Novartis AG

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Richard Vosser Analyst

Welcome to the Novartis presentation at the 42nd JPMorgan Healthcare Conference. I'm Richard Vosser, European pharma analyst with JPMorgan. It's my great pleasure to welcome Vas Narasimhan, the CEO of Novartis today. Before I hand over to Vas, I'll just everyone, we're going to take Q&A after Vas' presentation in this room. Vas, welcome to the conference.

Vasant Narasimhan Executive

Thank you, Richard, and great to be here today. Always wonderful to be at JPMorgan to start the year and give all of you an update of where Novartis is and where we're going. And what I'd like to do is give you an overview of a little bit of our journey over the last few years and then talk about the future and I think pretty exciting prospects for us as a company. Now when you look at our overall profile, in summary, we think we've come to a place where we really present investors an attractive story, a focused strategy with 4 core platforms -- 5 core platforms, 4 core TAs, strong capital allocation approach. We highlighted at our recent R&D Day, a commitment to grow 5% through 2027 as well as 40% plus margins really putting us at the top end of the peer set.

A robust pipeline with 10 Phase III positive readouts in 2023, and we'll go through that, as well 83 projects in the pipeline. We've slimmed down the pipeline, but we think the pipeline now is really filled with attractive assets and then a leader in ESG. We're a leader in many of the key indices and we take it seriously to continue to do the right things to contribute to society.

Now when you look at Novartis over the last decade, we've really now completed what was a substantial transformation of the company. In 2014, we were a diversified healthcare group, spanning a large number of sectors and progressively with the exit of Consumer Health, the exit of Alcon, the exit of Sandoz, each is now independent companies with attractive spins to shareholders that were tax neutral.

We end up as a focused medicines company today entering 2024. And when you look at that transformation and how it's impacted our financial profile, our margins have substantially improved to now 37%, marching up to that 40% as well as if you just look at the free cash flow generation of our business now at $11 billion for 3 quarters. We expect a strong quarter 4 as well, 32.4% of sales now getting into free cash flow. So it really shows that we are doing the right things that not only improve the strategy of the company, but also the financial return profile of the company. And when you look at our financial performance over the last 5 years, in spite of LOEs, in spite of challenges, we've grown sales at 7% on our Innovative Medicines business.

We've grown our core OpInc at 14% on that IM business and as I've mentioned, that core margin up 790 basis points. So showing that we can deliver that steady financial performance consistently over time now since 2018. Now as we look ahead, we remain very committed to our focused strategy, which we outlined really 2 years ago along the therapeutic areas platforms, 4 priority geographies with the big goals have raised our presence in the U.S., of course, delivering returns and being a leader on foundations and continuing to be strong on operational excellence. We continue a big commitment to culture. We continue to believe culture drives performance in the long run, and I think we're seeing that now start to come through in the operating performance of Novartis.

And we also stay consistent with our approach to capital allocation with a balanced approach investing in the business. We fully invest in R&D as well as our manufacturing and other capital needs and continue to do value-creating bolt-ons, about $33 billion over the last 5 years, while consistently growing our dividend in Swiss francs independent of the various spins that we've made, we've committed to continue to grow that dividend and a consistent approach to share buybacks. We have a $15 billion share buyback now ongoing following the past $15 billion share buyback we recently completed. And we've already talked about the exits that we've done in a shareholder-friendly way. We've also been active on the BD&L and M&A front.

And I wanted to highlight some of the deals we announced this morning. Over the course of the last year, we did about 15 strategic deals totaling around $600 billion, a few we announced this morning, Argo Biopharma, a partnership with an siRNA company where we've now brought in 3 different assets that we have, either options or will be licensing and developing within cardiovascular disease. We recently announced the partnership with [CKD] with an inhibitor in atrial fibrillation. This morning, we announced the acquisition of Calypso Bio with an anti IL-15 in immunology. So very excited about bringing that into our immunology portfolio.

