2022 Q1 results presentation and transcript

2022 Q1 results presentation

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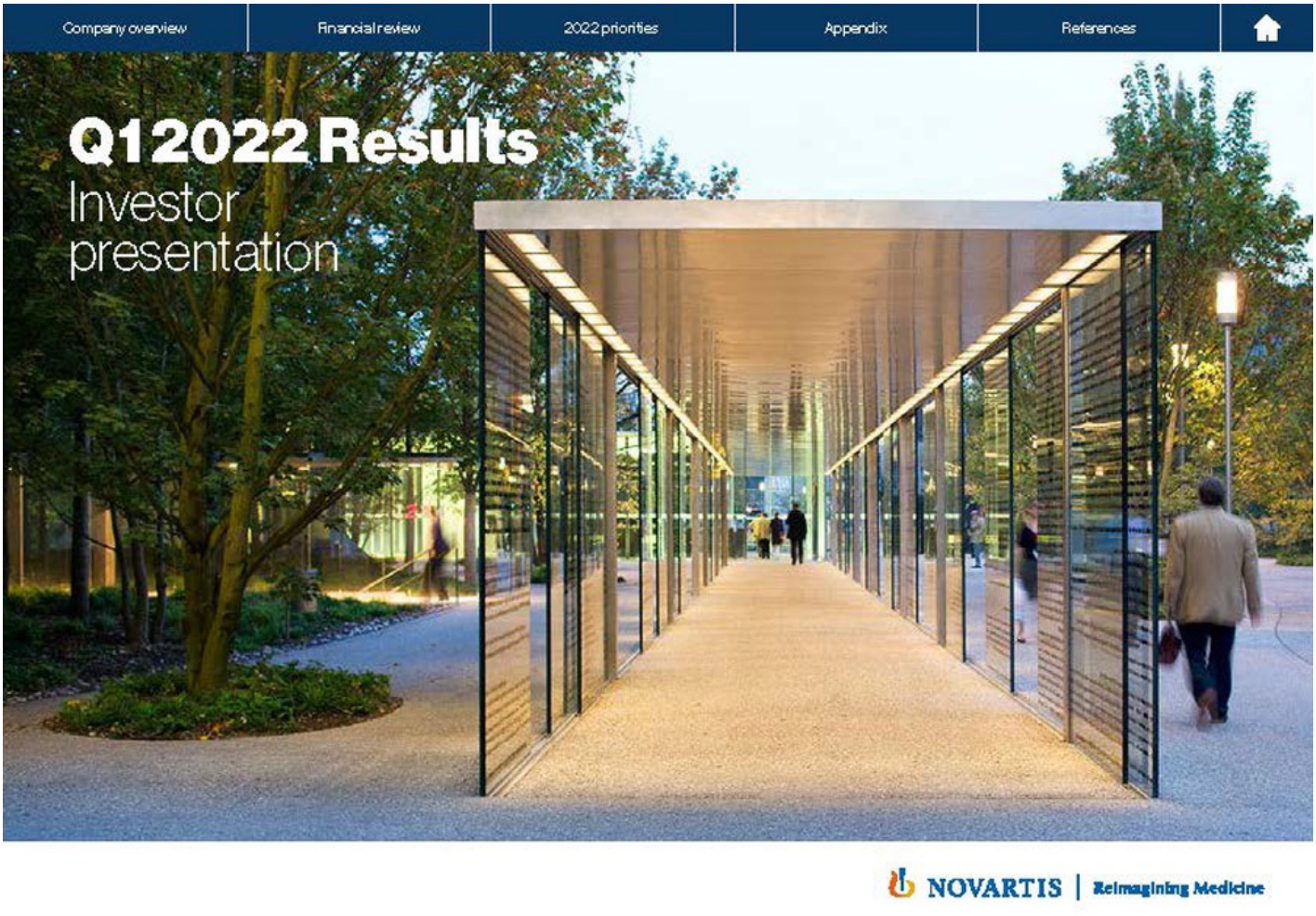
Transcript

View the 2022 Q1 results presentation and read the transcript slide by slide

Slide 1 – Samir Shah, Global Head Investor Relations



Thank you very much, everybody, and good morning and good afternoon to all participants. Thank you for joining us today for Novartis' quarter 1 2022 results.

Slide 2

Disclaimer

This presentation contains forward-looking statements within the meaning of the United States Private Securities Litigation Reform Act of 1995, that can generally be identified by words such as "potential," "expected," "will," "planned," "pipeline," "outlook," or similar expressions, or by express or implied discussions regarding potential new products, potential new indications for existing products, potential product launches, or regarding potential future revenues from any such products; or regarding potential future, pending or announced transactions, regarding potential future sales or earnings of the Group or any of its divisions; or by discussions of strategy, plans, expectations or intentions; or regarding the Group's liquidity or cash flow positions and its ability to meet its ongoing financial obligations and operational needs; or regarding the strategic review of Sandoz; or regarding our commitment to net zero emissions across our value chain by 2040; or regarding our new organizational structure. Such forward-looking statements are based on the current beliefs and expectations of management regarding future events, and are subject to significant known and unknown risks and uncertainties. Should one or more of these risks or uncertainties materialize, or should underlying assumptions prove incorrect, actual results may vary materially from those set forth in the forward-looking statements. You should not place undue reliance on these statements. In particular, our expectations could be affected by, among other things: liquidity or cash flow disruptions affecting our ability to meet our ongoing financial obligations and to support our ongoing business activities; the potential that the strategic benefits, synergies or opportunities expected from our new organizational structure may not be realized or may be more difficult or take longer to realize than expected; the impact of a partial or complete failure of the return to normal global healthcare systems, including prescription dynamics; global trends toward healthcare cost containment, including ongoing government, payer and general public pricing and reimbursement pressures and requirements for increased pricing transparency; uncertainties regarding potential significant breaches of data security or data privacy, or disruptions of our information technology systems; regulatory actions or delays or government regulation generally, including potential regulatory actions or delays with respect to the development of the products described in this presentation; the uncertainties in the research and development of new healthcare products, including clinical trial results and additional analysis of existing clinical data; our ability to obtain or maintain proprietary intellectual property protection, including the ultimate extent of the impact on Novartis of the loss of patent protection and exclusivity on key products; safety, quality, data integrity, or manufacturing issues; uncertainties involved in the development or adoption of potentially transformational technologies and business models; uncertainties regarding actual or potential legal proceedings, investigations or disputes; our performance on environmental, social and governance measures; general political, economic and business conditions, including the effects of and efforts to mitigate pandemic diseases such as COVID-19; uncertainties regarding future global exchange rates; uncertainties regarding future demand for our products; and other risks and factors referred to in Novartis AG's current Form 20-F on file with the US Securities and Exchange Commission. Novartis is providing the information in this presentation as of this date and does not undertake any obligation to update any forward-looking statements as a result of new information, future events or otherwise.

Before we start, just wanted to go through the safe harbor statements. The information presented today contains forward-looking statements that involve known and unknown risks, uncertainties and other factors. These may cause the actual results to be materially different from any future results, performance or achievements expressed or implied by such statements. For a description of some of these factors, please refer to the company's Form 20-F and its most recent quarterly results on Form 6-K that, respectively, were filed with and furnished to the US Securities and Exchange Commission. And with that, I'll hand across to Vas.

Slide 3 – Vasant Narasimhan – CEO of Novartis

Vas Narasimhan
Chief Executive Officer

Company overview

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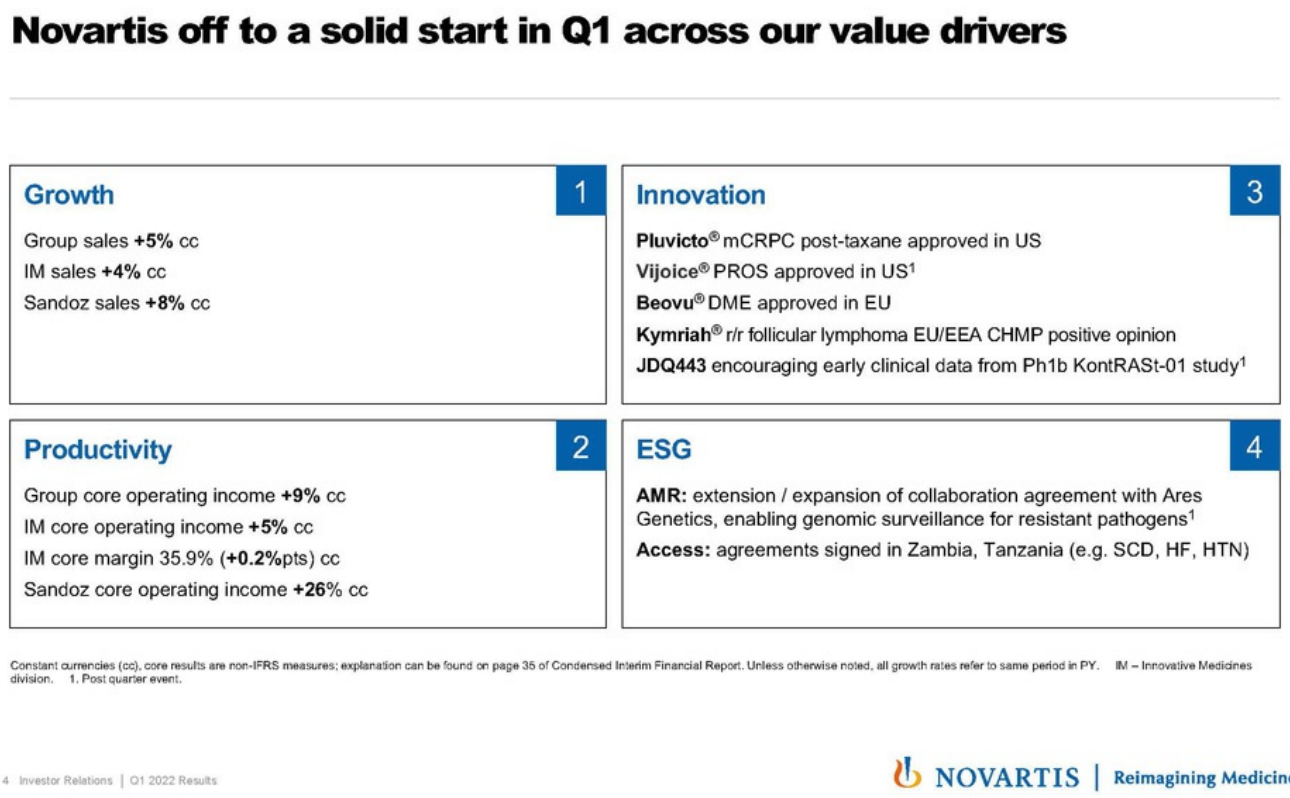
Thank you, Samir, and thanks everyone for joining our conference call today. If we could move forward a few slides. So with me today, I have Harry Kirsch, our Chief Financial Officer; and Karen Hale, our Chief Legal Officer.

