As Deborah already mentioned in her introductory comments, we had two approvals with FDA in the first half year, both of those together with our partner, Otsuka. The one I'd like to start with is the May 10 approval of the sNDA for Rexulti for the treatment of agitation associated with dementia due to Alzheimer's disease, for short, AADAD. This approval was preceded by a very supportive FDA external expert advisory committee discussion on April 14.

This approval constitutes a critical milestone, since it's 20 years since FDA last time granted a full approval of any NMA for the treatment of Alzheimer's disease. Moreover, this is the first-ever approved treatment for agitation associated with dementia, and, in fact, for any behavioural psychological symptoms of dementia. So an FDA-approved treatment of agitation is a very important addition to the care of this devastating disease, in particular since agitation is one of the most bothersome symptoms for patients to cope with and not in the least their caregivers.

In addition to the US, we have ongoing regulatory authority reviews of brexpiprazole for the treatment of agitation in dementia due to Alzheimer's disease in Canada, with the SNDS review with Health Canada expected to be concluded by the first quarter 24. Submissions have also been done in Singapore, Australia and Switzerland through the so-called Access Consortium process. Approvals in those three countries is anticipated during mid-24.

The second approval we had during the Spring was on April 27 for aripiprazole two-month ready-to-use long-acting injectable suspension for intramuscular administration. As

you heard, it is now marketed in the US under the name of Abilify Asimtufii for the treatment of schizophrenia in adults, for maintenance monotherapy treatment of bipolar, for the... Sorry. For the treatment of schizophrenia in adults or for the maintenance monotherapy treatment of bipolar I disorder in adults, thus the same population as for Abilify Maintena.

The basis for that approval was a large and robust 32-week pharmacokinetic bridging study, while the efficacy of this product builds on adequate and well-controlled studies of Abilify Maintena. As previously reported, this new extended-release formulation aripiprazole has also been submitted to EMA for the indication of maintenance treatment of adult schizophrenia patients.

The MAA review is progressing in Europe following a resubmission which allows CHMP to follow what they consider more appropriate regulatory procedure. We have a current estimate for H1, first half of the year 24, for finalisation of that review. The SNDS review of this product submitted to Health Canada is ongoing, but with an extended review period. The product has also been submitted in Australia and Korea.

The other major event during the first half of 23, as Deborah mentioned in the introduction also, was the announcement on April 19 that we had a very encouraging positive read-out of the first-in-class anti-PACAP monoclonal antibody, 222, in the HOPE trial in migraine prevention. I will get back to that in more detail. However, the next step for this exciting programme is to progress to a Phase IIb trial in order to better establish dose range and route of administration.

Finally, I'd like to highlight that we had released the new data on Vyepti from the DELIVER trial. The data further demonstrates not only the powerful action of the treatment of Vyepti, but also very nicely confirms its long-lasting migraine-preventive effects. So let's take some further look at that data. Next slide, please.

The Phase IIIb DELIVER trial was evaluating the safety and efficacy of Vyepti in hard-to-treat patients with two to four previous treatment failures. The trial included an open-label extension phase. The patients had chronic or episodic migraine.

We had previously reported the placebo-controlled part of the trial, which showed a robust effect of the drug in patients that had been on other migraine-prevention treatments. Now, the open-label extension phase of the trial confirms the long-lasting migraine-preventive effects of Vyepti and an excellent tolerability profile.

As you can see on the graph to the left, at the time of switching all patients to active treatment, the time point as you see here indicated by a dotted line, there is a clear and rapid onset of the therapeutic effect on the number of migraine days in patients previously treated with placebo.

This is followed by clear-cut therapeutic effects throughout the Vyepti treatment period, up to 18 months. In addition, the treatment during the open-label part of the DELIVER trial also reduced severity of headaches and reduced the use of acute medication. Next slide, please.

Naturally, we are very pleased with the performance of Vyepti as a fast onset-of-action migraine-prevention treatment and how well it works in patients that have failed to respond well to previous treatments. However, with the results from the HOPE trial with our first-in-class anti-PACAP monoclonal antibody, 222, we are looking forward to further build our efforts to deliver therapies for patients suffering from migraine that do not always find therapies that work well for them.

It's not often in R&D that I get a chance to be part of the positive proof-of-concept read-out, but the robust read-out in the HOPE Phase IIa trial is indeed a breakthrough for a new mechanism of action. 222 is a humanised IgG1 antibody against the receptor ligand, PACAP, which is known to act through at least three different receptors.

The PACAP biology is quite broad. Thus, this programme certainly adds an opportunity for Lundbeck to further expand not only our migraine franchise but also may lead to us to contemplate the molecule's potential in other pain indications.

The HOPE trial studied prevention of episodic and chronic migraine patients not helped by two to four prior treatments, so quite similar to the DELIVER trial in design. The patients received IV infusion of low and high doses in a 12-week trial.

The primary read-out, which measures number of migraine days at four weeks, showed clear statistical separation against placebo. Both doses tested appear to work. The secondary endpoints were also supportive. 222 was also well tolerated. The HOPE trial data will be presented at the International Headache Congress in mid-September, so we'll have the possibility to see more from this trial very soon.