We also announced our partnership with Isomorphic Labs on the AI front. That's a Google DeepMind company working on developing novel -- using AI to prosecute drug development

targets. So a broad range of deals. We'll continue to really look at those yields in that sub $2 billion, sub-$1 billion space to continue to build out the portfolio. Now turning to our growth profile.

We outlined at a recent R&D Day, our belief that we can grow at 5%, that's an upgrade from the 4% previous CAGR from 2022 to 2027, 40%-plus margin. That's driven that by primarily the growth drivers and the pipeline outpacing the LOEs that we have with Entresto, Tasigna and Promacta. And I want to get into a little bit more detail as well on this individual peak sales for some of those assets. And then when you look at the longer term, we believe we have the pipeline and portfolio to grow 5% to '27 and then mid-single digit and beyond. A broad range of de-risked in-market brands that you can see listed here, a number of pipeline assets, as I mentioned.

I'm going to walk through the 10 positive readouts. Just this morning, we announced Scemblix 1 in the frontline setting, hitting all primary and secondary endpoints against standard of care, choice of TKI Gleevec or second-generation TKI showing again the kind of assets that we're able to bring forward out of our portfolio. So turning into our in-market brands. We outlined at the recent investor meeting, our peak sales in each one of these in-line assets, upgrading particularly the guidance on Entresto now to $7 billion of peak sales, maintaining our Cosentyx at $7 billion, upgrading Kesimpta, with a belief that medicine can now get to $4 billion plus. Kisqali is solely in the metastatic setting, not in the adjuvant setting, we'll get to that on the next slide, $4 billion.

And then Pluvicto now as part of our radioligand platform, multibillion-dollar potential. And of course, Leqvio, our SiRNA in cardiovascular disease also with a multibillion-dollar peak sales potential. And I think what's really exciting about our portfolio is that many of these assets have now a next leg coming up with the recent data readouts. When you look at Cosentyx that $7 billion, but we continue to have, I think, some pretty exciting recent launches with Cosentyx. We launched Cosentyx IV, which is off to a very strong start in the United States.

We also had the approval of Cosentyx in hidradenitis suprativa, which gives us another exciting indication to move forward in dermatology. With Kisqali, we had the readout -- positive readout of the adjuvant indication, and I'll talk more about that. Pluvicto with multiple opportunities to move into earlier lines of therapy to add another multibillion on top of the multibillion we've already guided to. And of course, Leqvio with this outcome studies as well as moving Leqvio into the frontline setting as well gives an opportunity to drive stronger growth. So taken together, when you look at our strategy from a therapeutic area standpoint, we've defined specific diseases that we want to win in.

And these are diseases that we manage centrally now at the company aligned in R&D through commercial. And we, of course, constantly are thinking about which diseases we need to add or exit. We have anchor brands in each one of those therapeutic areas, which give us strong commercial, medical affairs and development presence in those TAs. And then we have multiple assets in those TAs that we can bring forward and continue to leverage that global commercial R&D and medical affairs infrastructure.

So now I want to turn to what I think was a banner year for Novartis in R&D. Over the course of the year, we had 10 positive Phase III readouts or data presentations on assets with

significant potential. These are all assets now that are either recently approved or in the process of getting filed over the course of this year. And we think can give more confidence not only in that 5% out to '27 but our belief will grow mid-single digits into the 2030s. I won't get into some of the earlier -- mid-stage pipeline and emerging Phase III that would read out in the '25-'26 time frame.

I think it's a great opportunity to review for all of you kind of these core assets. So starting with Kisqali at ASCO, we showed the Phase III NATALEE study, which demonstrated consistent benefit, and then we updated that at San Antonio Breast -- showing that -- Cancer showing that we had consistent improvement in iDFS in both Stage II and Stage III with a positive trend in OS. I can say now today, we have completed the filing of Kisqali in the U.S. following the file in EMA with a priority review voucher, we would expect to be able to bring this forward in the course of 2024. Again, a very strong profile overall, no new safety signals, a compelling profile that allows this medicine, we believe, to be used not only in high risk like the currently approved therapy, but also an intermediate risk.

