

H. Lundbeck

Transcript: FY 2020 results

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[00:00:00] Operator

Ladies and gentlemen, welcome to the Lundbeck fiscal year 2020 results conference call. For the first part of this call all participants will be in a listen only mode and afterwards there will be a question and answer session. Today, I am pleased to present Deborah Dunsire, President and CEO, Anders Götsche, Executive Vice President and CFO, and Johan Luthman, Executive Vice President of Research and Development. Speakers, please begin.

[00:00:28] Deborah Dunsire

Hello, everyone, and welcome to the Lundbeck Full Year 2020 results conference. As you've heard, I'm joined today by Anders and Johan, but also have Jacob Tolstrup, our Head of Commercial Operations and Peter Anastasiou, our Head of the North American operations, with us to answer your questions.

Next slide, please. You've seen this disclaimer many times before. I won't read through it. So let's go to the next slide.

2020 is a year that I am extremely proud to be part of Lundbeck for. We have accomplished so much in the midst of a global pandemic, and faced with significant currency headwind, our employees came together to ensure a seamless delivery of all our products around the world throughout the year. And that enabled us, in spite of the challenges, to deliver revenue growth within our guidance range of plus four percent and reaching seventeen point seven billion Danish kroner in line with our guidance. We also were able to save during the year, we weren't able to promote normally, and that resulted in savings that we could bring to the bottom line, our core EBIT improved to four point four billion with a margin of 25.1 percent. We grew our brands. Our strategic brands grew in total 13 per cent and we launched Vyxepti in the US in the midst of the pandemic and were able to move that brand forward, not as we would have liked indeed, but to get a lot done during the year. We've also had additional approvals in Canada and the UAE and initiated the regulatory review in Europe. Rexulti is on track for the interim readout

of the Phase three study in agitation and Alzheimer's disease, and that will come in Q2. So it was great to be able to get the patients in for that interim analysis, even in spite of the difficulties the pandemic has implemented on our clinical trials. The covid-19 impacts been across the business in many different ways, limiting patients from seeing physicians, limiting our promotion around the world, limiting our clinical trials. But the people of Lundbeck came together to make things happen, and we've been able to move forward regardless. We couldn't, unfortunately, do anything about the significant currency headwinds in the second half of the year, and that has had an impact that Anders will go through in more detail. But it is a year we're very, very proud of.

Next slide, please. When we look at the underlying performance for the major strategic brands, Brintellix/Trintellix grew to three point one million Danish kroner. And you can see that it grew 13 per cent versus full year nineteen. So at a slower rate. And you see the impact of the first and second half, very strong growth in the first half and the impact of the pandemic restrictions impacting the second half. But the market shares have been stable and in some markets even increasing. Rexulti also had a very strong growth year and achieved two point six billion DKK. We've continued to launch that brand in other markets recently launching in Brazil and Italy. The biggest business, of course, is still in the US and also Canada, where we have the major depressive disorder indication as an adjunct therapy. Abilify Maintena was very resilient through the covid pandemic and grew well at achieving two point two billion Danish kroner in sales. The LAI market, I think, has been growing well in the pandemic as LAI allow patients to come in less frequently. So Abilify Maintena benefited from that. And we shouldn't forget Northera achieving 2.5 billion the Danish kroner in sales with a growth of 10 percent.

Next slide, please. Focusing a little bit more on Vyepi, fourth quarter demand doubled compared to third quarter demand, showing that this brand is continuing its momentum, even though it is challenged by the limitations of the pandemic. We've had very, very positive testimonials from both patients and the physicians providing Vyepi to their patients that it really delivers on that powerful, fast and sustained relief from chronic and episodic and frequent episodic migraine. The work we did in our US operations to really get the bedrock of reimbursement in place for Vyepi was quite remarkable in a virtual setting. We've had the average sales price is now published and the permanent J-code was effective from October 1st. We had by the end of the year 130 million Americans covered lives by their insurance, providing

access to Vysepti with no branded step edits. And we've seen utilization not only in those people, but in people whose plans required branded step edits. They had to go through other brands because Vysepti can deliver relief where other brands have failed. So we also see that at the end of this graph here, the normal reset at the beginning of a year as the deductible resets for people in their new insurance year. So we're confident that Vysepti has the potential we expected when we made the acquisition of Alder. But of course, it has been impacted by the pandemic.

Moving to the next slide, please. This is a brand that we own globally and the global rollout is beginning, and we're also rolling this brand into different indications. There's a very big market for prophylactic migraine treatments around the world, and we expect it to grow considerably in the coming years. It's a market that has been served by older generic therapies for so long and they are inadequate. So we do anticipate that there is a lot of headroom for growth in the prevention of migraine market. As I said, we've achieved approval in three markets, the US, Canada, UAE and actually updating today we have now submitted for approval in 12 markets around the world, the latest being Thailand. We importantly submitted to the European Medicines Agency in December, right on track. And they have accepted the Lundbeck application for the marketing authorization, and we anticipate that approval in the first quarter of 2022. We've started the trial alleviate for the second indication in episodic cluster headache, and Johan will talk about a bit more about that and got also our Asian development activities underway with trials starting in China and pharmacokinetic trials starting in Japan. So we're very excited about the potential for Vysepti to expand globally and then expand into further indications.

Next slide, please. Anders, over to you.

[00:08:01] Anders Götzsche

Thank you, Deborah. Our five largest products have been quite resilient, growing 10 percent in 2020, and that is indeed a strong achievement considering the pandemic, but also the currency headwinds we have experienced during the year. The four key product delivered double digit growth in 2020, despite the impact from the limitations we have seen due to the pandemic. There has been less patient interactions with health care providers and we also have had a reduced ability to conduct normal promotional activities. The lower activity level and the patient interactions with health care givers, health care providers has reduced the new to brand prescriptions, which has impacted the growth negatively, especially in the second half as

Deborah also alluded to in the previous slides. It is important to highlight that we have seen strong recovery and also uptake in periods where countries have opened up and society has been more back to normal.