The path toward the HOPE trial was facilitated by early experimental medicine studies characterising the target engagement in humans of 222. Moreover, we have

previously shown good pharmacokinetic properties of 222 when given subcutaneously. So we have the potential optionality in terms of route of administration.

A Phase IIb study is currently being designed and planned to start in early 24. The aims of this upcoming trial is to establish subcutaneous efficacy and further explore optimal dose range. Next slide, please.

In this call, I'd also like to highlight two programmes in Phase I that are progressing well towards the possibility to initiate Phase II proof-of-concept trials in the coming year. First, some words about our differentiated CD40 ligand antibody-like drug candidate, 515.

The role of CD40 ligand is well documented and it's assumed to play a key role in auto-immune diseases in which activated T and B cells cause pathology. The CD40-CD40 ligand interactions mediate T-cell priming and T-cell dependent B-cell responses and promote proinflammatory activities. By blocking the CD40 ligand and its interactions with CD40 and the co-stimulatory signalling, you can block the downstream effects on immune cells.

Our drug candidate, 515, is a recombinant, bispecific fusion protein that is not only binding to the CD40 ligand but also the human serum albumin through the so-called SAFA technology platform. 515 aims to provide a long half-life and is expected to show an improved safety profile due to the albumin binding.

The clinical development programme for 515 was initiated in March 22 and is progressing swiftly throughout the target engagement and dose escalation studies. Phase II is expected to commence in 24, where we will explore several potential neuroimmune indications. So we're really excited to bring forward this differentiated CD40 ligand binding. Next slide, please.

I'd also like to talk a bit more about our D1/D2 agonist programme in Parkinson's disease. It's a legacy programme from our strong background in monoamine neuropharmacology. The new chemical entity, 996, is an innovative, orally available product for the generation of a broad-acting D1/D2 receptor agonist.

Through this mechanism of action, we aim to provide continuous dopamine receptor stimulation. This is expected not only to lead to improved efficacy on reduction of off-time in comparison to other D2 agonists, but also improve tolerability against L-DOPA, and obviously substantially improve convenience compared to pump administration of

the D1/D2 agonist, apomorphine.

996 is progressing very well, and it's concluding its Phase I this year, with a solid data set that includes regular healthy volunteer studies but also an open-label experimental medicine investigation of its profile in patients with Parkinson's disease. We are planning to commence Phase II trials next year with 996. Yes, next slide, please.

Regarding other pipeline programmes, I'd just like to remind you that I have previously announced that we finalised the recruitment into the two trials, '71 and '72, that are exploring the efficacy and safety of brexpiprazole in combination with sertraline in post-traumatic stress disorder. We're therefore looking forward to obtaining the data from the evaluation of the PTSD indication within this ongoing quarter.

So you hear that we are expecting to progress well also in the second half of the year, with several interesting programmes. This is naturally facilitated by our transformed R&D organisation. We have now a strong presence in our four biological clusters. We're also fully employing experimental medicine studies, supported by biomarker-driven clinical read-outs for stringent go/no go decisions and early de-risking.

Obviously, we are very happy that we have this year already been able to deliver on several critical late-stage lifecycle management programmes, such as Abilify Asimtufii and brexpiprazole in a new, impactful indication for Alzheimer's disease patients. But we are also, importantly, advancing very well in the further build-up of our mid-stage pipeline, with the potential to move two to three assets into Phase II during 24. With that, I'd like to hand over to Joerg.

Joerg Hornstein

Thank you, Johan. We have new microphones. Thank you, Johan. We continued to deliver an excellent performance, with the strongest first-six-months' revenue Lundbeck has ever delivered. The plus 13% of reported revenue growth is driven by a growth of 10% in constant exchange rates coming from the strong underlying performance of all of our strategic brands. The positive FX effect is driven predominantly by the increase of the US Dollar, the positive contribution from hedging due to a narrowing of hedging rates versus actual rates year over year.

Our gross margin is 1.3 percentage points lower compared to 2022, negatively impacted by the additional amortisation of product rights related to the EU approval of Vyepti as well as by the provision for Vyepti inventory obsolescence of 245 million recognised in the first half of 2023.

For that reason, it is much more insightful to look at the development in our adjusted gross margin. Adjusting for the aforementioned provision and the amortisation and depreciation linked to sales, the adjusted gross margin in the first half of 2023 is higher by two percentage points, reflecting the positive sales volume development.

Sales and distribution costs grew plus 14% at constant exchange rates. The increase is driven by higher Vyepti sales activity in the US along with its global roll-out in approximately 15 countries this year, as well as costs for the launch preparation of Rexulti AADAD.

R&D costs declined by minus 14% at constant exchange rates, mainly impacted by the planned lower late development and reduced pace for activity for Rexulti and Brintellix/Trintellix so far in 2023 compared to 2022. All of these effects contributed to an EBITDA growth of plus 19% at constant exchange rates.