Slide 4



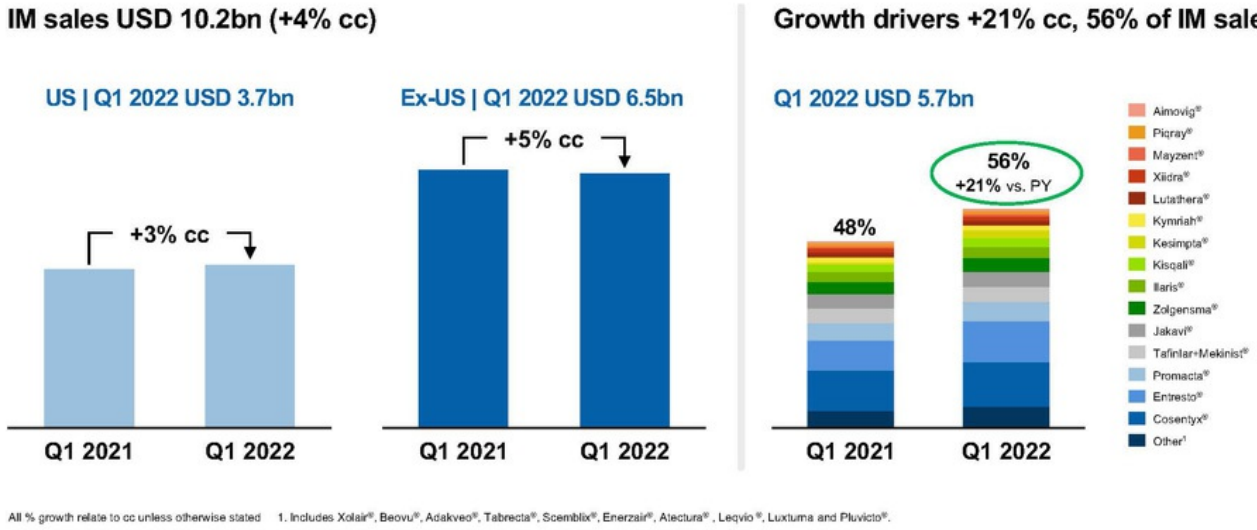
If we go to Slide 4. Overall, the quarter came out with a solid start for Novartis across all of our 4 key pillars. From a growth standpoint, good sales growth both at the IM and Sandoz and, of course, the overall group level.

Good productivity, group core operating income, up 9% on a constant currency basis as well as a solid result in both IM and Sandoz. Some important innovation milestones, I'll go through those in a bit more detail. And we also continue to advance our ESG agenda in AMR as well as Access to Medicines agreements in Africa. So I think a solid quarter that we can build on over the course of this year.

Slide 5

1 GROWTH

Q1 Innovative Medicines (IM) sales grew across US and ex-US, driven by our in-market growth drivers



All % growth relate to cc unless otherwise stated 1. Includes Xolair®, Beovu®, Adakveo®, Tabrecta®, Scemblix®, Enerzair®, Atectura® , Leqvio ®, Luxturna and Pluvicto®.

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Moving to the next slide. Our Innovative Medicines sales grew across both our US and ex US geographies, 3% in the US, 5% ex-US in constant currencies, with growth drivers now accounting for 56% of our IM sales. Growth of those – growth drivers, up 21% quarter-over-quarter. So a nice demonstration that we continue to replace our sales base with newer and newer products.

Slide 6

1 GROWTH

Strong performance of Entresto®, Kesimpta®, Cosentyx®, Zolgensma®, Kisqali® and launching Leqvio®...

Q1 sales[1]

	Sales USD million	Growth vs. PY USD million	Growth vs. PY cc
Entresto	1,093	304	42%
Kesimpta	195	145	nm
Cosentyx	1,159	106	12%
Zolgensma	363	44	18%
Kisqali	239	44	28%
Xolair	368	33	17%
Ilaris	285	29	18%
Promacta	491	28	9%
Jakavi	389	26	14%
Scemblix	25	25	nm
Mayzent	79	24	47%
Leqvio	14	13	nm

Constant currencies (cc) is a non-IFRS measure; explanation of non-IFRS measures can be found on page 35 of Condensed Interim Financial Report. Unless otherwise noted, all growth rates refer to same period in PY
nm = not meaningful 1. Innovative Medicines division

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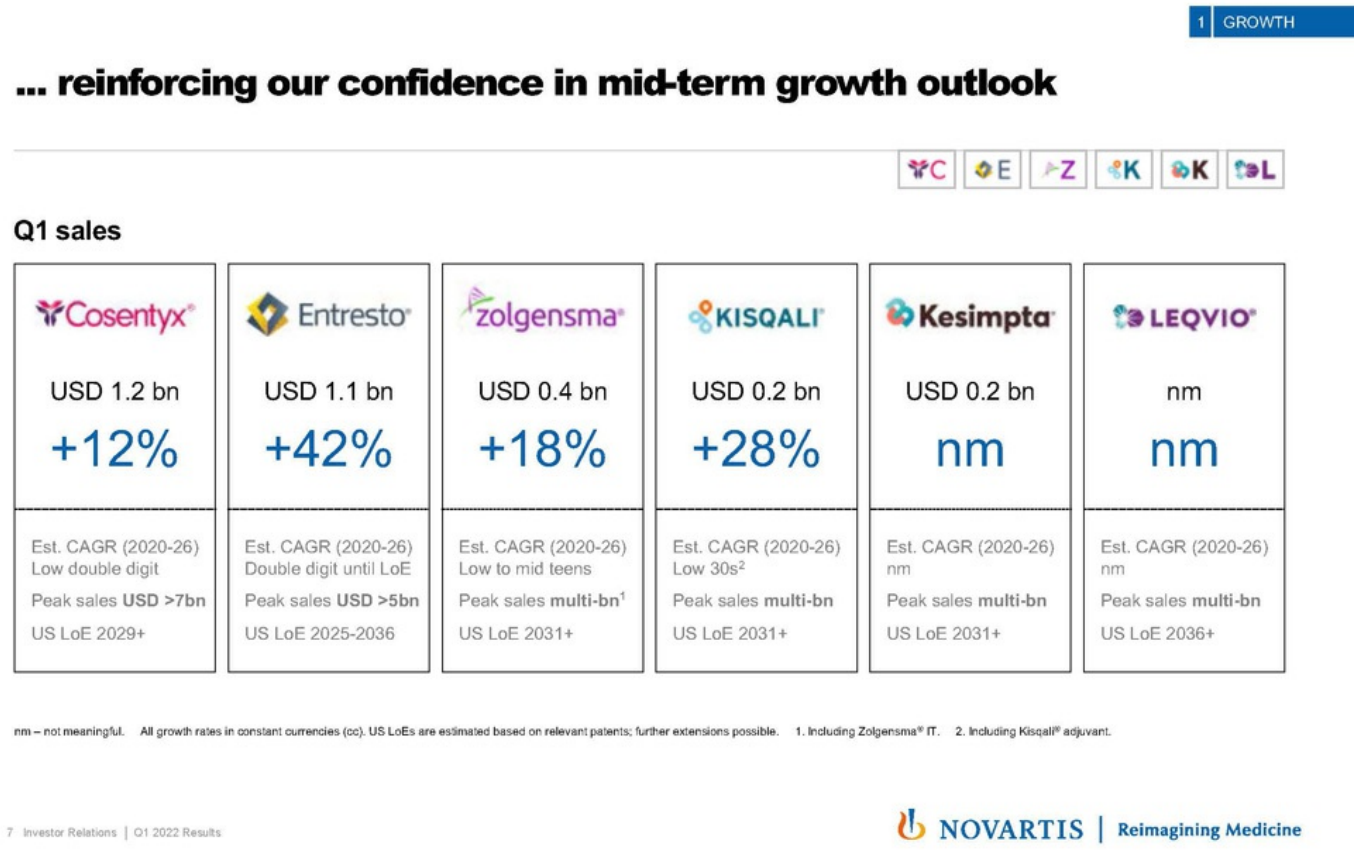
Now moving to Slide 6. We saw strong performance on our key growth drivers, the 6 brands we've been consistently highlighting, and I'll talk about them in a bit more detail. But you can see really across these key brands growth that ranged from the high single digit to the double-digit range. So again, pleased with the broad-based performance. Of course, there were pockets of weakness, and we can talk more about that. But overall, we're pleased that we're off to this solid start on the key brands.