Next slide, please. For 2020, the growth in net sales amounted to four percent and thereby we are actually meeting the expectations that we laid out in the market in the beginning of year before the pandemic actually started. So to achieve four percent in unprecedeted year, we are superheavy with that. The core gross margin increased with one percentage points during the year to approximately eighty six percent. The reported gross margin was a bit lower than we expected. And that is, of course, due to the addition amortization of Rexulti of approximately three hundred million. The increase in SG&A and also R&D is a consequence of two things; The fully correct writedown of eight hundred million, as you are aware of, and then investments in additional clinical trials for Vyapti and also additional sales and promotion activities as we started the launch of Vyapti in April 2020. If we adjust for this, then the cost development would have been flat between 2019 and 2020. So when we look at the underlying performance, without these investments and the write down, our reported EBIT margin would actually have been above twenty five percent. It's also important to emphasize that we delivered a very solid core EBIT of four point six billion, which is also the reason for the strong cash flow, which I'll come back to in a minute. The effective tax rate for 2020 has been a positive surprise as it ended much lower than anticipated due to a couple of positive impacts. It was increase in Danish R&D tax incentives. It was faster integration of the acquisition and a faster utilization of in NFLs and also a positive tax impact on transfers of IP rights to Denmark. All in all, we are pleased with the financial performance for 2020, which is also seen in this light. So please turn to slide nine.

As you know, Lundbeck has more than 50 percent of our business in the US, we have a 24 percent in international markets and then the rest is coming from Europe. Our main currencies are US dollar, Chinese yuan, Canadian dollar. These three exchange rate together constitutes about 70 percent of our currency exposure. We have seen declines across all these, including some very steep depreciations on some of the more exotic currencies during the year. The impact of sale from depreciations in currencies was very visible in the fourth quarter. Reported revenue from the US was negatively impacted with seven percentage points, and in international markets, the impact was negatively all, which was the impact of nine percentage points negatively. That depreciation of currencies is expected to impact Lundbeck's revenue with

approximately eight hundred million in 2021. It's also important to highlight that our assessment, based on the currency rates we have now, is that a five percent change in the US dollar will impact Lundbeck's revenue by approx. in a range between 250 to 300 million kroner.

Next slide please. As you can see from the left hand side of the slide, free cash flow in 2020 was very solid and is a testament to the strong underlying growth and performance by the business. To the right of the slide, you can see that acquisitions made in 2019 increase the net debt to around six point six billion that has during 2020 due to the strong cash flow being reduced to four point one billion at the end of 2020, leading to a net debt to EBITDA ratio a bit less than one. We expect that net debt during the year will end or at the end of twenty one will end in a range between three to three point five billion Danish Kroner.

Next slide, please. We believe that the 2021 will continue to be impacted by the pandemic and we assume a gradual return to a more normal market situation by mid 2021. So we expect to regain momentum with double digit growth for the key brands during the second half of 2021. We delivered approximately seventeen point seven billion kroner in 2020 of our revenue of seventeen point seven billion kroner. And in 2021 we expect revenue to be in a range between 16,3 and 16,9. And we have tried to illustrate the moving parts in the bottom of the slide. And as you can see, we have maintained our expectation around 50 percent decline in Northera sales due to loss of exclusivity, which is approximately a decline of 1.3 billion Danish kroner. The other key brands are expected to show high single digit to double digit growth during 2021. And then we expect that the mature brands will decline around 10 percent. And that is due to two things; It is continued generic erosion and then its VPD in China. The net effect of that is a total gross and revenue of around 8-900 million for the key brands and the mature brands in local currency. We assume, as I said before, negative currency effect of around 800 million and a hitching effect that goes in the opposite direction of 200, which means the net effect will be around 600 million in 2021. In reported EBIT we got 1.8 to to 2.3 billion, despite having elevated investments both from a SG&A perspective but also from an R&D perspective in 2021 compared to 2020. For the full year, you should expect finance and items to be a net expense of 250 million to 350 million kroner depending on currency development. With that, I would like to hand over to Johan for going through the R&D Pipeline.

[00:16:38] Johan Luthman

Thank you, Anders, please turn to slide 12.

while we continue to maximize our brands, including running critical life cycle activities, we are simultaneously focused on filling the pipeline with innovative programs, with an increasing focus on niche and rare diseases affecting more defined subpopulations of people, where the unmet medical need is the highest. With regards to Vyepti, some of the recent activities I like to highlight are that we started a Phase three clinical study in episodic cluster headache. We also submitted by the end of the last year the European marketing authorization application for the preventive treatment of marketing and others, which means that we can expect to see a CHMP recommendation by end of the year and the formal EU Commission approval of Vyepti in Europe around a year from now. By the end of last year Vyepti was approved in the UAE as our second approved market, followed by the very recent approval in Canada. In addition to the present three approvals, we have to date submit the Vyepti 12 regulatory authorities for review and we plan to submit to over 10 other authorities during 2021. For us Rexulti Alzheimer's disease, we have, as communicated earlier, somewhat changed this study with the introduction of an interim analysis. We have completed the recruitment of the patients needed for this planned interim analysis, and it's on track for the second quarter. I'll come back to some more details of that program in a minute. We continue to progress innovative programs in our research organizations involved in Valby and La Hoya to build up a steady and dynamic early stage pipeline. While our early development programs are progressing with a systematic experimental medicine approach, we are also dealing we also diligently, swiftly closed down less promising programs if we do not see what we expect to see. We continue to see a very fluid situation related to the covid-19 epidemic. Many of our trial sites closed initially, then open up and now some are closing down again. This is primarily impacting studies, especially in the early development studies where we depend on very few sites. Nevertheless, overall, we have a strong, sustainable phase one set of assets. For example, we have a strong momentum in the MAGLipase inhibitor programs.