Our adjusted EBITDA that eliminates the provision for Vyepti inventory obsolescence actually grew by plus 32%, improving the margin by 7.5 percentage points to 33.4% compared to last year. Please bear in mind that approximately three percentage points of the margin improvement relates to the lower R&D costs, as expected. Next slide, please.

Our EBIT grew by plus 38% in reported rates, reflecting the high revenue growth and strong operating leverage, improving our margin by plus 3.9 percentage points. Our net financial expenses decreased for the first half to DKK 138 million. The lower expenses are mainly driven by the non-recurring DKK 278 million fair value adjustment of the CVR to Alder shareholders in Q1 last year, triggered by the Vyepti EMA approval and, of course, lower debt levels. These are partially offset by higher foreign currency exchange effects.

The effective tax rate has increased to 23.5% compared to last year's 22%, in line with full-year expectation, reflecting the reduced deduction from the Danish R&D incentive. Net profit increased by plus 61%, DKK 1.5 billion, and adjusted net profit increased by plus 36% to DKK 2.5 billion.

The adjusted EPS growth is in line with the underlying performance, after adjustments relating primarily to the amortisation of product rights and the fair value adjustment of CVR to former Alder shareholders in Q1 2022. Next slide, please.

The cash flows from operating activities landed at an inflow of DKK 1.6 billion in the first half of 23 compared to an inflow

of DKK 711 million last year. The operating cash flow is, of course, a reflection of the strong EBIT performance, further benefited by higher adjustments for non-cash items of DKK 1.4 billion, which is driven by higher amortisation in 2023 and the provision for Vyepti inventory obsolescence, but negatively impacted by higher change in working capital of DKK 1.5 billion.

This was mainly driven by increased receivables, driven by higher sales, and increased inventory, primarily driven by Vyepti inventory build-up due to the fixed-term agreement that expired mid-year 2023, partially offset by changes in short-term liabilities.

The cash flow from investing activities were an outflow of DKK 265 million, driven by paid-out sales milestones. Just for your reference, the first six months of 22, in comparison, included an outflow of DKK 1.2 billion for the CVR payment to Alder shareholders.

The cash flow from financing activities were an outflow of DKK 1.3 billion in the first half compared to an inflow of DKK 480 million in the same period last year. This is primarily driven by the continued repayment in 23 of the last part of the 2022 loan, connected to the CVR payment to Alder shareholders, and, of course, the higher dividend payment in 23, connected to the improved net results in 2022.

Our net debt position continues to develop very favourably and lands at DKK 1.4 billion in the first half of 2023 compared to DKK 4.3 billion, the same period last year, reducing the leverage to 0.3 for the rolling four quarters, continuing our progress of deleveraging the company. Next slide, please.

Lundbeck raises its full-year guidance on revenue to DKK 19.5 billion to DKK 20.1 billion while at the same time increasing the adjusted EBITDA to DKK 5.2 billion to DKK 5.6 billion. The raised guidance is reflecting the strong momentum of our strategic brands, which is expected to continue in the second half, despite the continued erosion of the mature brands. We expect current exchange rate level as a positive hedging effect of approximately DKK 135 million due to more favourable hedging rates in the second half.

We have some timing effects in the first half of this year from which the mature brands benefited. However, we see especially around Cipralex, Lexapro in Japan, Deanxit in China and Sabril in the US a bit more of a faster erosion in the second half of this year.

From a profit perspective, let me reiterate the following. The forecast of amortisation of product rights remains unchanged at approximately DKK 1.6 billion for the full year. The expectations on sales and distribution costs reflect the necessary investments in the important launches of Vyepti in approximately eight additional markets, Rexulti for AADAD and the Abilify LAI franchise.

R&D full-year costs are expected to be broadly stable, considering higher investments in the second half of 2023, mostly to develop clinical material ahead of planned initiation of clinical studies. Finally, as previously mentioned, the provision of approximately DKK 300 million of Vyepti inventory obsolescence is reflected in the guidance for 2023. With that, I hand over to Deborah.

Deborah Dunsire

Thank you, Joerg. It's great to be able to report such strong momentum in the business. So we have made progress maximising our strategic brands. Those four brands grew, in aggregate, 18%, and it's great to see momentum across the world and across the brands. The Vyepti global roll-out is on track, with nine more markets to come in the second half of this year, and we're looking forward to the momentum building in those recent launches in the US.

I think it's fair to say that R&D has had the most productive first half in, I'm sure, Lundbeck's history, and we look forward to the PTSD results coming in the balance of the third quarter 2023. We've made good progress with a very high-potential, early development portfolio, rebuilding the Phase II pipeline, and potentially more molecules entering that in 2024, but also some very interesting additions to the Phase I portfolio coming in. And that is coming out of the transformed and highly innovative research portfolio.

We've seen an improved profitability in the first half. But as Joerg has said, we do expect higher spending in the second half, given that we have the full load of the launches, the costs coming in the second half, and we anticipate the startup costs for some of our Phase I and II trials, notably the preparation of the monoclonal antibodies, to make R&D costs higher in the second half than the first, given that we finished a large number of Phase III clinical trials during the first half of 2023.