I'd say that Kisqali is doing extremely well in the metastatic setting. Right now, we are leading an NBRx share in the U.S. with a steady progress in TRx as well. And then we also see multiple markets outside the United States, Kisqali is getting to the point in the metastatic setting to being the market leader. On Pluvicto, we read out the PSMAfore study, which showed robust efficacy, great safety and efficacy profile overall.

We nearly doubled or doubled the median rPFS, very consistent benefit, whether it's in patient benefit with time to worsening, the FACT-p or the BPI-SF. Overall, I think a really nice trial to support the broadened use of Pluvicto. We will be working now to get to the next information fraction cutoff of 75% event in the early part of this year, which we hope will then allow us to move forward with the filing with FDA. As a reminder, this is a study with really high rates of crossover of over 80%. And part of that is because the medicine is doing so well right now in its current line post chemo in the U.S.

and in Europe. So we guided to $1 billion of -- roughly $1 billion of sales in '23, and we expect that March in its current indication to continue forward. On Friday, we announced that Pluvicto, new manufacturing site in Indianapolis is approved, giving us yet another large-scale manufacturing site. It's our largest in the world. And that allows now for radioligand therapy, we fully supply unconstrained both for Lutathera, Pluvicto and our pipeline.

Now moving to Fabhalta. This is iptacopan, our factor B inhibitor, which showed outstanding data in the APPLY and APPOINT studies for efficacy and safety in PNH. We received approval in December for Fabhalta in the U.S. with a very attractive label, which allows us to be both frontline, add-on or a salvage therapy for these patients and now are in the active approach of launching this medicine in the U.S. with plans then ultimately to bring it around the world.

I'm very excited about this data. And I think it demonstrates that we can raise the standard of care for diseases like PNH with an oral therapy twice a day with an attractive profile. Iptacopan demonstrated later on, last year, positive data in the C3G trial, a rare kidney disease, but again demonstrating that it had a clinically meaningful and statistically significant impact on proteinuria reduction in this patient population. Again, a very good safety profile consistent with what we saw in the PNH setting. We'll be presenting this data later this year,

but this will be the next leg for iptacopan to continue to expand across a broad range of indications.

We have ongoing studies with iptacopan in other indications such as membranous glomerulonephritis as well as atypical hemolytic uremic syndrome amongst others. But importantly, with iptacopan, we also read out positively in IgAN, which gave us the third positive readout on this medicine in a single year.

Now we have 2 assets with positive readouts in IgAN over the course of 2023, both iptacopan and atrasentan read out positive. We are now in the process of filing both of these medicines in the U.S. and then eventually around the world. And this allows us to really build out a next leg in our cardiorenal portfolio having multiple assets with iptacopan, with atrasentan to give patients with kidney disease, the next better therapies that they, of course, all need to avoid transplant and some of the other adverse consequences of renal disease. And then in the mid-stage pipeline, we continue on our Phase III study of Zigakibart, which is a monoclonal antibody that we're currently evaluating, and that would give us yet another asset within the IgAN portfolio.

We also read out positive data on remibrutinib. This is our BTK inhibitor in the REMIX-1 and REMIX-2 studies in chronic spontaneous urticaria. Here, the data demonstrated we would argue near biologic-like efficacy with a very good safety profile without any signals within liver disease -- with liver signals of any concern. This gives us the opportunity to not only move forward with a submission in 2024 with remibrutinib, but also to take remibrutinib now into a further range of immunology indications. While we do have the multiple sclerosis studies ongoing as well, we see the opportunity to expand this medicine in multiple immunology indications given it's strong safety profile as well as high efficacy.