Next slide, please. As I mentioned previously in the ongoing Agitation and Alzheimer's study, we have recruited a 255 subjects needed for the interim analysis, and I'm therefore confident that we can conduct a planned interim analysis sometime during the second quarter. The main analysis is a pooled analysis of the 2 and 3 milligram doses. With upcoming analysis, it might be worth worthwhile to recap on what has been published prior from the two conducted Phase three studies on Brexpiprazole in patients with agitation and Alzheimer's dementia. The program was initiated to assess the efficacy of Brexpiprazole on agitation measures, as well as safety and

tolerability in two 12-week randomized, double blind, placebo controlled parallel arm studies. One of these studies, study 293, was conducted at 81 sites and in seven countries and recruited 433 patients. The second study, study 284, was a flexible dose study with 0.5 to 2 mg per day of placebo of Brexpiprazole, and conducted at 62 sites in nine countries, recruiting 270 patients in a care facility or community based setting. In study 283, Brexpiprazole 2 mg per day demonstrate a statistically significant greater improvement in the Colon Mansfield Agitation Inventory, total score from baseline to week 12 compared to placebo at the level that is also considered to be clinically meaningful. In study 284 Brexpiprazole 2,5 did not achieve statistical superiority over placebo. However, a benefit was observed in the post hoc analysis among patients treated to the maximum Brexpiprazole dose of two mg per day compared with placebo patients. Combined with our broad knowledge about the molecule, it's therefore my view that Brexpiprazole has the potential to be efficacious, safe and well tolerated in the treatment of Agitation in Alzheimer's disease.

Next slide, please. This is our current pipeline. We have a line of products according to our strategically prioritized biological clusters. In development, we are currently active in three out of four of those clusters. During the second half of 2021, we plan to start phase two programs. One on PACAP on migraine, and another planned on eight to four two two, our alpha synuclein, Monoacylglycerollipase and multiple system atrophy or MSA for short. With that, I like to turn over to Deborah again.

[00:22:14] Deborah Dunsire

Thanks, Johan. Next slide, please. As you know, at Lundbeck, our purpose is to tirelessly dedicate ourselves to restoring brain health so every person can be their best. While we do that, we want to do it as part of a global community committed to moving the world forward. We support the sustainable development goals and we make an impact on a number of them. A very important one that we are focusing on is our commitment to carbon neutrality. And we have committed to the Paris climate agreement and aim to be carbon neutral definitely before 2050, by 2050 or before. And we have new science based targets approved that we're talking about in our sustainability report to keep moving us along that journey. In 2020, we made significant progress reducing our CO₂ emissions in spite of the fact that we are increasing production volumes and a 14 per cent cut in the carbon emissions from our production versus 2019 even, and we've over exceeded our annual target by four per cent. So we're a company that's working hard to become

carbon neutral. We made these reductions even without purchase certificates of origin in 2020. And it's our goal to continue to do that. We also have made progress in creating a workforce that's even more diverse and an environment where people can be their best that is inclusive of all as we make progress against the Sustainable Development Goals 5 and 10, looking at gender equality and the reduction of inequalities. Generally we're a company where discrimination is not tolerated. We've also formed a donation partnership with International Health Partners to help bring our medicines to places that don't have access to medicines for brain disease or mental health. And we're constantly looking to reduce the stigma associated with mental health so that people facing brain disease can get equal parity of care.

Next slide, please. We released today our sustainability report for 2020, and you'll find that on our website and you'll see that Lundbeck has significantly improved our ESG ratings during 2020. In this new reporting format, we list our information on what we're doing. According to the Task Force on Climate Related Financial Disclosures, the TCFC Reference Index so that you as investors can easily track our commitments and our goals regarding sustainability. We were very proud this year to be listed for the fifth year in a row as an A-list company by the Carbon Disclosure Project for our work on climate.

Next slide, please. Turning to looking to the future, we've made significant progress on our expand and invest to grow journey. And you know that we expanded our disease operating space in 2019, during 2020 focused our internal discovery in four very promising areas of biology to yield new medicines for neuroscience. And in the future, where we'd like to go with that is always addressing the highest unmet medical needs, which are typically specialist indications. And we want to be able to bring that innovation forward for patients in those select segments that allow us to bring transformative improvement in brain health. We want to do it in selected patient populations where we've got biomarkers to measure the progress and give us predictability, or where we may be able to use a biomarker to select a group of patients where we can focus a medicine on that disease. That gives us more tractability in development and helps us reduce the size of our development programs. When we focus on bringing forward transformative medicines in these niche psychiatry, niche neurology indications, we also know that it helps us have a focused footprint around the world. And as a mid-sized company, it enables us to be able to afford the commercial footprint to bring those medicines as Lundbeck around the world. And we're looking to be able to bring our medicines to all countries, given the

transformation that we're looking for. You know that we have great medicines. Just Trintellix is a phenomenal drug. But there are some countries we can't launch it because we can't get pricing and we want to change that as we go into the future.

Next slide, please. So here's the trajectory. Expanding the disease operating space, focusing our internal discovery in the most promising areas, and then focusing as we develop medicines in indications in niche neurology, rare disease, neurology and niche psychiatry.

Next slide, please. We're on a journey and we are very ambitious. We look to be number one in brain health and that will come through trends providing those transformative outcomes to patients in the most high unmet medical need areas in neurology and psychiatry. We want to be recognized by patients and other stakeholders as their partner, their number one partner in brain health. We want to be recognized for having a pipeline filled with premier neuroscience and having a commercial organization that partners with health care providers and patients around the world on those targeted areas of niche neurology, niche psychiatry and rare disease neurology. We're working to become a more digitally enabled company to be able to use data and digital to improve patient outcomes, never forgetting that we're part of a global community. We need to be on track to be in carbon neutral by 2050 and deliver sustainable growth in revenue and profitability so that we can address all our stakeholders needs. So we look forward to communicating with you over the years ahead on our journey to be number one in brain health.