We have been able to raise the financial guidance, given the strong momentum in the strategic brands, in spite of some headwinds on some of the mature brands in the second half of the year. So Lundbeck is extremely well positioned to deliver sustainable, profitable growth for some years into the future. And so it is with great pride that I look back at the five

years that I've had with Lundbeck.

As you know, next slide, please, we have announced that I will be leaving Lundbeck at the end of August. Charl van Zyl will join us as of 1 September, 2023. He brings a lot of experience in the neurosciences from various experiences within the industry, most recently at UCB. And of course, he has to be good, because he's South African.

So, with that, I am going to bring this to a close. A great, great first half for Lundbeck in 2023. So now, we'll open the floor to questions. And in addition to Johan and Joerg being with us, we also have Jacob Tolstrup, who you know very well, and Tom Gibbs from the US, who you're getting to know very well, who I'm sure you will have many questions for. So, with that, let's have the first question.

Operator

Ladies and gentlemen, at this time, we will begin the question and answer session. Anyone who wishes to ask a question may press star followed by one on their touchtone telephone. If you wish to remove yourself from the question queue, you may press star and two. If you are using speaker equipment today, please lift the handset before making your selections. Anyone who has a question may press star and one at this time. Our first question comes from Michael Novod from Nordea. Please go ahead.

Michael Novod

Thank you very much. Michael Novod from Nordea. Two questions, please, two in opposite directions. First of all, on Trintellix. So it's sort of a never-ending story around continued sluggish sales performance. And still, you're trying to do whatever it takes to ramp up your efforts with Takeda and the reorg on the sales force, etc. How should we be thinking about this in the next two years to three years? Is it just that it's at best flat, or perhaps even gradually declining in the US?

And then on the other side, with regards to Rexulti in Alzheimer's agitation. So I recall you've been saying something like \$500 million to \$800 million in aligned sales, or up to \$1 billion, but your partner is saying significantly high numbers, if you calculate on their assumptions for penetration rates in AAD in the US. So are you willing to give a bit more flavour to how you see Rexulti in AAD develop over the next five-six years? Thank you very much.

Deborah Dunsire

Thank you, Michael. Tom, would you like to start on Trintellix?

Thomas Gibbs

Sure. Deborah. Thank you, and thank you for the question, Michael. As you saw, the top line number was a 7% decline during the first half of 2023 versus first half of 2022.

However, I think it's important to recognise that there is some noise in the revenue line, with some gross-to-net adjustments that did occur. So what I'd like to do is focus on demand, which I believe is the most important element to understand brand performance. And demand for the first half of 2023 did decline by 3% versus the previous year.

As Deborah had stated, and I think it's important to put into context, back in the first half of 2022, our alliance partner, Takeda, who is responsible for 80% of the promotion for Trintellix, did downsize their sales and marketing investment in Trintellix in response to the Vyvanse going off patent. And this was with the goal of increasing profitability for Trintellix.

Lundbeck also adjusted the promotional levels of our sales and marketing efforts to reflect the revised sales and marketing investments of our partner. These type of adjustments, as we've talked about previously, do cause some disruptions, especially when you're looking at it through the lens of our customer-facing model.

As Deborah had stated, the strategic choice did achieve the intended objective of increasing profitability of the brand, but however, and not surprising, this strategic choice has created some pressure on the top line demand, which you normally see, for a late lifecycle product, emerging at six months to 12 months. And that's what we're seeing now.

As we talked about, Lundbeck is working very, very closely now with our partner, Takeda, to ensure that we have our rebased resources optimally deployed, from a sales point of view, from an omnichannel point of view, to reignite growth from these levels. And we're starting to see some positive signs, albeit early, when we look at first quarter 2023 to second quarter 2023, where we did see an increase in both TRxs and NBRxs.

Deborah Dunsire

Thanks, Tom. And then on Rexulti, what we have said is that we believe that across the alliance, gross sales of this product in this indication will achieve over \$1 billion. So we see this as an immense opportunity for the brand. We're investing as a big opportunity, and we intend to grow it as far as possible.

Can it be bigger than that? Possibly. This is a very high unmet medical need, and we certainly will do all that we can to grow the market. And maybe, Tom, I'll hand over to you to talk about how we're thinking about that growth, and how things are going.

Thomas Gibbs

Yes. Thank you, Deborah. And I think if we look at it based upon the work that we did pre-launch to understand the

market, and our experience in the market since approval, we believe that there is a substantial unmet need that exists within the AAD market. And we are aligned with Otsuka that there is a significant opportunity for this brand with AADAD.

Additionally, Lundbeck, along with Otsuka, are committed to investing the necessary resources to maximise this opportunity. And when we think about our first priority to be able to deliver on this opportunity, it's really about driving market penetration of Rexulti in the current diagnosed and treated patient population for AADAD.

And this is going to take significant efforts, as we've talked about, in terms of raising awareness and appreciation from both physicians as well as caregivers about the prevalence, the disability associated with this disease, and most importantly now, that there's an FDA-approved agent to treat this debilitating disease.