So we're very excited to provide updates on those Phase III starts as we make them over the course of 2024. Next, turning to our radioligand therapy slide and this one was a little bit under the radar but something we're quite excited about. Lutathera readout positive in its Phase III NETTER-2 study. This is in the frontline setting in combination with high-dose Sandostatin, gives us the opportunity to take this medicine, which is already a $500 million plus medicine in later-line therapy of neuroendocrine tumors and move it into the frontline setting. What's exciting about this in the U.S., we already have a broad label that allows us for the medicine to be used in that frontline setting.

We just didn't have the data yet. So this is the medicine that met its primary end points. We will be presenting this data at one of the ASCO satellite meetings in the first quarter of this year, so at ASCO GU. And we believe this gives us an opportunity now to have, given our long history of Sandostatin LAR in the frontline setting, a next-wave medicine that redefines the standard of care for these patients and give us the next leg of growth within radioligand therapies and within that whole treatment of neuroendocrine tumors.

This is also a medicine now we're taking forward in small cell lung cancer in combination with PD-1 inhibitors. And we also have ongoing studies in glioblastoma multiforme to give us the kind of next leg next to Pluvicto for radioligand therapy. One of the things we did highlight in our R&D Day was a very strong portfolio of RLTs behind these 2 frontline medicines.

And let me turn to Scemblix. So this morning in the slide we just updated right before my presentation, we announced that in the ASC4FIRST study, Scemblix hit its primary and secondary endpoint, clinically meaningful and statistically significant improvements in MMR rate versus investigator choice TKIs, Gleevec or second-gen TKIs, safety -- favorable safety and tolerability profile. I mean, from our perspective, as the company that brought Gleevec to the world in 2001 and redefined the opportunity to treat patients with targeted therapies in cancer, then bringing forward Tasigna to now once again raise the standard of care in the frontline setting with an oral medicine, I think, is one of the triumphs of Novartis' scientists and Novartis' chemistry. So we're very excited about this data. This will build on our third line data ongoing Phase IV studies in the second line, both mono and in combination and now in the frontline setting.

We think we'll make this medicine special, not only high efficacy, but a very strong safety profile. So this is obviously data we'll be presenting later this year at an upcoming medical congress with a submission plan in 2024 and a significant medicine, we think, now for Novartis. So thinking together, we expect 15 key submissions in our core therapeutic areas by 2027. You can see here the full range, I talked about many of them. One of the ones I didn't talk about, what we're excited about is ianalumab, which is a CD40 ligand, BAFF receptor CD40 ligand inhibitor, so we think pretty exciting medicine as well within our immunology portfolio, amongst others.

I did want to say a word on our next wave platforms that we think can drive our long-term growth, and you see a lot of BD&L activity from Novartis on this front. Radioligand therapies, we've talked about CAR-T in immunology you heard in the last presentation, but we also believe that we have a unique asset with our YTB medicine that has the opportunity to deliver significant clinical outcomes for patients with immunological disease. So we continue to expand out our clinical trials as well, and we think this will become a very significant space. We've already presented our first 3 patients in treating SLE at a congress last year and demonstrated, I think, very, very compelling results consistent with what the German investigators have found and they, of course, are now at 18 months, 2 years showing full remission in these patients. And lastly, siRNAs not only in cardiovascular disease, also in neuroscience.

We did DTx earlier last year. And then I mentioned Argo Biopharma giving us, I think, more and more assets within siRNA, ASOs alongside our partnership with Ionis as well, giving us, I think, a pretty attractive early portfolio to use these medicines in treating neuroscience and cardiovascular disease. So in closing, I just wanted to also highlight our strong commitment within ESG, something we take seriously at the company. We've really repositioned Novartis as one of the leaders, both in terms of how we create value for society with the work we do, but also ensure whether it's in the environment ethical standards or other enablers, we're doing right things for the world and how our company operates. And just to close with the story, I feel a lot of pride in as a public health physician, leading an incredible company like Novartis, our commitment to malaria spans decades.

We took Nobel prize winning work from a Chinese scientist and brought the world Coartem. We are now at over 1.2 billion courses of Coartem provided to patients around the globe at no profit to Novartis including 400 million children. We've created formulations and new

programs. We also have the most of the malaria pipeline in the industry.