Next slide, please. When we look at the news flow coming this year, the first half, we've already achieved one goal, which was the Canadian approval of Vysepti. We're looking forward to the next after in the middle of the year, Australia. The interim analysis for Rexulti in Alzheimer's agitation in Q2. In the second half of the year, the MSA trial with our 82422, the alpha synuclein antibody kicking off, will start the phase two with our PACAP antibody in migraine and then hope to finalise the study with Rexulti in borderline personality disorder as long as clinical trials can accelerate their approval and as the pandemic lifts. First half of 22, it will be a big milestone to have Vysepti approval in the US, in the EU and then finalising the post-traumatic stress disorder trial with Rexulti.

Next slide, please. I think we probably are done with presenting and now we can go to your questions.

[00:30:07] Operator

Thank you. And ladies and gentlemen, if you do wish to ask a question, please press zero and then one on your telephone keypad now. First question is from Wimal Kapadia from Bernstein. Please go ahead. Your line is open.

[00:30:20] Wimal Kapadia, Bernstein

Oh, great, thank you very much for taking my questions. I am Wimal Kapadia from Bernstein. Could I kindly ask you to talk about the upcoming interim for Rexulti. So firstly, what is the bar? And I'm assuming reasonably high and, you know, just tied to that, you know, what are management expecting in terms of primary outcome, in terms of C.M.A reduction, you know, is a good benchmark. The previous six study where we saw close to twenty point change. And secondly, can I just push a little bit on the target population? Clearly, there are a lot of a large number of patients, but how do you think which are the most likely to receive the products? And really just curious to hear how you think about the dynamics both in the care home institutional setting? You know, on label drug use is very important, but also in the community setting where carers are really trying to delay institutionalization. And then my second question is just on Vysepti, just like in your release, that the manufacturing has been shown to be more cost effective and thus production costs will be lower going forward. Could you just help us better understand that in terms of accretion dilution versus the group costs and what that could mean moving forward in terms of benefit? Thank you.

[00:31:38] Deborah Dunsire

Ok. That sounded like a lot more than two questions, but I'll kick off with the target population, and hand over to Johan to talk about the trial. We know that agitation is the symptom that causes people to have to move out of community care into care homes. And it's very difficult to manage even in those settings. So we'd anticipate that this would be able to be used in both settings. We showed a very good tolerability profile in the previous two studies. And so we anticipate it could be used in the community to maybe enable people to stay with their families for longer, but also be used in the care homes to make the management of patients much better, both for patients and staff in those settings. So we really look across both. And then Johan, perhaps you can comment on the other parts of the question.

[00:32:32] Johan Luthman

Yes. One more word about the population. So the population we're studying in this particular trial that's ongoing, is actually the same population we started in the two previous trials. And this is a mix of about 50/50 people that are institutionalized in nursing homes primarily, and people that are our patients living at home. So that is the population we're targeting also in the trial and document in this trial work. In terms of the interim, obviously, this is a very classical interim. There are three possibilities here. Success, fertility, or trial continues. And as you may recall, we talked about the trial going out to 330 subjects. Now the interim is at 255 subjects. The bar. We don't go into details all the statistics here, but the fertility bar is set pretty high because there is really no reason to believe that we will hit fertility. We have previous data from the two previous trials. In terms of the primary outcome measure and decisive effect. We actually aim for similar effect as in the previous trials. And the effect size is what is considered, as I mentioned before, clinically meaningful effect. And the absolute effect is also similar to what you saw in the previous trials. So that's what we're aiming for. We are going to see the results by Q2 and obviously we can only communicate details whether it's a progression of the trial or death to a different outcome, success and fertility at that time point.

[00:34:19] Deborah Dunsire

On the Vyapti question, perhaps, Anders you can answer.

[00:34:23] Anders Götzsche

Yes, so what we have said before is that we have had a pretty nice improvement in our costs for producing Vyapti. But, of course, it's not something that we are willing to go into if it changes the accretion dilution. What we can say is that what we have said in the past is that the gross margin that we have for Lundbeck, around 70 to 80 percent, that will not be changed by launching Vyapti. So that is the indication we have said before.

[00:35:03] Operator

Next question is from James Gordon from JP Morgan, please go ahead, your line is open.

[00:35:09] James Gordon, JP Morgan

Hello, this is James Gordon from JP Morgan, thanks for taking the questions. One on the agitation and also just one on growth trends. For agitation, and if you repeated the efficacy you

saw in the previous studies with the two big dose in phase three, would it be fair to assume that would clear the statistical hurdle that you have at the interim? And also, could you just remind us? I think one of the interesting differences is that the current phase three had a different geographic involvement. You've taken out the Russian involvement. It was a bit of an issue in the two previous trials. If you look at the previous trials and you did take out the Russian involvement, how much better does the data look? Do you still think that is a big confounder for those previous trials? And the second question is just on Rexulti and Trintellix. With the post covid-19 rebound. So I know there is a bit of an issue from covid-19 in 2020 for these drugs in the US. But early this year it sounded like you were seeing the encouraging trends so far is continued. And could they be double digit growth in the US again this year?

[00:36:14] Deborah Dunsire

Great, James, thanks for the for the questions. I'll have Johan hand start with the Alzheimer's agitation, and then I will move to Peter for the commentary on what we saw in the fourth quarter and what we're seeing in the first half.

[00:36:27] Johan Luthman

Yeah, if I got your question right, you're really after whether it will be sufficient at the interim? We had progressing, for example, with filing and we have a good understanding with the regulators that this would be the case. This, as I said, is a pooled analysis or 2 and 3 mg. And we have, as I said, 255 subjects is a two-two-one. So we have a sufficient subject dose at that time point, including the critical 3 milligram dose that is there really to create the headroom for safety. probably that's what you're asking me if I got your question right. Can you confirm that was what you're after that?

[00:37:08] James Gordon, JP Morgan

Yes, because I'm aware that when you take an instrument that can be a statistical penalty. So we know just how many patients you've got. But if you're splitting the alpha and sometimes the regulator or ????. And so that's the highest hurdle to success, that interim versus the final result. So my question is, do you need it effectively need even better efficacy than you saw previously because it's an interim or the extra patient? You know, ???, the power sufficiently that even in the interim you only just need to repeat what you showed in previous trials were to make.