Slide 7

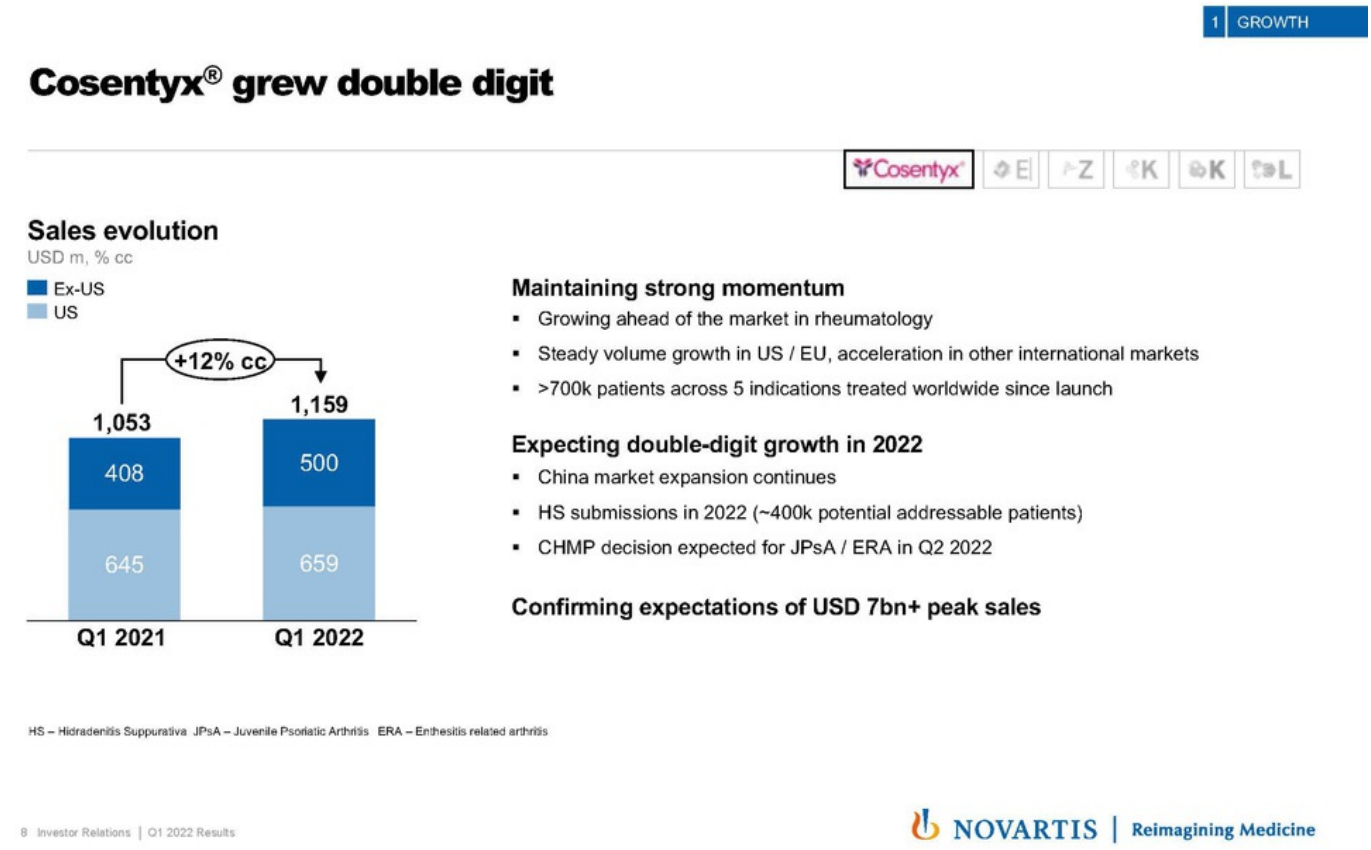


But let's go a bit deeper on the 6 key brands. So moving to the next slide on Slide 7. You see that on Cosentyx®, Entresto®, Zolgensma®, Kisqali®, Kesimpta® and Leqvio®, we had good growth on the major brands that we really believe will drive our midterm sales performance and, of course, continue to maintain our peak sales guidance on these brands.

Importantly as well, Kesimpta® has now demonstrated in Q1 the potential we expect of this brand, to really reach that multibillion-dollar potential with very strong growth in the quarter. We'll talk more about that.

And with Leqvio®, continue to build the solid foundation base for what will be a multiyear journey to get to the multibillion-dollar sales potential. But I think the initial foundational elements are starting to come in to play. So again, it will be a longer-term journey for this brand.

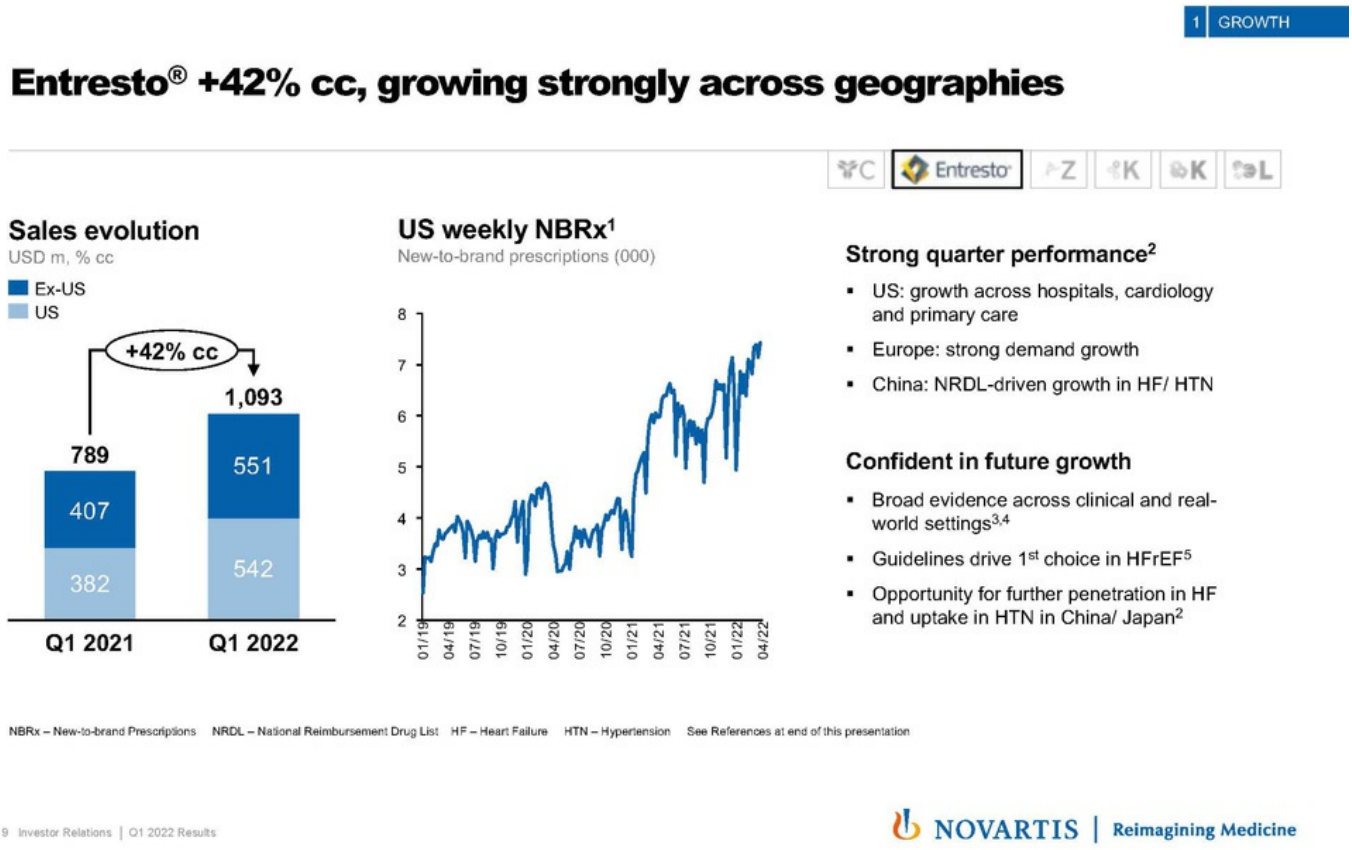
Slide 8



Moving to Slide 8. And going to each one of these brands, brand-by-brand. First with respect to Cosentyx®, double-digit sales growth, 12% on the quarter, really driven by our ex-US performance. When you look at the specifics on the growth momentum, we saw steady volume growth in the US and EU. We have 700,000 patients now across our 5 indications treated worldwide since launch. Very good performance in rheumatology across geographies.

We expect double-digit growth in '22, driven by our China market expansion. Year-to-date, our China performance has been good. We also will, in the medium term, be driven by our ability to get new indications online. We're on track for our hidradenitis suppurativa submission this year, and we do expect CHMP decision on a couple of additional indications later in quarter 2. So we confirm our USD 7 billion-plus peak sales expectations for Cosentyx®.