And then we recently announced we'll be starting a study to be able to treat infants, new born infants from malaria with our medicines. I think this is the kind of work we want to do alongside the other work to demonstrate we're a company that really drives health improvements for the planet.

So in closing, coming back to where I started. A focused strategy, clear and attractive growth prospects with assets that can drive that growth a robust pipeline, demonstrating that we have the R&D engine with 10 positive readouts in 2023 and an ESG leader doing the right things for the world. So look forward to taking your questions, meeting with many of you over the course of the day and then keeping you updated on Novartis over the course of this year. So thank you all very much.

Richard Vosser Analyst

Thanks, Vas. We're moving to the Q&A portion. So if you have a question, I think, raise your hand, otherwise maybe I'll kick off. And you highlighted this raising of your growth rate. So maybe you could just talk about the pushes and pulls around that and how confident you are, what could deliver more growth than you expect?

What are the risks?

Vasant Narasimhan Executive

With coming out of 2022 or as you're aware, we did a pretty significant restructuring of the company, focused down. In 2023, we saw a significant rerating of how we were performing our in-line brands as well as all of these positive pipeline readouts, which led to the 3 guidance upgrades we gave over the course of the year. So a lot of ways that 4% to 5% is just mathematical from that step-up that we saw in 2023 and I think that's really underpinned by those assets I talked about. Those big growth drivers as well as now having confidence that Kisqali, Pluvicto, iptacopan, Lutathera and Scemblix will all come through in that period alongside some of deals we did like the Chinook acquisition. That gives us that confidence of 5% plus is really within reach.

And obviously we want to do even better. I think for us, the next part of the story, and we discussed this in London when we were together is really giving more confidence in that '28 to '33 period. And I think proof like Scemblix today, Scemblix is a drug that is not exposed to it's an orphan disease. So we have a runway through the 2030s on a market that historically has delivered $3 billion to $5 billion medicine. So I think we need to get a couple of more of those, I think, to give everyone more confidence on that next wave.

We have it. We also have to demonstrate to all of you.

Richard Vosser Analyst

Next question over there.

Ruojing (Angus) Liu Attendee

Thank you. Angus Liu, Fierce Pharma So just looking at the summary, [BD] summary, slide. It

struck me that I think Novartis right now, the only major oncology player that hasn't done any [deals] in ADCs. So I was just wondering because I understand you have some ADCs within your pipeline and it is not your priority technology, but just how did you resist the temptation?

Vasant Narasimhan Executive

We have a long history within research of ADCs, but we have not been successful, I think, to be clear. We -- a part of our focused strategy is looking at places where we think we can create long-term sustainable leadership. And we are investing in radioligand therapies and we believe that the therapeutic index on radioligand therapies when you find the right target, gives you a pretty wide window to get a therapeutic effect without some of the safety issues. We saw that with Lutathera. We saw that with Pluvicto.

I didn't highlight it, but I think Richard saw it in London behind Pluvicto we have multiple actinium-based compounds, which give us the next wave of assets within -- in the prostate cancer space. We have 3 or 4 other targets [indiscernible] folate bombesin, integrin all in the clinic.

And then when you think about some of the successful ADCs, we now are advancing HER2 and HER3 RLTs into late preclinical, and we hope to get into the clinic with the belief that, as you all know, some of these ADCs have some pretty extreme toxicities. We saw that in the data at ESMO, I mean, you have Category 5 toxicities, which are deaths. And if you can avoid that with radioligand therapy, but still get that high efficacy and given we have completely unconstrained supply now with all the investments we made, we think that's a better place to focus our capital versus overindexing on ADCs at the moment.

Ruojing (Angus) Liu Attendee

Maybe some build there on the radioligand therapy and around Pluvicto, what's the physician response and how wide adoption can you get given they are quite technical to give within the hospital setting?