Deborah Dunsire

Thanks, Tom, and thanks, Michael. Next question.

Michael Novod

Thank you.

Operator

The next question comes from James Gordon from JP Morgan. Please go ahead.

James Gordon

Hello. James Gordon, JP Morgan. Thanks for taking my two questions. First question was R&D spend, and maybe one for Joerg. So you reiterated the guidance for broadly stable R&D in 2023, but I noticed R&D was down 14% in H1. And I heard the comment about preparing some antibody trial material for Phase II, but that seems like a lot to seek for R&D just to be stable.

So can you break out, how much extra spend is there going to be on preparing trial material in H2? And could it be the guidance is also including room for you to do some in-licensing and spend a lot more on R&D and projects that you don't yet have? So the first question, if you could help us better understand where this extra R&D is going to come from in the second half, please.

And then the second question for Deborah. As you retire from Lundbeck, thanks for humouring all my questions over the last few years. My question is, you've given a guidance for strong medium-term performance in the company, but how are you seeing the company position longer term, so beyond the next three or four years? Do you think the growth can be maintained, or should we be thinking of a significant slowdown? And what do you think the key challenges are going to be for Charl, please?

Deborah Dunsire

Okay. Thanks, James. I'm going to hand over to Joerg first.

Joerg Hornstein

Thank you, Deborah. Well, I think we don't break out specifically what is the CMC element out of clinical trials. But I think if you go back to the presentation from Johan, we talk about a very promising pipeline, with a number of projects that basically we bring forward. So you talk, in the end of the day, on starting of trials as well as starting on clinical materials.

Plus, on top, don't only think that investment is tied to clinical trials and CMC. You also have ongoing significant trials that also have quite some milestones to achieve in the second half of the year, especially around our Vyepti in Asia programme.

Deborah Dunsire

Great. Thanks, Joerg. James, Thank you for the question. You always have entertaining questions, and this is a good one. Lundbeck is well positioned as we go forward with these four strategic brands, and we are going to be growing mid-single digits through the middle of the decade. And we have a pipeline now that is building to bring in a number of opportunities that have multi-indication potential. So from within our own pipeline, we would see, towards the end of the decade, some of those coming into play.

We have always said that our business will be built in both internal and continued external licenses, partnerships or M&A, and with a preference for the bolt-on M&A. And nothing has changed about that. I think what you've seen over the years at Lundbeck, before I arrived and since I arrived, is that the management, working together, have been very successful in bringing in good assets through the years.

From the Ovation acquisition, the Chelsea acquisition, the Otsuka partnership, there's a number of successes. We've had, I believe, a great success with the Alder acquisition. Of course, that's still growing and adding to our portfolio. So the future will, in some ways, be that of the past, that our business will build from the inside and the outside, which the company has successfully done over many years. So I would say bet on Lundbeck to continue growing. Next question, please.

Operator

The next question comes from Marc Goodman from Leerink. Please go ahead.

Marc Goodman

Hi. First up, can you give us an update on 909 and how you see that product differentiated versus some of the competition? It's a little bit ahead. And then can you just give us a little more colour on the agitation indication and just the confidence that you're actually seeing some uptick because of that indication? You mentioned something about some

data that you had. I was wondering if you can go into a little more detail on it. Thank you.

Deborah Dunsire Sorry, you were a little hard to hear there, Marc, but I'm going to ask Tom to start on the agitation question. Did you hear it adequately, Tom?

Thomas Gibbs Yes.

Deborah Dunsire And then Johan...

Marc Goodman Yes, the agitation question...

Deborah Dunsire Can comment on the pipeline assets.

Marc Goodman Yes, the agitation question was how we know that we're seeing...

Thomas Gibbs Thanks for the question, Marc. As we all know, it's still very early in the launch. But I would say that the launch is progressing as we expected. And I'll first speak from a quantitative perspective. As I stated during the last earnings call, the best data that we have to look at until the claims data become available is the 65-plus weekly TRx data, which Deborah spoke about during her presentation. These data suggest there's a meaningful uptick in this segment, which is having, in my view, a positive impact on the overall brand performance.

And I think as you probably have seen, for the week ending July 21, Rexulti achieved its highest record to date TRx share, highest NRx share, and we also achieved our highest recorded new-to-brand prescriptions. So all very positive signs, both from the 65-plus, but also, more importantly, on the overall brand performance.

And then I think, from a qualitative perspective, our experience to date is that it confirms that the AADAD market is a large opportunity, with significant unmet need. However, and we've talked about this, it's also a nascent market that's going to require developing this market, both from Lundbeck and also with our partner, Otsuka. And we are committed to making those necessary investments to make this a truly substantial opportunity for Lundbeck and Rexulti.

Deborah Dunsire Thanks, Tom. Over to you, Johan.

Johan Luthman Yes, I believe you asked about 909. Can you confirm that? Yes? Okay.

Marc Goodman Yes, correct.

Johan Lutman So that's the programme I didn't talk about in this presentation today. That's the anti-ACTH antibody that we got through the Alder acquisition. And we've taken that into

phase Ib. It's being evaluated in congenital adrenal hyperplasia patients right now, and we are progressing well with the dose panels there.