Slide 9



Moving to the next slide. Entresto® had an outstanding first quarter, growing 42% on the quarter, driven by both US and ex-US performance. You can see here the US weekly NBRx showing a nice steep ramp as we come out – particularly as we come out of the pandemic period.

This growth has been driven across hospitals, cardiology and primary care, so really broad based in the US, primarily driven by reduced ejection fraction, especially with the new guidelines that are now in place, but also supported by the preserved ejection fraction indication. We have strong demand growth in Europe for the brand. And in China as well as Japan, the launch of our hypertension indications and the NRDL listing in China have helped drive this growth.

So longer term, we expect the continued development of evidence base, the continued drive of the guidelines that place ARNI as a first choice for physicians treating reduced ejection fraction heart failure as well as for further penetration in China and Japan to drive the momentum for Entresto®.

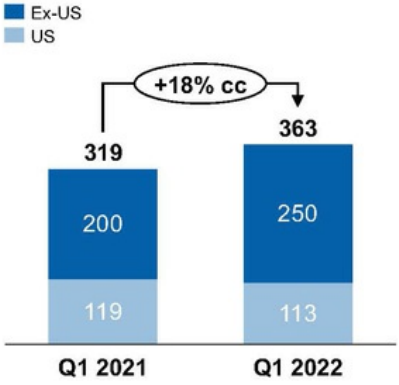
Slide 10

1 GROWTH

Zolgensma® grew 18% cc with increasing access ex-US

Sales evolution

USD m, % cc



Q1 highlights

- Ex-US sales grew +32% cc, while US sales steady
- Over 2000 patients have been treated worldwide

Future growth drivers

- Increase in newborn screening: currently at 95% in US, 25% in EU
- OAV101 IT data[1]: STEER currently enrolling; STRENGTH to start in 2H22

New data at MDA 2022 reinforce Zolgensma IV clinical benefit

- Age-appropriate motor milestones in pre-symptomatic children with 3-copy SMN-2 backup gene (SPR1NT)
- Post-hoc analysis (START and STR1VE) of children with Type 1 SMA achieved / maintained important measures of bulbar function

1. With investigational OAV101 intrathecal administration

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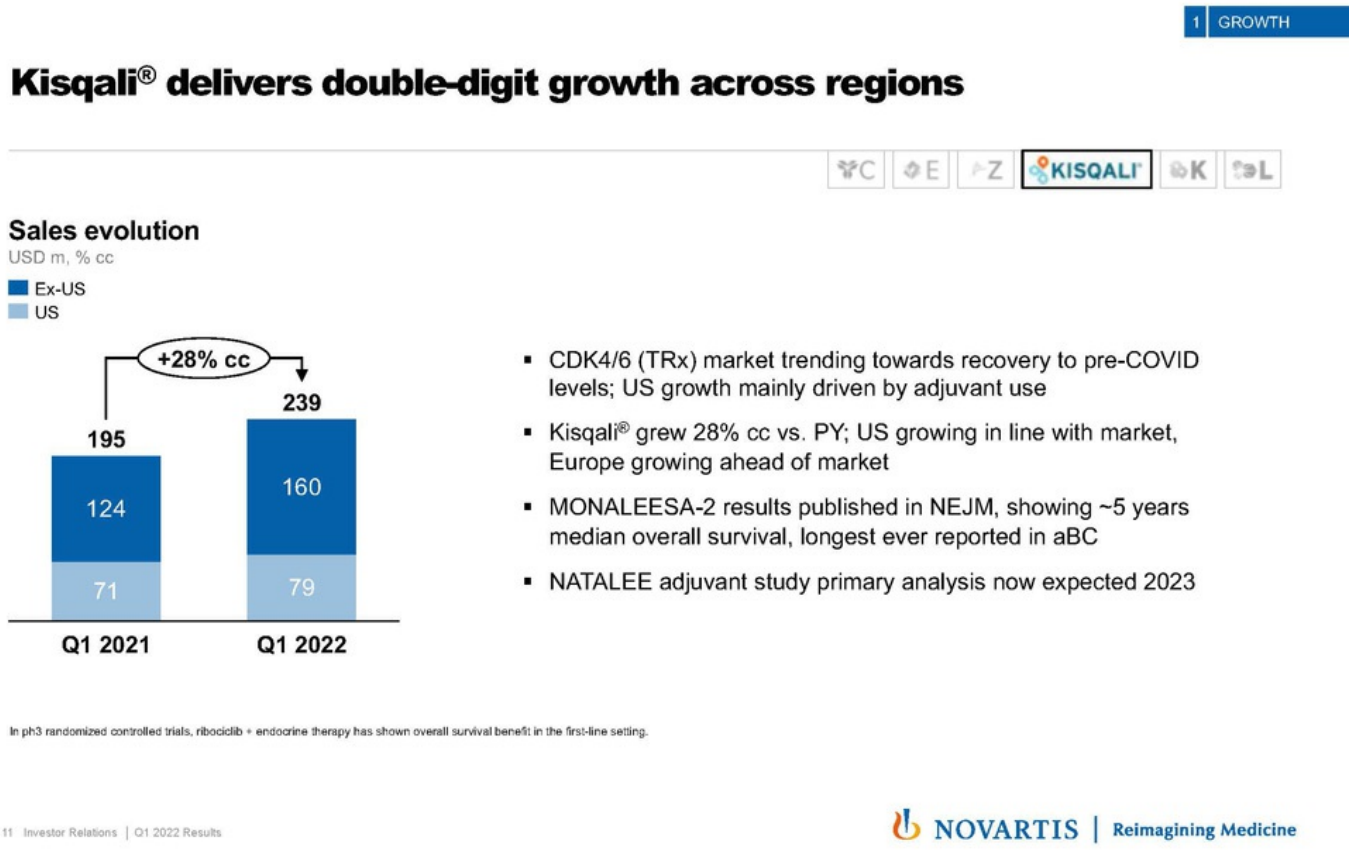
Moving to the next slide. Zolgensma® grew 18% on the quarter, with increasing access outside of the United States. The Q1 highlights were really the ex-US, where we had sales growth 32% in constant currency. While the US remains steady as we continue to drive up the newborn screening rates. So right now, we have over 2,000 patients treated worldwide, which I think demonstrates the profile of this gene therapy and the confidence providers are having using this medicine.

In the future, our growth will be driven by continuing to penetrate in the US the under 2, really getting to high market share. We expect to have over 90% of children who are diagnosed in newborn screening receiving Zolgensma®, that's our goal, and continuing to drive up that newborn screening in the EU above 25%.

Our next phase of data studies or data generation is on track, the STEER study with intrathecal in older children is currently enrolling. The STRENGTH study to further profile in the IV setting is starting in the second half. We also rolled out some additional data at MDA, which supports the overall profile of Zolgensma® IV. So this will be a steady ramp towards our goal to be towards the USD 2 billion product over time. But overall, the signs and signals are good.