Vasant Narasimhan Executive

It's a good point, especially as we move to the pre-taxane setting and then our goal ultimately to move into the hormone-sensitive setting with the PSMA addition study. We will need to move from about 300 centers today that can administer Pluvicto, we think to around 500 and continue to build out capacity within the community, both in urology as well as in nuclear medicine to provide the therapy.

So that's a big, big focus. I think that will be a constraint early, but then eventually what we see is in general patients and physicians have the experience of a 4 to 6 cycle drug that gives you high efficacy and a nice safety profile relatively speaking. I mean if you look at the PSMAfore data across all comparisons with all of the caveats, certainly, our data looks pretty good versus ARPIs.

And so I think -- from a safety standpoint, I think one of the trends in cancer care right now is that patients not only want high efficacy, but they want more tolerable drugs. They want drugs that don't mean a complete sacrifice in terms of how they're living their lives. And I

think we can deliver that with Pluvicto.

Richard Vosser Analyst

Got a question over here? Question [Morten]?

Unknown Attendee Attendee

[Morten Castelo] Copenhagen, Denmark. A market leader such as Novartis, can you talk a little bit about what's the precision medicine and how you're incorporating that into the pipeline, because I did not really see that on any of the slides?

Vasant Narasimhan Executive

Yes. I think on precision medicine, we've taken the approach. We did have the large investments, we even had divisions within Novartis that were generating precision medicine tests. We've largely divested those, and we take much more of an asset-based approach that based on a given asset, we will partner typically with precision medicine companies to develop the relevant biomarkers, et cetera, or try to bring those tests in as we get into translational medicine.

We realized some of our peers make very large in-house internalized that capability. We believe that doing it more through a network of partnerships that makes sense. It's very relevant within the world of RLT, not really the typical precision medicine, but you need a diagnostic always next to the RLT to be able to identify the patients. And while we do have internal capabilities for both PET and gallium-based diagnostics, we take the approach of using a network of partnerships, and I think that's how we do things going forward.

Richard Vosser Analyst

We've got another question over there.

Unknown Attendee Attendee

Thank you for great presentation. [indiscernible] from RadioMedix. What is your vision about other types of alpha-emitters in radioligand therapy?

Vasant Narasimhan Executive

Yes. It's a very good question. And of course, I think, as you heard from the previous presentation, RayzeBio being an alpha-emitting company. Now I think for those of you who want to spending a lot of times during radioligand therapy science. Beta emitters and alpha emitters have very different profiles.

Beta emitters have a broader, more diffuse radiation, less concentrated on the target. Alpha emitters are very potent at a short distance and have less potency as you move a little bit further away. The other things we see with beta and alpha emitters, which is the absolute key, is xerostomia. So what knocks out the salivary glands and then also with respect to renal and bone marrow, can you find a clear safety profile in which to dose up. So to date, alpha emitters, I think the verdict is still out.

We have our own alpha emitters in-house. We've also licensed them in. We acquired some with Endocyte as well. We are developing alpha-emitters both on PSMA as well as other targets because we think we need to have that. There are other alpha emitters other than actinium, as you surely know as well, which we also evaluate.

But the question for us now is, in which settings would beta emitters make the most sense and in which settings would alpha emitters make the most sense? Can you give alpha-emmiters after beta-emitter? So right now, our actinium PSMA lead program is in a post-Pluvicto setting. So patients who progress on Pluvicto or beta-emmiter, then you move them on to an alpha emitter. So these are all of the scientific questions, I think, that have to get clarified over the coming years to really know which emitter is going to be better for which setting.

But there's no question you need both in your portfolio to be a leader in RLT.

Richard Vosser Analyst

Maybe just before the next question, maybe logistics as well and half-life. I mean maybe you want to touch on that some of the differences that you found with the Pluvicto on the logistics.