[00:37:35] Johan Luthman

So without going into details there, we're looking for the same treatment effect across the study at the total end, 330 and at the interim, that's as much as I can comment on that bit. The bar is higher. And obviously with fewer subjects you have more viability and that's taken into account. So it's a pretty robust approach to the interim as well as the final readout if we have to go that far. And geography. You worry about that. You had the Russian sites in the previous program. We don't have that now. This is the US and Ukraine based study where we have experience. In terms of taking out different subgroups etc. in the previous study, obviously, Russia is a well known problem in our semi-trials. So if you look at the totality of the data versus taking out the Russian sides, there are differences. But I think the most important thing is now with the ongoing trial, we have a good set of sites, high quality sites, and we have experience with those sites before from the two previous trials. So we're pretty confident that we're picking the right geographies this time.

[00:38:51] Deborah Dunsire

To put a fine point on it. The flexible dose trial from 0,5-2 milligrams without the Russian sites, the overall intent to treat was positive. But that's a post hoc analysis. So we can't claim anything from that. But we have excluded the Russian sites. And then, Peter, would you take the question on what we saw when the society was opening up in the fourth quarter and then what we're seeing in the first place?

[00:39:23] Peter Anastasiou

Yeah, thanks for the question, James. The short answer to your question is yes. We believe we will get back to double digit growth with those brands, but it's very dependent on covid about when that happens. And as Deborah mentioned, in Q3, Q4, where we saw the lock down, these patient volumes were coming back, our reps were getting close to back to full promotion, although about a third of those calls were coming from virtual versus face to face. When we were approximating some normality, we saw the NRx go back to their pre-covid levels. So that's why we have the confidence that as this thing lifts, that those brands are going to recover. The big question is when.

[00:40:10] Deborah Dunsire

And I think in the first quarter, we've seen a much lower ability than the fourth quarter to be able to be out promoting, and that's also, of course, affecting patients willingness to come into physicians and physicians offices being open. So I think we're seeing not as deep a impact in the first quarter as the second quarter of twenty, where it was a much harder lockdown. But we have less availability to go out than we did in the fourth quarter.

[00:40:41] Anders Götzsche

So if I can add then so so when you look at the phasing of the growth for the strategic brands in in 2021, you should definitely expect also due to the strong currency or the strong dollar and the beginning of the year that the growth will be muted in the first couple of quarters, and then it will gain momentum in the second half of the 2021.

[00:41:14] Operator

And next question is from Trung Huynh from Credit Suisse. Please go ahead. Your line is open.

[00:41:22] Trung Huynh, Credit Suisse

Hi guys, Trung Huynh from Credit Suisse. I have a few on guidance and then just one on the Trintellix pattern proceedings. So on guidance, if you have a look at the 21 guidance at the sales level, it looks quite conservative. So I was just wondering what the push is or pulls you expect to get to that upper end, but more importantly, that lower end of your guidance. And for 21, what are your expectations for that other pharma portfolio? Looks like consensus has a decline of 8 percent. Do you think that's an appropriate decline? And then on the EBIT level. There is clearly an increase in costs coming through here. I wonder if you could just take us through some of those other aspects of the cost structure beyond COGS that we should expect to the group in 2021 and then on the Trintellix patent infringement proceedings. I see you've settled of eight people. There's a remaining six. I was previously expecting a decision in the first half of this year. But you're released today suggests a decision within seven months after the trial. So is an expectation for that decision in the second half of this year, now or even in 2022? And is there any comment you can make about the case? Thanks.

[00:42:38] Ok, Anders will take all the numbers questions.

[00:42:42] Anders Götsche

OK, so our expectations for the cost ratios in 2021 is that we anticipate that the cost of sales will be in a range of 20 to 23 percent. We anticipate that the SG&A will be in a range of 41 to 46 percent and then that R&D will be between 22 to 24 percent. And it is important to say when you look at the, and then you can take the mid range and then then you get kind of what is the middle of the guidance we're giving here. So if you look into the sales and distribution costs, we will use more money on Vysepti in in 2021 compared to 2020, but then we will make some savings on other costs. So Vysepti is basically the only reason for increase in SG&A and the rest will be absorbed by efficiencies. When you look into R&D, it's pretty straightforward that if you compare with 2020, then if you take out the foliglurax, then you are more or less on the midst of the ratio. And then within the portfolio, then there will be a substantial additional spend for Vysepti due to cluster headache, the trial for that, the deliver study, and then we will reduce the spending on other programs. On other pharmaceuticals we had anticipated to be declining a bit more than 10 percent. And that is, of course, due to pricing. But what we have seen what we have seen in 2020 is, of course, a mature brand showing a really, really strong performance. And it is a bit difficult to predict what will the performance in 2021 be? The underlying structural performance should indicate five to 10 percent decline because you will see generics coming in. But then, of course, you also have the VPB in China that is taking out some 20 million, 150 million kroner or something like that. That is definitely meaning that the mature brand portfolio will have a decline around 10 percent or more in the totality of the mature brand portfolio will decline 10 percent because we have the VPB on top. And on finance acquisitions, it definitely needs to go to the bottom of the revenue guidance then or the lower end, we will be hit more by the pandemic that we will not regain momentum, that the pandemic will not lift in the second quarter, and we will not see a rebound into single digit double digit growth in the second half. That could be could be a reason. A reason could also be if Northera is declining more than 50 percent. And that is basically the two biggest uncertainties. As Peter alluded to, we have seen a very, very strong uptake when we are back in the market and in the field, then products are regaining momentum immediately. And hat is also why we have a strong belief that we will regain double digit growth with the key brands because there's a strong need for the products in the market.

[00:46:34] Deborah Dunsire

I think the other thing, we don't hope that we'll see more of his currency decline, but that's another wildcard.

[00:46:40] Anders Götzsche

Yeah. And that that's also why we gave you some indication of what is a change in dollar actually meaning with the five percent sensitivity. And then it's also important that the hedging guidance we have given you of course, the hedging will impact Q1 and Q2 mostly, because that is where we had the high US dollar rates last year.