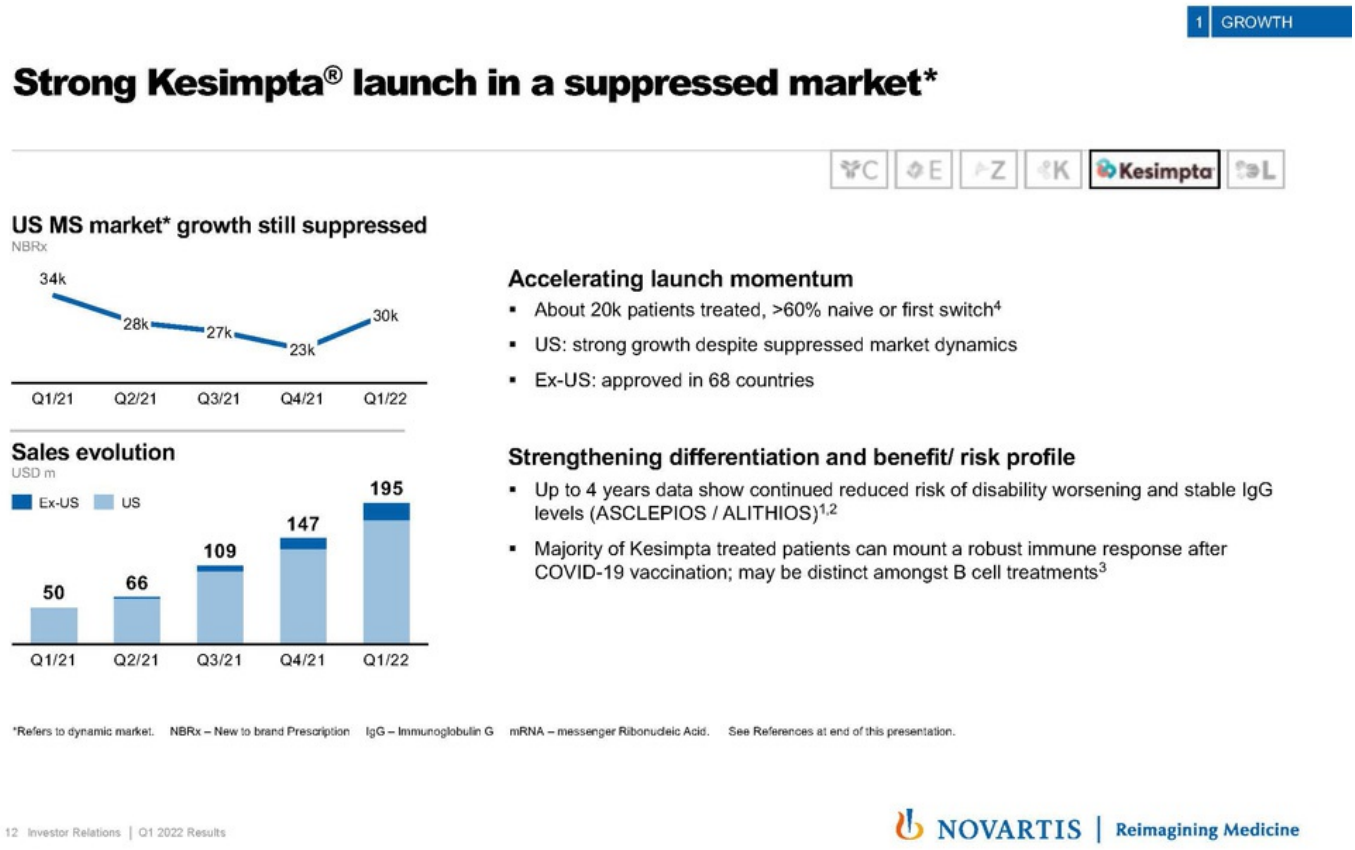
Slide 11



Moving to the next slide. Kisqali® demonstrated – delivered 28% growth on the quarter, primarily driven again by ex-US performance. The market trends show a recovery to pre-COVID levels for CDK4/6 TRx, but we continue to see a suppression in the NBRx part of the market. And so we'll have to continue to watch to see that recovery, which will be critical for us because a lot of our growth is dependent on new-to-brand patients.

Kisqali®'s growth in the US is in line with market, but in Europe, we continue to grow ahead of market. And I'll speak more about the NATALEE adjuvant study update that we provided today in an upcoming slide.

Slide 12



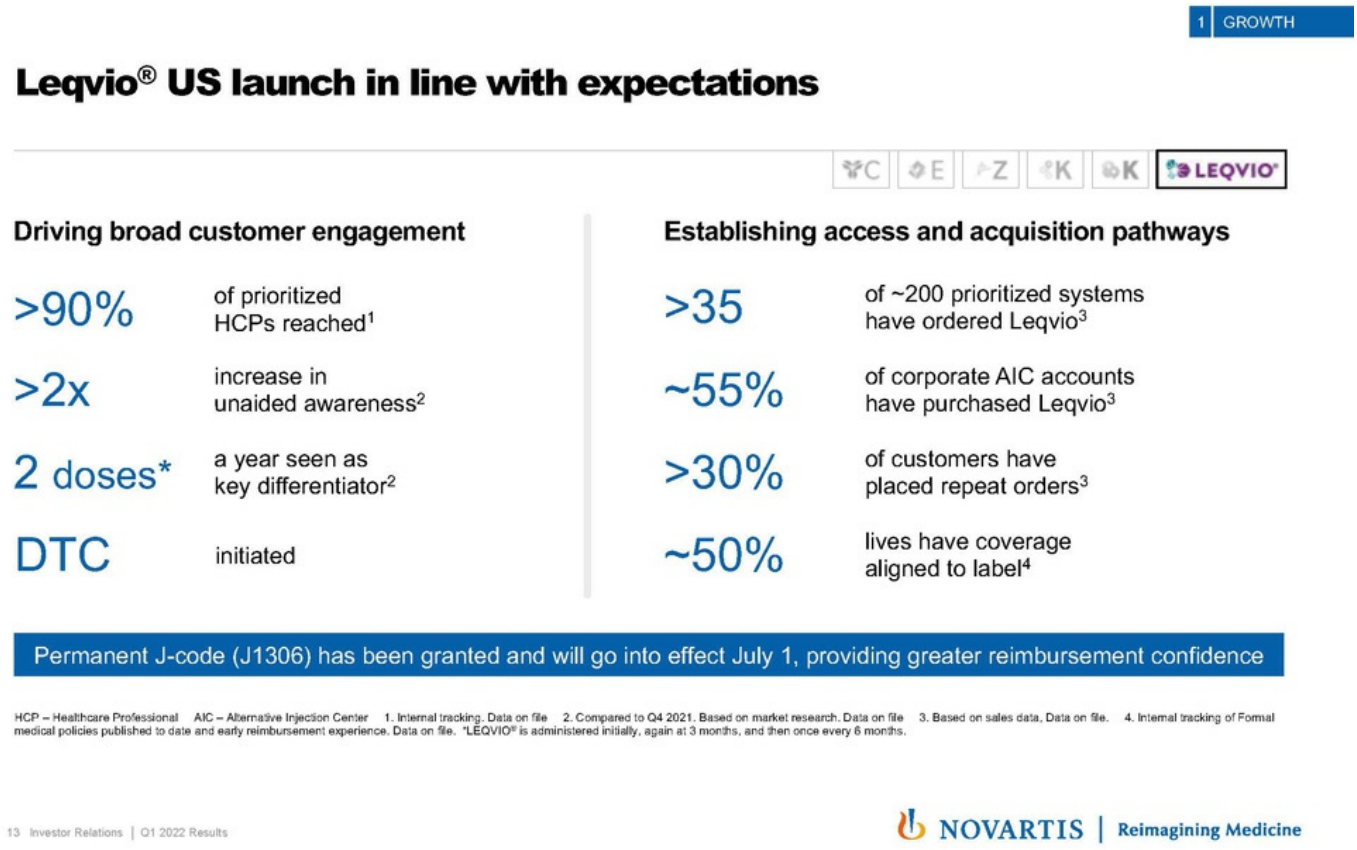
Moving to Slide 12. Now turning to Kesimpta®. Kesimpta® really, I think, had a strong quarter. We have 20,000 patients treated. Over 60% are naive or first switch. In the US, we see really strong growth dynamics. Despite a suppressed market, you can see in the upper left-hand side of the slide, the US MS market growth remains below its pre-COVID levels. Nonetheless, we see Kesimpta® continuing to gain momentum.

And now outside of the United States, we're approved in 68 countries. So over the course of this year and really starting in 2023, we would expect the ex-US contributions to the brand to start to increase.

We again rolled out additional data in the quarter now at 4 years out showing the ability to reduce disability worsening, with stable IgG levels as well as data that supports the use of Kesimpta® in patients who need to be treated with COVID-19 vaccination.

So overall, I think a strong start to the quarter, a lot of good momentum with Kesimpta®, and we'll look forward to delivering that momentum or accelerating that momentum over the course of the year.

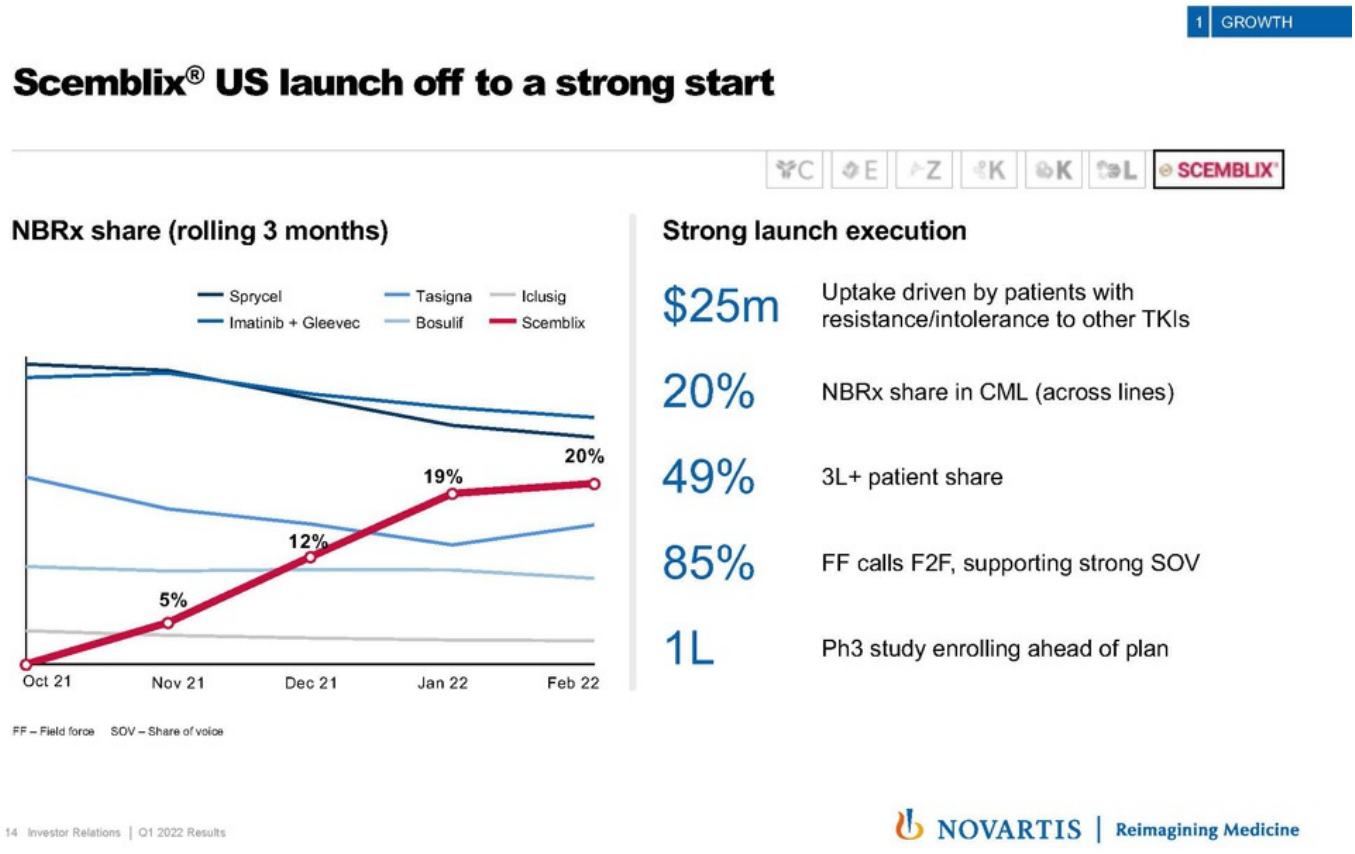
Slide 13



Now moving to the next slide, Slide 13. Turning to Leqvio®. Again, early days, particularly in the US, but I think the leading indicators point to the foundations being put in place to have this brand become a very significant brand for the company.