It's a really exciting programme. I couldn't talk about everything we do in Phase I. It's a little behind the ones I talked about that are more closer to Phase II starts, but it's not so substantially behind, because this is obviously a mechanism going for the so-called HPA axis and going for hormonal modulation. So we go quite quickly into patient studies, and expanding patient studies. What we've seen so far in the very early, early data we obtained are actually very promising findings. So it looks like it's very much a molecule that is alive.

Deborah Dunsire

Thanks, Johan. Next question, please.

Operator

The next question comes from Dominic Lunn from Credit Suisse. Please go ahead.

Dominic Lunn

Hi. Thank you. So following on from the earlier question on costs. So clearly, the adjusted EBITDA at 2Q was much better than the market expected, and guidance was raised only modestly. So that implies a step-up of costs into the second half.

So would it be fair to assume that the second half cost level is a good proxy for next year, given you'll still be needing to support the launches and fund R&D? And then could you also provide an update on the timing of the transition to the lower-cost cell line for Vyepti production?

And then, secondly, on the overall Abilify franchise. So there are a number of moving parts, looking forward. So we'll see the tumour formulation ramping up, the European LoE for the Maintena version kicking in from mid-25, and then US LoE potentially after that.

So how could we think about the sales profile for the rest of the decade, given the moving parts, i.e., can we expect continued year-on-year growth for the franchise, or should we factor in some erosion in the latter part of the decade from the generics? Thank you.

Deborah Dunsire

Great. Joerg, would you comment on the cost profile?

Joerg Hornstein

Yes, absolutely. I think you had a couple of questions. I think the first one was why is the adjusted EBITDA in the first half better than consensus, and probably growing a bit stronger than EBIT? First of all, keep in mind, we have booked DKK 245 million of inventory obsolescence. We originally guided towards more than DKK 200 million for the first two quarters. We're not changing the full-year guidance. That remains in

place at DKK 300 million. But you had a bit of higher adjustments than originally anticipated in Q2, around the Vyepti inventory obsolescence.

The second piece is we also had pretty much DKK 15 million of restructuring costs we booked due to the closure of the sterile plant in France. So these adjustments you have probably not to the full extent factored in.

The second part of your question was, I think, around phasing. We've always talked about fully supporting the launch of AADAD in the US. And having had launch commencing in May, you see predominantly the full launch costs in the second half of this year.

Of course, you have a little bit as well in H1, because you start to hire reps, etc. But of course, the guidance reflects, as originally communicated, more of a spend level in the second one. I don't think we give further guidance on SG&A ratios next year. So with that, I would hand over to Johan around your question on the transition.

Johan Luthman

Yes, I think they are more technical. Yes, if it's more a technical, scientific question, I can't answer it. There's also, of course, a cost estimate in this. But I think it's very important to say that we're progressing well with this. The wholesale switch from *Pichia pastoris*, which is the yeast cell manufacturing platform we have right now, to the Chinese hamster ovary platform is the critical one, because that brings us into a much more established type of cell platform to work on.

We have generated very, very strong in vitro data and are really supporting very much what we're doing. But at the end of the day, it's really a data-driven and regulatory-driven switch. And when I say this is all going well, I think we are looking forward to see that switch occurring in the coming year.

Deborah Dunsire

Yes, one thing I would add on that switch. Remember, we have this contract that delivered all of the *Pichia* supply within five years that is just sunsetting now. So it is our intention to utilise, as fully as possible, that *Pichia* supply before transitioning to delivering on the CHO supply. I think you should also bear that in mind. And then on the Abilify franchise, would you like to comment from the US, and perhaps you from an ex-US perspective, Jacob?

Thomas Gibbs

Sure. Thank you, Deborah, and thank you for the question, Dominic. As we see the Abilify long-acting injectable franchise, we see this as an important growth lever for the US over the coming years. And the addition of Abilify

Asimtufii has really enhanced the overall clinical value proposition that we bring to physicians and patients. And we see this as an important contributor to growing the overall franchise.

Deborah Dunsire

Great. Over to you, Jacob.

Jacob Tolstrup

Yes, a similar comment also from my side. It's an excellent addition to our franchise, and I think there will be many patients that will be suitable and will benefit from a two-month version. Longer term, I think that was also part of your question, we have had tremendous success with the Abilify Maintena one-month. And I think it will be too much to hope for that you can expect the total franchise to continue to grow once we see generics on the one-month, when and if that happens.

Deborah Dunsire

Next question, please.

Operator

The next question comes from Charles Pitman from Barclays. Please go ahead.

Charles Pitman

Hi. Charles Pitman from Barclays. Thank you very much for taking my questions. Could I just ask on Rexulti, as we're coming up to the readout of the PTSD trial, whether or not you could just give us any more insight into how confident you are in the potential for a positive result on this trial, what you're really looking for in terms of benchmark results? And maybe if you could speak to what your expectations could be in terms of any sort of commercial opportunity for the indication relative to the other indications Rexulti is already approved in.