[00:47:06] Deborah Dunsire

And then to the Trintellix patent, obviously, the most the strongest patent for any product is the compound patent, and that's the 2026-27 expiry. The court case if we are litigating the other very important innovations that we've put around Trintellix, and so the outcome of that is what's being litigated in the court case. And we don't provide guidance on ongoing litigation, but we have innovated around Trintellix. And so we will defend those patents accordingly. As to when we will see an outcome of that, we can't tell. We do know that there had been delays because of the pandemic leading up to this. And there may be there may be more. So I wouldn't really hazard a guess as to whether we'll see it this year or early next.

[00:48:08] Operator

And next question is from the line of Michael Novod from the Nordea markets. Please go ahead. Your line is open.

[00:48:15] Michael Novod, Nordea markets

Thank you very much, it's Michael Novod from Nordea. So maybe a bit of a strategic question to sort of your European launch and rest of the world launch of Vysepti. There's been a lot of focus whether you could do more M&A, but maybe you could talk a bit about whether you could consider doing more sort of product in licensing for drugs that are very close already on the market in order to support. So the range of products that your sales force is going to target the market with, given that you are probably going to invest anyway in significant promotion activities for Vysepti. So more of a strategic question. And then secondly, we've seen your Abilify maintainer a two months formulation and we're waiting for a production ramp up. But what about the Brintellix long acting version? I know you have one in the pipeline as well. How do you see the progress for that? And if that's successful, how would that also fit into a potential

Alzheimer's education indication? And also regarding the length of the IP protection for a long acting injectable of Rexulti.

[00:49:37] Jacob Tolstrup

Yeah. So hopefully I'm answering correctly, Michael, just to start on Vysepti. So as you know, we will be starting at the end of this year and the first markets outside of North America, which is obviously exciting. So the first launch will be the Arab Emirates and then we'll move into Europe in early twenty two and there will be a phased rollout of my Vysepti over some time, some years, as you normally well aware of for Europe. It's also a different launch for us this time compared to what you've seen in the past, that this is more of a hospital based, few clinics opportunity since it is an IV product, that also means that we will positioning it towards a specific segment of migraine patients where we believe the benefit speaks the most and will we have good data also compared to the other CGRPs in the market. So for the strategic point of it is that we will have Vysepti launching in 22, rolling out over the next two to three years after that in Europe. And then at the same time, we will in 2024, lose Abilify Maintena to exclusivity. But that still means that we will have two large scale promotable brands in Europe, and we would obviously like to add to that portfolio. And that's where we come to the BD part of that question that we are constantly looking for opportunities to add to our product portfolio. And we have been looking at opportunities that are very close to market or even on market basically, during 2020. And I'm sure we will continue to look for those in 21. So you have to absolutely right. If will be good go add something more to our portfolio in Europe where we have a full, full scale infrastructure.

[00:51:24] Deborah Dunsire

Yeah. Just, you know, we will continue to look externally at things that might have global rights. We've said that we'll look for license, we look for partnership, we'll look for M&A. We would be prepared to do regional deals. So it's a question about finding the right strategic fit for us at the right price. And there are a number of things that are a little bit priced to perfection right now. So we'll be disciplined in how we invest, but definitely looking to supplement from external innovation. Johan, maybe I can ask you to comment on the brakes LAI.

[00:51:59]

[00:51:24] Johan Luthman

Yes. Well, first of all, the Abilify maintainer we delivered very good clinical data that we think are supportive. And that gives you the answer to the Brexpiprazole needs good data. And this is a very early stage program, obviously in collaboration with Otsuka, we're exploring a lot of formulation and possibilities. But it's too early to tell. In that program. We're exploring different options formulations and we have ongoing clinical studies to see whether we can deliver upon the pretty challenging demand to put some long acting molecules into the right space and format.

[00:52:35] Deborah Dunsire

And I think if we do find a formulation that works, it's been a challenge, Brexpiprazole and aripiprazole don't formulate in the same way they are different products. So it's been a lot more challenging with Brexpiprazole, but that would carry its own protection around that formulation. And we would anticipate bringing it forward in a number of different indications. And you're perfectly right, a longer acting formulation in an agitated Alzheimer or dementia population would be a benefit. So I think we could see lots of different possibilities there. But first of all, we need the formulation to deliver the parameters that make it worth investing in.

[00:53:29] Michael Novod, Nordea markets

But can you say whether you are seeing progress in the formulation work done on Brex, that was my sort of my feeling that in recent discussions that you've seen some progress in this formulation.

[00:53:42] Johan Luthman

It's too early to tell. Quite frankly, we are still running and we have gone through a number of formulation and test. And, you know, as Deborah alluded to, not every molecule is made the same way. And there are some technical challenges with this molecule, quite frankly, to make a long acting. In terms of the question of different indications, I may add to what Deborah said, that traditionally this kind of molecule has not been very big for long acting because the tolerability issue. So obviously we hope to be able to deliver better tolerability, which we've seen in the two previous trials in agitated Alzheimer. But it's an area where you to have stayed away from long acting injectable because of the tolerability challenges.

[00:54:29] Operator

And next question is from Michael Leuchten from UBS. Please go ahead. Your line is open.

[00:54:37] Michael Leuchten, UBS

Thank you. It's my pleasure to be here. Two questions. One for Anders and one for Deborah. Anders, as you referred to, tax benefits from the acquired companies is wondering if that's something that's a one off just from the top or if that's an ongoing process that could help you with your tax rate going forward. And then for Deborah, I think in Q2, maybe Q3, you talked about how the mental health issues coming out of the pandemic might lead to a benefit for you, but patients have to go through the generics first. Is that part of the dynamic you're seeing early in the year with a slightly more dynamic behaviour of your portfolio in the U.S., or is that yet to come? Or is it just impossible to say because this is not something that can be analysed?