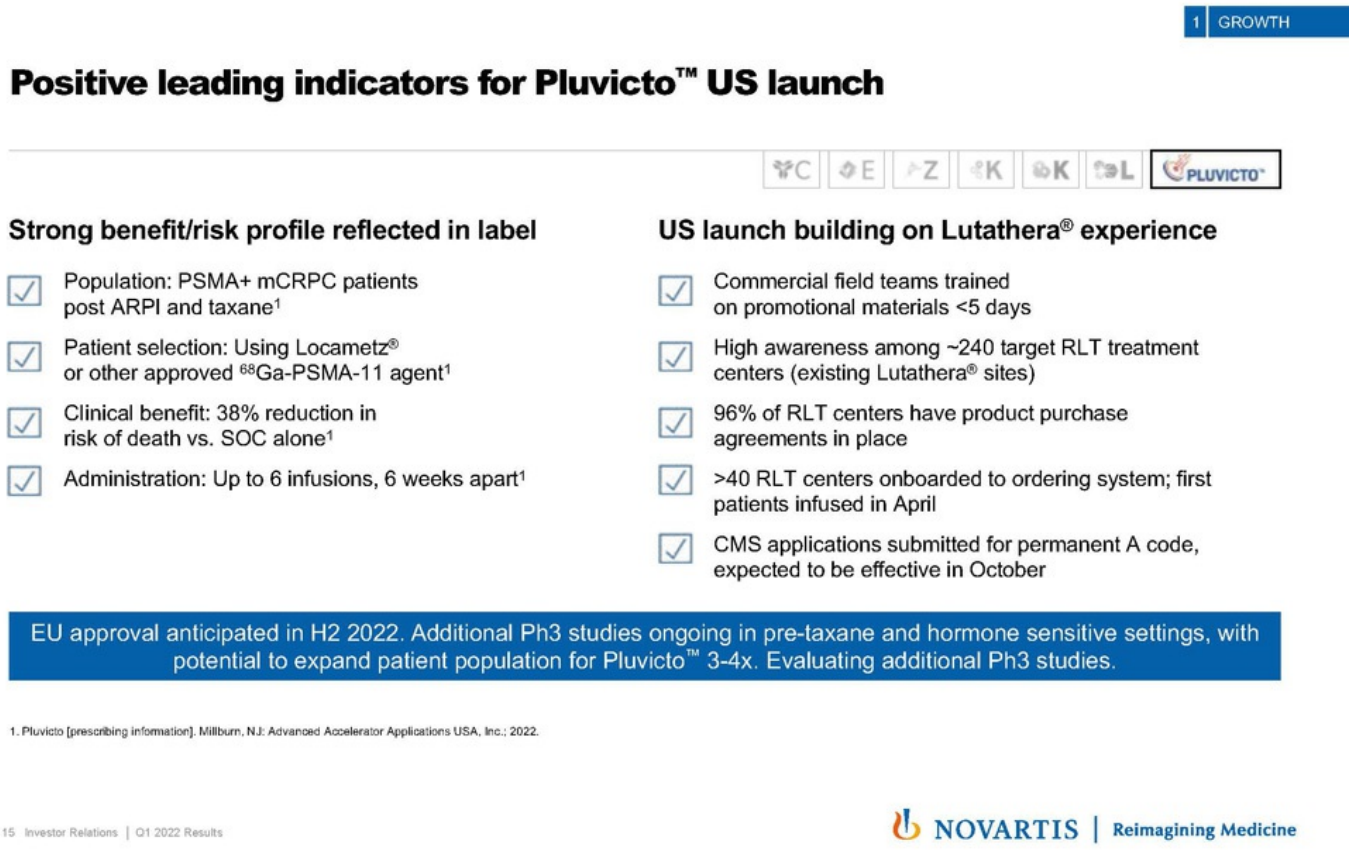
We reached over 90% of HCPs. We have good unaided brand awareness. Our DTC is now initiated. We've also established access in over – it's actually over 50 of the 200 prioritized systems. So it's 35 on the slide, but we're up to 50, have ordered Leqvio®. Our focus very much is in driving more depth in those accounts. We have 55% of our alternative injection sites accounts now have purchased Leqvio®, 30% repeat orders. And importantly, our permanent J-code has been granted and will go into effect on July 1. So all of this to say that the foundations are in place for the second half. In the second half of this year to begin to see more acceleration in growth for Leqvio®, going into what we expect to see further acceleration in the coming years.

Slide 14



Now moving to the next slide. I just wanted to say a word on our two recent launches in the US. Scemblix®, our BCR-ABL inhibitor, STAMP inhibitor showed nice performance in the quarter in the third-line setting. Here, you can see our NBRx share has reached 20% through February. Still small numbers, but I think it points to the potential of this medicine given its strong efficacy and safety profile. We're up to 49% third-line patient share. And our first line Phase III study is now enrolling ahead of plan. So we remain optimistic that we can deliver an over USD 500 million brand in the third-line setting, but our focus in the longer term is hopefully with positive data move into the frontline setting.

Slide 15



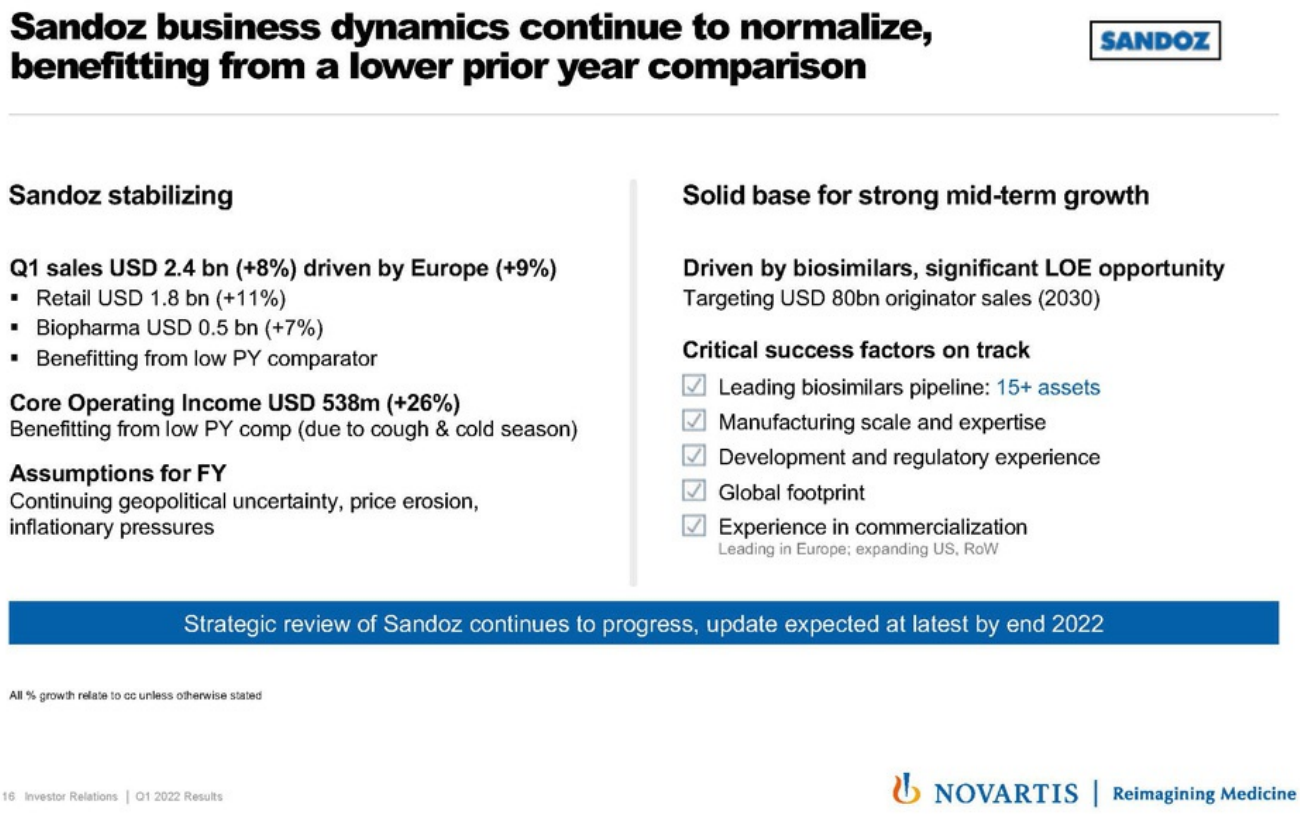
Moving to the next slide with Pluvicto®. So we at the – towards the end of the quarter, I received approval for Pluvicto®. And I think on the US launch, we're off to a good start and getting again the key elements in place to really drive this launch. As a reminder, the population is metastatic CRPC patients who are post relevant chemotherapies.