And then just secondly, on Vyepti. Looking at that global... The geographic roll-out chart, I was wondering if you could just dive a little bit more into the key differences of growth for Vyepti's share in Europe, and why Germany and UK share gains seem a little bit more limited, whether or not there's anything we need to appreciate here in terms of increased competition, and whether or not you can really get to that same level of share seen in those other geographic areas. Thank you.

Deborah Dunsire

Thank you. I think, Johan, you can start on the PTSD clinical side, and then Tom on the opportunity/ And then Jacob will take the Vyepti question.

Johan Luthman

I've been commenting on this before several times, so obviously I can add a little bit more element to it but not much. As I said, we finished the enrolment, and we are just waiting for getting the results. So it's too late to speculate. It could be 0%, it could be 100%, and nothing in between. There could be a gray-zone version, of course, because

there are two trials ongoing.

But important for all these kind of estimates, what could work out and not work out, is prior information. And that's what I've been talking about before. For the Alzheimer agitation indication, we had substantial prior information and a very, very solid data package already from two prior big trials. Here, we are working with much less from an exploratory Phase II trial, so it's definitely coming with higher risk, as it does when you have less prior information.

Deborah Dunsire

Over to you, Tom.

Thomas Gibbs

Thanks, Deborah. And if the data are positive, we do see PTSD as a meaningful opportunity to really enhance the overall value proposition of Rexulti. If we think about the magnitude of the opportunity, I think we start with the annual prevalence which is about 3.5% in the US. And that compares to an annual prevalence of 8.3% for MDD, and then something right around 1% if you look at schizophrenia and schizoaffective disorders. So we see the magnitude of this opportunity between that of the schizophrenia indication as well as the MDD indication.

Deborah Dunsire

Great. Thanks, Tom, and over to you, Jacob.

Jacob Tolstrup

Yes. And on Vyepti, showing the volume market share is always good to give an indication of the progress and the performance in the different markets. It's also important to say that every market is different, and the volume market share can be distorted in different ways, and one example being Germany, where our competitor, Aimovig, had an expansion of the market due to a clinical trial they did. And that means that the whole market has grown tremendously in Germany, but also means that our market share looks more depressed than for other markets. I would say both for the UK and Germany, we are ahead of our internal plans.

Deborah Dunsire

Great. Thank you. Next question, please.

Operator

The next question comes from Michael Leuchten from UBS. Please go ahead.

Michael Leuchten

Thank you. Two questions, please. Deborah, just interested in your comment on the US rep count. Do you think that is a Lundbeck-Takeda-specific issue, or is this actually more broadly across the industry as everybody tried to go down the digital path and is now figuring out that boots on the ground is actually the more effective way of marketing products in the US still, whether we like it or not?

And a question for Johan, PACAP. You're very firm that this is a Phase IIb that you're thinking about. So is that a plain-

vanilla Phase IIb dose range study, or is this a potential Phase IIb/Phase III trial design that would still allow you to accelerate the programme? Thank you.

Deborah Dunsire

Thanks a lot, Michael. I'm actually going to ask Tom to comment on the Trintellix and the sales force question for you.

Thomas Gibbs

Sure. When we look at Trintellix, we may have talked a little bit about the rebasing of our overall sales force footprint, but I see that as more of a surrogate for the overall promotional spend that we put behind the brands. And I think, philosophically, what we do know is that the sales force continues to be an important element to the overall marketing mix, but it is not sufficient, and we are seeing greater efficiencies and effectiveness with complementing sales force efforts with omnichannel customer engagement.

Deborah Dunsire

Thanks, Tom. And over to you, Johan.

Johan Luthman

Yes. Thanks for the question. Yes, we call it Phase IIb because we're actually shifting the exploration now from an IV dose that we had prior in the HOPE PoC trial now to a sub-Q exploration. So it's an element of technical transition here. Of course, we had good data to support that transition, but there is a certain element in this.

So we're not rushing into a pivotal trial directly, based on that shift, and obviously we need to find the dose range that is most fitting for the product. And whether we're going to have one or two doses eventually in a Phase III, that's still up for discussion, but we'd really like to make sure we're picking the right doses. So that's why we call it IIb.

The shift. I mentioned that we're still working on the design, so the shift between the two could be within the same protocol or two different protocols. That's always possible. But I think we'd like to have a clean data set first on the sub-Q and the dose range, before we really make any further decisions.

Michael Leuchten

Thank you.

Deborah Dunsire

Great. Thank you. Next question, please.

Operator

The next question comes from Vineet Agrawal from Citi. Please go ahead.

Vineet Agrawal

Yes, hi. Thanks for taking my question. Just one more on Rexulti. I think, in the past, you said that the subnational data shows that the utilisation for ages 65 and above has been pretty consistent around 12% to 14%. I was just curious if you can maybe share any utilisation data post the AAD indication launch. And then the second question was just on

Vyepti. I wanted to check if you can provide us any updates on the SUN studies and ALLEVIATE cluster headache trial. When should we expect to hear more on these trials? Thank you.