[00:55:29] Anders Götzsche

So if I start with the tax question, you should expect that our reported tax rate, from a structural point of view, will be around 23 percent going forward. What we have done here is, of course, also to optimize our tax payments. And so for the next three to four years, you would see way lower cash tax rates. And then, of course, on a more long term basis, it will be around 23 percent, but it's simply to optimize cash flow. So it's not that you should expect that it has a sustainable impact on lowering the corporate tax rate that will be around 23 percent.

[00:56:09] Deborah Dunsire

And then on the impact on mental health, we're still seeing that there's a tremendous discussion about the impact on mental health. As society opens, some of that diminishes. We've seen in multiple places, a difficulty for patients to get in to see physicians, to be diagnosed. So Adrup, a Cuvier data in the US, suggests that there's a drop in patients and new patients coming into seek care by up to 40 percent in some categories. And so we would see that reverse. So I think it's going to be dependent on how much of the mental health impact that the pandemic has had based on isolation, concern about jobs, those kind of things, whether that resolves when the pandemic resolves or whether we see people coming through and requesting care and going through the first generic SSRIs. And so I think the dynamism we saw in the fourth quarter, we see as a return to a much more normal. We don't see that as sort of a wave coming through after the pandemic. It's a normal a normalization of patients seeing physicians.

[00:57:40] Operator

Next question is from Peter Sehested from Handelsbanken. Please go ahead. Your line is open.

[00:57:48] Peter Sehested, Handelsbanken

Thanks for taking my questions. I came a bit late to the call, so I apologize if they have been posted. So please just listen to the replay. But I have three, if I may say. Performance in Q2 to Q4 has actually shown positive growth rates in cost exchange rate terms. Is that a trend that you see going into 2021 as well? That was my first question. On the upcoming interim analysis; With the target samples to 255, it basically corresponds to that upon which the two prior studies were designed and they were designed with 85 per cent power and a five percent level. But I guess that you are probably using a spending function as your interim, which all else equal suggests that bar for efficacy is higher than we have seen in the first two studies. So my question is here is this. Is it clear, that the powerful is higher? Or conversely, can you confirm that you're using a spending function in data analysis? And secondly, with respect to adaptation. What is the effective I guess you're getting some sort of data exclusivity, but what is sort of the effective exclusivity period on this particular indication? Thank you very much.

[00:59:28] Deborah Dunsire

Ok. So Anders is going to start.

[00:59:31] Anders Götzsche

The annual growth you have seen in 2020 is more or less what we anticipate in 2021. That is with the assumption that only one generics in the market, if more generics enters, and that might be the case, then, of course, the negative growth can be accelerated because then you don't know what the second generic will have of pricing strategy and all the other stuff. But if it's the same one generic play, then we assume it will be more or less the same growth. Negative growth rates.

[01:00:09] Deborah Dunsire

Yeah. On the interim analysis spending function.

[01:00:13] Johan Luthman

Yeah. I mean obviously there is a spending with an interim analysis, but the way it's structured, it's not a major penalty for alpha hit if that's what you're asking about. The overall trial is slightly increased in sample size, 330. That's for many reasons. First of all, we like to make sure that we have a strong trial at the end to really make sure that if the drug works, we detect it. But it's not the big impact. The spending function is not that high. It's not a big impact on it. It's a handful of patients more basically. In terms of the corresponding data and sample size. Obviously at the interim, we have somewhat fewer patients than at the end of the study. But remember, I went through number of patients we had in the previous studies and those were split between different treatment times, etc.. Here we have a pooled analysis, which means that already at the interim we're going to have a pretty sizable cohort of about 150 subjects versus placebo or so slightly more than that. Even so, it's not a small sample size. And the effects we are after in terms of statistical details, I'm not going into details, but you can assume we're operating with similar assumptions.

[01:01:30] Deborah Dunsire

Right, and then there is the third question on agitation and exclusivity. Yeah, so there is data exclusivity, but we also know that that the compound patent is the strongest patent always. And while we defend our patents, I think we would still guide you to the 2029 compound patent for Rexulti.

[01:02:04] Operator

Next question is from Carsten Lønborg Madsen from SEB. Please go ahead, your line is open.

[01:02:10] Carsten Lønborg Madsen, SEB

Thank you very much for taking the time here. I have a little bit of more of a conceptual question left. If I look at Lundbeck's average R&D to sales ratio over the last 15 years, and it has, of course, jumped up and down, but on average, it has been 22.5 five percent. And on top of this, you have made several acquisitions. But even on the back of these investments, that it sort of feels like Lundbeck is not in tip top shape. Before you accuse me of being to bearish, then you are guiding for a relatively bleak outlook here in 2021. So my question is; longer term is 22 to 24 percent. Is that really enough to make Lundbeck an interesting case, not only the next couple of years, but also on the 10, 15 year horizon? That was the first question. And then secondly, I was just interested in hearing whether there are some Schütz patient differences in the trials we've seen

already, the 283 and the 284 studies, simply because when you look at the absolute responses, it seems like data is less impressive into a three versus 284 response much more in terms of the reduction in the scores.

[01:03:49] Deborah Dunsire

We are a company that keeps looking at building strongly forward. I think we've had a great success in the past with molecules that have come out of our internal pipeline, Lexapro and Trintellix, Cipralex, and with things that we've brought in from the outside. And we've had a sustained compound annual growth rate over the last, you know, I guess since 2007 or something, on 7,4 point percent. And we will continue to be able to do that in the future through a combination of the drugs that are moving through our own pipeline. And we have quite a robust Phase one pipeline and we're working with new biologics that will continue to yield an opportunity to bring new molecules forward. And then we will continue, as we have in the past, to make license's partnerships, acquisitions, to supplement the growth where we've been very successful in the past with the innovation acquisition, the Chelsie acquisition. So like almost every other pharma company in the world, we're built on a combination of both internal and external innovation. Anders, I'll hand it over to you on the ratio's.