Vasant Narasimhan Executive

So first, I would say this is not for the faint of heart. If you have no inventory -- if you think about all the companies that all of you are following we live in a world, we typically have 6 months of inventory or 1 year of inventory, so that if we have supply disruptions, you just no issue, you have the inventory at your hand. Here, we have no inventory on these medicines. In the case of Lutathera, it's 3 to 4 days. In the case of Pluvicto, we have 5 days and you're in a very short window to get the medicines to patients.

We've now successfully built up through our supply chain the ability to get these medicines to patients. And now we target 1 day before administration that's our goal to get the medicine. But it's been a 3-, 4-year journey to build out that supply chain. So to your point, Richard, alpha-emitters, beta-emitters have different profiles, depending on how they're formulated in terms of time, but I would say regardless as a company, you have to be able to navigate between 4, max 6 days between production run release and then getting it to the patient anywhere in the globe.

Unknown Attendee Attendee

Edmonds from [Ulti]. Had a quick question on your cardiology franchise. Obviously, with Entresto coming off and [Questran] finally starting to really kind of see some traction. Could you just talk about where you see Novartis' cardio and kind of capital deployment? And how you're thinking about the strategy?

Vasant Narasimhan Executive

First on Entresto, different time lines in different parts of world. We have the appeal ongoing in the U.S. We continue to guide to a mid-2025 for forecasting purposes LOE for Entresto in the U.S. In Europe, we have till 2027. In China, it will be in the '24-'25 time frame.

In Japan, where the medicine is doing extremely well, we have till 2033 give or take. So obviously, a lot of room, which is why we upgraded Entresto to $7 billion. On Leqvio, slow and steady uptake, but we do see that steady trend now continuing to climb in the U.S., in Europe, but we also see very strong update in China. And we also see now the opportunity in Japan to bring Leqvio forward in a pretty exciting way, so that's next. And then on the pipeline side of things, Lp(a), of course, pelacarsen is now on track, continues to be on track for a readout.

And that's going to be, I think, the next wave for us within cardiovasculars to get that Lp(a).

And then behind that, the deals that we're doing within siRNA on the one hand. And we continue to believe getting to once yearly dosing on HMG-CoA reductase, on PC SK9 on angiotensin II, those are the deals we just announced this morning give us an opportunity for next wave, especially we'll see how IRA unfolds, but certainly on a race to get a next gen Leqvio there before IRA hits. So that's a big, big priority. And then you've seen also some of the activity we have in atrial fibrillation as well. So a big focus as well within research on trying to get this next wave of assets forward.

Unknown Attendee Attendee

And did you learn anything kind of from -- the question, I mean, obviously, you bought medicine company. I don't think the market developed as fast as you thought. Obviously, you had to put a lot of work into it. Is that the way you kind of look when you think about the future of cardiology, it is these markets with innovative medicines that are -- you have to develop. And that's really going to be the next drive is bring the innovation and then create the markets?

Vasant Narasimhan Executive

Yes. I think it is a challenge when you think about IRA and cardiovascular disease. There's no question because these markets take time to develop. Entresto took 7 years, 6, 7 years before we hit a strong inflection point. Certainly, with Leqvio we are hoping to get that to happen faster.

If you have a 9-year pseudo genericization, then on the other you're on a tight, tight time line. Part of the -- our strategy, again flex the siRNAs, ASO-related technologies. And we continue to be hopeful that we can shape both the IRA generally to move from 9 to 13 but also specifically within genetically targeted therapies, there's bipartisan legislation out there to try to get the legislation to recognize that siRNAs ASO should be viewed differently than typical small molecules. And that's a huge priority for us as a company.

Richard Vosser Analyst

Maybe on IRA, it was mentioned the -- or you mentioned the LOE for Entresto but it's also is one of the first drugs on the IRA list. So maybe you could tell us how you're seeing that negotiation, if there's anything -- or what's coming?