Deborah Dunsire Hey, Vineet, we were really having trouble hearing you. We can make out that there's a question on AADAD and one on Vyepti, but we really can't tell what the questions were. I don't know whether you're on a headset and you can take it off to get a better connection. But could you try to repeat your question?

Vineet Agrawal Okay. Sorry. Is it better now?

Deborah Dunsire Yes.

Vineet Agrawal Oh, I was just checking on the... In the past, I think you have said that the subnational data shows the utilisation for ages 65 and above to be pretty consistent around 12% to 14%. I was just curious if you can share any utilisation data for the AAD indication launch. And then secondly, on Vyepti, I was wondering if you could provide any updates on the SUN studies and the ALLEVIATE than the ALLEVIATE cluster headache trials in terms of when should we expect to hear more on these.

Deborah Dunsire Okay, great. I'm going to have Tom start on the update on the AADAD.

Thomas Gibbs So thank you for the question. And you're right, if we looked at the overall utilisation for 65-plus prior to the indication, it was teetering between 12% and 14%. And what I can say, and you saw within the data that was shown by Deborah, is that there's been a meaningful and significant increase in the overall 65-plus utilisation.

Deborah Dunsire And then, Johan, when can we expect to hear data from the cluster CHRONICLE and ALLEVIATE?

Johan Luthman So for the cluster indication, which obviously is an attempt to have an indication expansion really go into a new indication, which has been a really, really hard indication to crack the nut on, several of our competitors have struggled with this, and it's also a hard indication to run, quite frankly, trials in, but we have two trials ongoing, the CHRONICLE and ALLEVIATE trial. The CHRONICLE is in chronic cluster headache and ALLEVIATE in episodic. And both trials are basically ongoing. We're waiting for data to see, out of some of these trials, and that's going to guide us in the future.

Deborah Dunsire Next question, please.

Operator The next question comes from Manos Mastorakis from Deutsche Bank. Please go ahead.

Manos Mastorakis Thank you for taking my question. A question on the CD40 assets. I want to clarify if that is going to be a single trial, a basket trial including multiple indications, or if it's going to be multiple Phase IIs. And basically, what are you thinking in terms of which indications that will include? But in general as well on CD40, what can we expect in terms of read-outs? Thank you.

Deborah Dunsire Thanks, Johan.

Johan Luthman Thanks for that question. As you heard, we are very excited about this molecule. When it comes to technically progressing this forward, we are contemplating a number of neuroimmunology indications. And yes, I'm a big fan of the basket trials, if it's possible. But when we go through the indications we are contemplating, they are pretty distant from each other. In basket trials, you have generally a benefit of when you have similar read-outs and a similar sort of disease course. So that's the benefit of doing basket trials, when you have very closely associated indications.

Here, we're contemplating more distant from each other, so it's most likely going to be separate patient studies that we're going to initiate. And in terms of what indications, we are going to gradually look through a big box of various things. As you know, there is prior information in this field that we obviously take care of and look at carefully. But we'd also like to explore new indications here.

Deborah Dunsire Great. Last question, please.

Operator The last question comes from Suzanna Queckbörner from SHB. Please go ahead.

Suzanna Queckbörner Hello. Suzanna Queckbörner, Handelsbanken. I'd like to ask about the monthly fluctuations that you have in your Vyepti sales. So when you look at the US hospital data, is this down to hospital purchasing patterns, or is there any seasonality when patients actually seek treatment in hospitals? Perhaps you can give us a bit more of an insight here on Vyepti.

And then the second question relates to the mature brands. So you said that you're seeing faster erosion in the second half. Perhaps you could expand on this and specifically how we should think about that going forward.

Deborah Dunsire Great. Tom, will you take the Vyepti question, and Joerg, the mature brands?

Thomas Gibbs Sure. When we look at the performance of Vyepti over the course of the last seven months, what we have seen is a continuing strong momentum upwards in terms of overall demand. Now, there could be some fluctuations, for

example, when a price increase is taken, where you could see some additional purchasing prior to a price increase. But as it relates to any seasonality, we just don't see that in the data.

Deborah Dunsire

Joerg?

Joerg Hornstein

With your question regarding mature brands, I think it has, in principle, two components. The first component is that, yes, we see a bit faster erosion, especially in CipraleX, in Lexapro in Japan, in Sabril and in Deanxit in China. And then, of course, mature brands are always a bit impacted by timing effects, timing effects related to government tendering, a full year volume already in the first half, or changes you have in your distributor structure.

There are certain timing effects also in the Q2 numbers. I think if we would specify a number here, we would probably talk around DKK 100 million to DKK 200 million that we may not see materialising in the second half, besides the topics I just mentioned on Sabril, CipraleX, Lexapro and Deanxit.

Deborah Dunsire

Great. With that, I'd like to thank you for your questions, for attending the Lundbeck first-half results. It has been my privilege and pleasure to work with this team at Lundbeck and also to meet and answer your questions over the years that we've interacted. So I appreciate your continued interest in Lundbeck. And bet on Lundbeck to drive the frontier in neuroscience and to grow. Thank you.