[01:05:18] Anders Götzsche

I think I will not go into any kind of speculation in R&D to sales ratios for the next 10, 15 years. What we have said is that we believe that the next six to eight years will deliver a nice growth numbers. We also believe that we will see a margin expansion. We need a margin expansion over the after having invested heavily in Vysepti, as we said when we made the old acquisition, then you would see a substantial marketing margin improvement of both reported and core earnings. And I think it's important to emphasize that the core margin for this year is 25 percent and it will expand over the next couple of years. So that is what we are aiming for. And then another time we can look into data for the next 15 years.

[01:06:06] Johan Luthman

Yeah, maybe I can comment on The percentage is a little bit first. Obviously 15 years from now, things have changed tremendously and how we run trials, what we do and what populations, and you heard about our strategy when we go more to niches and rare diseases, that means that you have different clinical pathways. You have different requirements on the study. I wouldn't

say there are lower bars in any way, but sometimes smaller studies, more directed studies. So you can get more bang for the bucks, if I may say so, also for our R&D. I guess you're looking at study 283 and 284 and the graphs and you see that they look slightly different than the outcome there. For someone who's been in this business a long time with psychometric readouts like the DC Mice Score, this is what you normally see between studies. I think it's actually more encouraging to see that there's a robust treatment effect in both of those studies. The absolute difference is, yes, they are slightly different here. There's also the influence of, as we talked about, different countries and geographies that could also have an effect. It's well known in our semi-trials that you have country differences. And as I told you, we had seven countries in nine countries in the two different studies and that this is just basically what you expect randomly across two studies like this. The populations were aimed, inclusion criteria were aimed to be identical between the two studies. And that's also the third study we're running.

[01:07:58] Deborah Dunsire

And remember that the 284 is a post hoc subset analysis. Right. So the next question, unfortunately, needs to be the last one.

[01:07:58] Operator

So the final question is from Mark Edmund from SVB leerink there. Please go ahead. Your line is open.

[01:08:06] Mark Edmund, SVB leerink

Yeah, a couple of questions. Number one, can you just talk about your alpha synuclein and how it differs? Biogen announced that they had stopped theirs and obviously Roche had some disappointments last year. So just so we understand the difference in the products in the way that you approach it. Second, on borderline disorder, just give us a sense of how enrolment has been. I'm just trying to get a sense of how much demand there is for that type of therapy. I'm just trying to get an understanding of that market, you know, so that you can tease out if Covid had a major impact or if you believe everything is, you know, pretty exciting there as far as demand. And for Vysepti, is there any way you could just give us the actual number of patients that were on the product and a sense of, you know, was January stronger than December, which was stronger than the previous month? Just, you know, any type of trend from a patient perspective. Thanks.

[01:09:03] Deborah Dunsire

Right. So Johan is going to start talking about alpha synuclein and the borderline enrolment and then Peter will comment on Vysepti. But I will preface this by saying we won't be giving you actual patient numbers.

[01:09:19] Johan Luthman

So for alpha synuclein. Yeah, I understand your question because it was just a very recently Biogen announced that they were stopping that program. That's the new immune antibody. And it's actually a binder to the one to 10 domain residues of the ??? molecule, a very different binding domain than we are targeting with this one. We are actually at this C terminal domain with our antibody, which is mechanistically a very big difference. The Roche molecule is targeting about the same area as we are. So we're kind of in that broad range, more mechanistically. And as you may know, the Roche patina study showed some interesting data on the ??? score, particularly at the higher doses, and they showed also some effect on progression over time. So there are very different molecules, basically, and that's how we view them right now. In regards to borderline, yeah, that's a study that was hit quite a bit by the pandemic, and so we had pretty and it was also at an early stage of the start up of the trial. Otsuka and we have jointly worked very hard in trying to regain the momentum of this study. We are not really clear on the timelines. We are talking about delays, obviously. We don't know exactly how long delays we're going to face because the efforts done recently seemed to have an impact on the study. So we're gaining momentum. But with recent events in the US and the studies, the US based one, it's very hard to tell really where we are.

[01:10:59] Deborah Dunsire

And I think in terms of using the study to think about, you know, the ultimate size of the market and demand, I don't think it's going to give you a clear picture. Borderline is a very difficult disease. There's nothing approved for it. It's almost a diagnosis of exclusion and a difficult patient group to treat. So this is, I think, a very it's a very challenging bar for the study, but a high unmet need. Peter, do you want to comment on Vysepti?

[01:11:31] Peter Anastasiou

Yeah, thanks for the question mark and as Deborah said, won't give specific information on patients, but I will point out what we said in the release, and that is that each quarter we have doubled the amount of demand and volume that we've been on the market. So a good growth trajectory, albeit off of a lower base. And as we know, in the fourth quarter, as we were starting to get some normalcy, as we were starting to get patient volumes come back, one might even argue that there was a little bit of an acceleration in the fourth quarter, as you can see on the demand curve that Deborah showed in the deck. So all that is progressing well. The types of patients we are typically getting are like in many launches, a little bit sicker at the beginning because people are trying new therapies on partial responders. I think it's particularly true here. Because of the pandemic, the risk benefit ratio of patients who are willing to come out and get treatment tends to be those patients who are a little bit sicker. But as doctors are getting experience and the drug is delivering even in the sicker patients that have been unresponsive or partially responding to other therapies, they're getting good results. We're getting very good feedback from both the patient and the physician community. So I expect as the product becomes more familiar with customers, as patient volumes continue to come back, that it will move earlier in the algorithm.

[01:12:57] Mark Edmund, SVB leerink

Are these patients on CGPR already?

[01:13:01] Peter Anastasiou

Some yes, some have been, certainly some have been I mean, almost everybody has been on a previous preventative or one of the older therapies that's required by payors. But, yes, we've received patients who have tried dissatisfy and have had dissatisfaction outcomes with other CJRes.

[01:13:25] Deborah Dunsire

So unfortunately, that I will have to call the end of the meeting as we have another meeting backlog onto this, so thank you, everybody, for your interest. And again, I'll just summarize by saying I'm so proud of the year that Lundbeck delivered in 2020 and we look forward to continuing to grow the business in 2021. Thank you.