Patient selection is driven by a Gallium PSMA-11 agent to identify patients who would benefit from Pluvicto®. There was a 38% reduction in the risk of death in these patients. So a lot of physician and KOL interest in the medicine in the prostate cancer space. 6 infusions, 6 – 6 week – over 6 weeks, which really gives the opportunity for a onetime therapy over that period of time and then patients derive the benefit.

We're building on our Lutathera® experience with this medicine. Our commercial field teams are in place. We see high awareness already in the 240 treatment centers that we're targeting initially. 40 RLT centers are already onboarded into the ordering system and many of these centers have experience with us. And we've submitted the application for the permanent A-code for this medicine.

Now in Europe, we expect approval in the second half of '22. And we also are progressing on track with our Phase III studies in the pre-taxane and hormone sensitive setting and we're also – which would expand the patient population 3 to 4x and allow us to target a patient population to enable this to be a multibillion-dollar brand over time. And we're evaluating additional Phase III studies in the earlier-line setting.

Slide 16

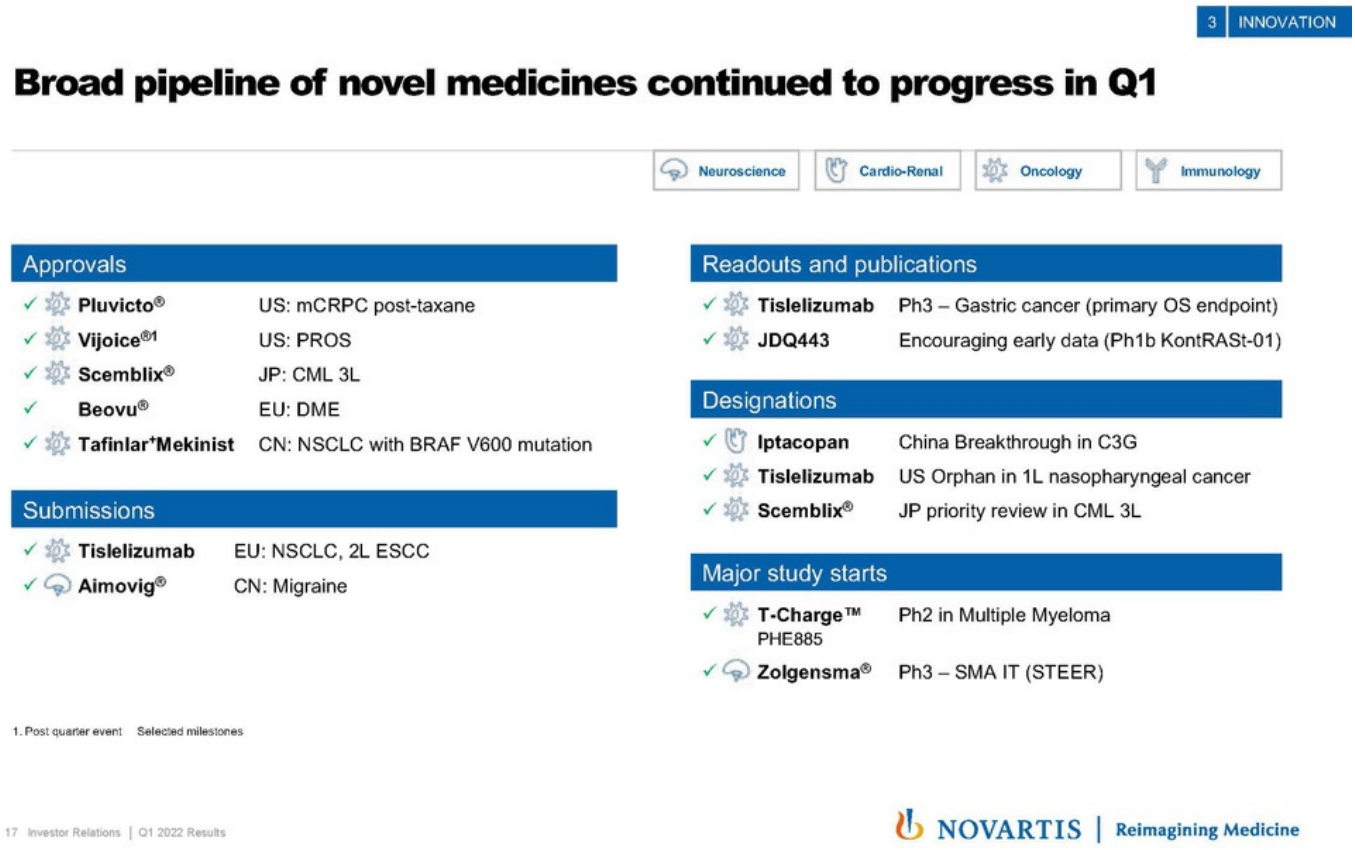


Now moving to the next slide. Wanted to say a word on Sandoz. Our business dynamics in Sandoz, as you saw, in the quarter have really stabilized. We are benefiting from a lower prior year comparison. Nonetheless, it is a positive time to see now stabilizing Sandoz business, with good growth, 8% overall. It was driven by performance in Europe at 9%. So we do see now moving towards the bottoming out of the US business as we look to get that region back to growth. Very good biopharma performance and retail performance. Core operating income was up quite significantly, but again benefiting from both prior year comps as well as certain one-timers.

And so overall, given the geographical uncertainties, price erosion and other inflationary pressure in Sandoz spaces, we're maintaining our guidance for Sandoz on the full year, but we'll, of course, continue to monitor to see how Sandoz performs.

Just as a reminder, we continue to view Sandoz as having the potential to be the leading generics company in the world driven by its biosimilars' presence and strength as well as key success factors which we reviewed on the previous call. Overall, our strategic review remains on track, and we would plan to provide an update on the strategic review at the latest by the end of this year.

Slide 17



So moving to the next slide. In terms of the pipeline, some important milestones, but I'll really dive in on just a handful.

Pluvicto® was our key approval in the quarter that we had some other approvals around the world, as you can see here. In terms of submissions, we are continuing to move forward with Tislelizumab in the EU and our filing is on track in the US as well. I'll go through in a little bit more detail, our JDQ data on the subsequent slide.

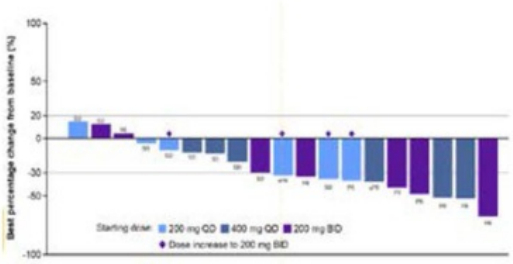
We continue to see good interest in Iptacopan around the world as we head towards our first Phase III readout in the second half of this year and we're on track. We've already started our T-Charge Phase II study in multiple myeloma and plan to start in Phase III in DLBCL in the second half of the year. And I've already mentioned the Phase III start of Zolgensma®.

Slide 18

JDQ443 showed early sign of clinical activity with acceptable safety and tolerability

KontRASt-01: Phase 1b/2 study of JDQ443 in advanced, KRAS G12C-mutated solid tumors

Best ORR across all doses in NSCLC



JDQ443, a novel KRAS G12Ci, demonstrated a competitive safety and efficacy profile in NSCLC

- ORR of **57%** (4/7) at the RD of 200 mg BID
- ORR of **45%** (9/20) across all dose levels
- No Grade 3 or higher treatment-related AEs at RD

JDQ443 achieved high systemic exposure

- PK/PD modelling predicted sustained, high-level target occupancy at the RD

Further development ongoing

- KontRASt-01 actively recruiting into SHP2i (TNO155) and anti-PD1 (tislelizumab) combo cohorts
- KontRASt-02 Ph3 JDQ443 monotherapy vs docetaxel in NSCLC opening soon

Data presented at American Association for Cancer Research ORR – Objective response rate RD – Recommended dose BID – Orally twice daily