Vasant Narasimhan Executive

I'm not sure I'd characterized the real negotiation. We've submitted a lot of documents, and we continue to submit our case for why we believe Entresto is unique and should -- the value

should be properly recognized. So that's why we also guide that, look, the LOE is going to happen somewhere between '25 and '27 and also probably in '26 time frame you're going to have a price set on this medicine in any case. I think some of the interesting dynamics on Entresto for just understanding the IRA legislation, this is a medicine where we give significant gross to nets anyway. And so depending on how you interpret the legislation, we no longer are going to give those gross to nets to Part D plans and instead give them to the government, then it's a net neutral proposition.

And I don't know if the government really has thought through yet how it's going to manage this. And I think that's something that we'll be watching, I mean the whole sector has to watch because, in our view, it should not be stacked on top of rebates we are already providing these PBMs. Rather, it should be in lieu of in which case on highly rebated drugs, it could be neutral, right, depending on the situation.

Richard Vosser Analyst

Makes sense. You mentioned -- we got one question over there.

Vasant Narasimhan Executive

I guess we didn't give you an interview, I guess, so we're going to do it here.

Unknown Attendee Attendee

You better be. I think you guys -- the team was kind of put on spot during the R&D Day when the FDA about that CAR-T investigation. After going through that FAERS database, Kymriah appeared to have the most T-cell lymphoma cases. I know given the various limitations of the database, I was just wondering how you think that might -- that perceived imbalance a higher rate of T-cell lymphoma will affect the next wave of the T-Charge and the next wave of T cell therapy setting [indiscernible].

Vasant Narasimhan Executive

It's a good question. And I think we have to take it seriously. Just to be clear though, I think what FDA is specifically looking for is integration events. So are these cancers -- so in general, in these patients who have DLBCL, FL-related cancers, they do have high rates of recurrence because you are conditioning the bone marrow. And so when you do bone marrow conditioning, you do increase the rates of cancer recurrence, hematological malignancies in these patients.

It's sort of a consequence of that. The question is when you use lentivirus, are you seeing integration events that are pro cancer. And if you remember, even at the first Kymriah AdCom many years ago, that was a big question. I can say within our assessments, we don't see integration events within Kymriah. I don't know about the other companies.

And I think certainly with YTB within immunology, we will have to keep watching carefully as we take that into a range of immunological diseases, we see those integration events. I think the real question now for CAR-T and immunology is how early are you going to be able to go. I mean, these results are staggering. When you talk to patients and you hear the stories of patients who are in the final stages of some of these immunological conditions and if

complete remissions in 3 months, it's something you just don't see in medicine.

So amazing results right now restricted to very late-stage patients in these diseases. The question is, can we demonstrate the safety to allow us to go earlier. Can we reduce conditioning so that it's less onerous so you reduce the rate of some of these cancers, could you use bispecifics, trispecifics, other approaches to get similar results? I think that's where the next wave of effort is going to have to be to really enable more patients ultimately to benefit for these type of therapies.

Richard Vosser Analyst

You talked about the rollout of Leqvio in China, maybe you could give us an update on how the China business is going and what the growth potential is there. I mean there's been some problems with obviously the Chinese looking at -- and doctors not prescribing drugs.

Vasant Narasimhan Executive

Yes. Overall, in China, we set out a goal back in 2018 to double the business. We're on track to do that. So approaching a $4 billion business within China, second largest for the company, growing in the high teens. Entresto growing extremely well.

Cosentyx. Now we have Kisqali approved. So a lot of growth drivers in China. With Leqvio, it's been very interesting to see that within the private market, we're seeing self-pay for this medicine. And it does point to the opportunity you have when you have such a large middle class that you can have self-pay opportunities with medicines like this.

So overall, we're optimistic on China. I think in order to win in China, you have to be able to have the commercial execution to ramp quickly and then manage well when you do get into the value-based pricing system that you can manage the decline. So I don't believe that this will be like genericization events in the U.S. I think you can manage the decline in a thoughtful way, but that's a lot of the work that you have to do, I think, in the market.

Richard Vosser Analyst

Excellent. I think we're out of time. So thank you very much.

Vasant Narasimhan Executive

Thank you all very much. Wish you a great conference.