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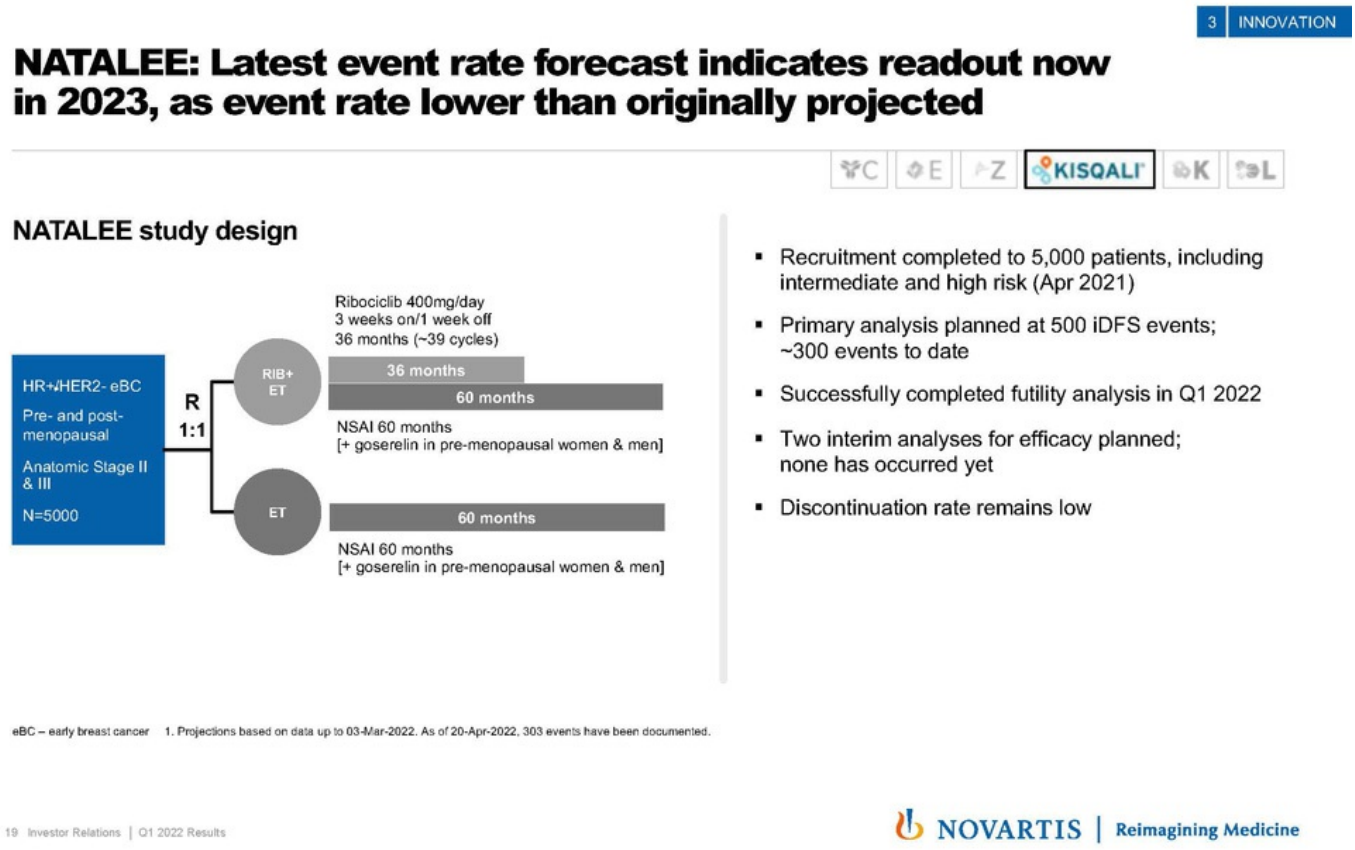
So let's move for a moment to JDQ. So at AACR, on the next slide, so we showed early signs of clinical activity with acceptable safety and tolerability for this KRAS G12C. As a reminder, we have a unique structure to this medicine versus the other G12C inhibitors which we believe allows us to optimize the PK/PD for the medicine.

When you look at the data set, we demonstrated a competitive safety and efficacy profile, though, again, with a caveat that this is a small study, 57% ORR at the target dose of 200 milligrams BID. No grade 3 or higher treatment-related AEs, so really nice safety profile.

When we look at the modeling of the overall PK of this medicine, high systemic exposure, high target level occupancy. So we're pleased with how the medicine has performed thus far.

So we're moving forward rapidly in recruiting our combination study with SHP2 as well as another separate study with anti-PD-1. And so both the studies are moving forward. And we're also preparing to start our monotherapy Phase III program in small cell lung cancer versus chemotherapy which we plan to open shortly.

Slide 19



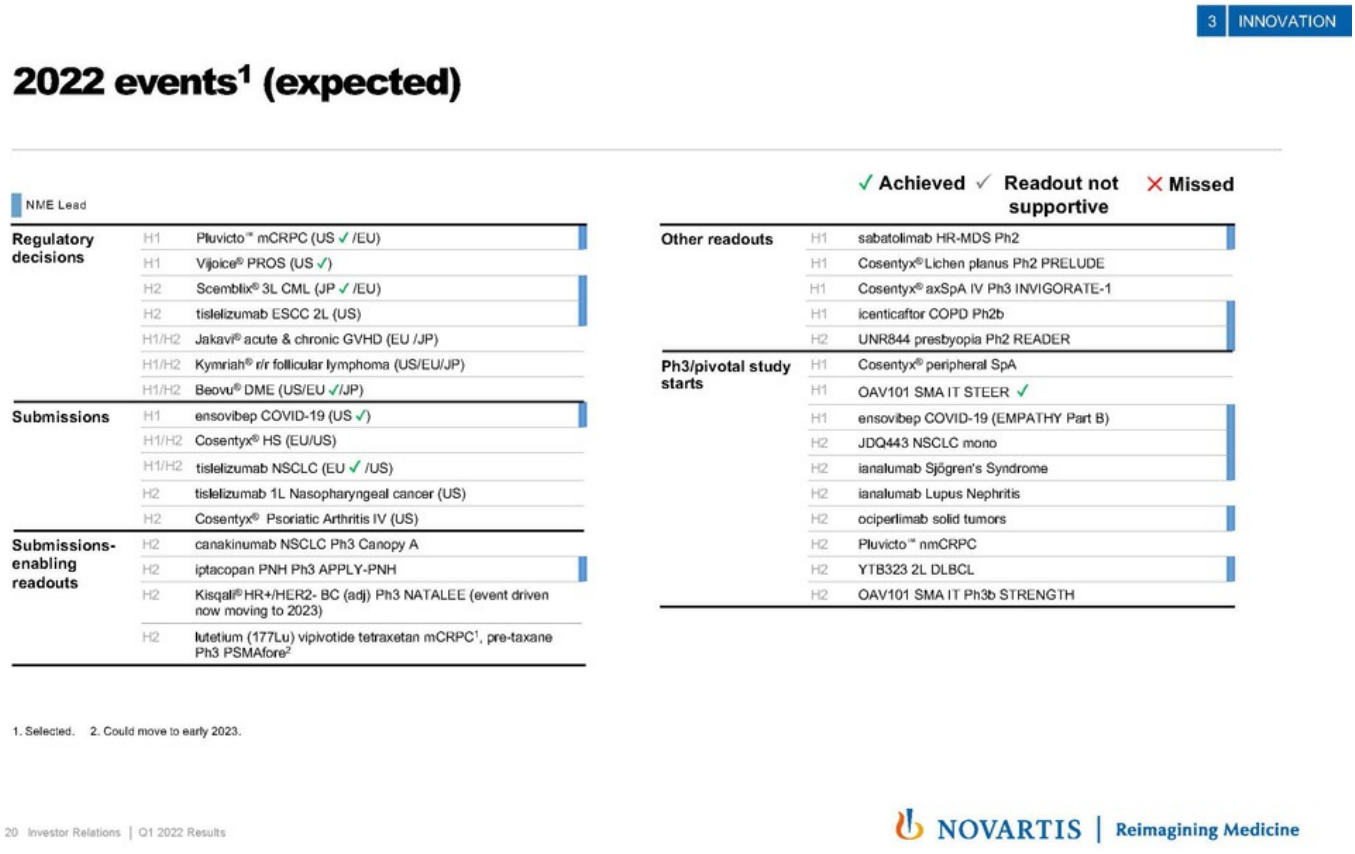
Now moving to the next slide. We also wanted to provide an update on NATALEE. So based on our regular update of the number of events that we are accruing, we now forecast the trial to complete in 2023 as the current event rate is lower than our originally forecasted event rate for the study. This is a regular process we go through. And now when we look at these forecast versus – or look at our actuals versus our forecast, we're currently predicting a 2023 completion of the study.

On the left-hand side, you see the study design remains unchanged from our previous update, 5,000 patients randomized 1:1 to ribociclib plus estrogen therapy versus estrogen therapy alone. Patients receive Kisqali® 400 milligrams per day for 36 months. So a longer treatment duration, a lower dose than the metastatic setting to really try to ensure we keep patients on therapy and keep them on therapy longer to drive the efficacy signal.

So in terms of the recruitment, we completed 5,000 patients in April 2021. Our primary analysis is that 500 events. We have 3 – approximately 300 events to date. In the quarter, we successfully completed a futility analysis. We have two interim analyses planned between now and the end of the study, but neither has occurred yet. And the discontinuation rate remains low in the single-digit percentages, which I think demonstrates the overall profile in terms of safety and tolerability of the medicine.

So all on track. We'll continue to keep you updated as we progress this important study. As a reminder, the opportunity here is significant. We estimate in 2027 that the market for – in the adjuvant setting could be USD 7 billion. And the ability to target both the intermediate and the severe patients is significant in that we estimate there are 3x as many patients in the intermediate risk versus the high-risk patient population. So this would offer us, if successful, a significant medicine for the company.

Slide 20



Moving to the next slide. So our overall events are on track. I won't go through the slide in detail. We'll continue to keep you updated as we progress on these events across our regulatory decision, submission, study readouts and study starts. So moving to the next slide. With that, I'll hand the mic over to Harry. Harry?

Slide 21 – Harry Kirsch – CFO of Novartis

Harry Kirsch
Chief Financial Officer

Financial review and 2022 guidance

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Yes. Thank you, Vas. Good morning, good afternoon, everyone. I'm now going to walk you through some of the financials of the first quarter. And as always, my comments refer to growth rates in constant currencies unless otherwise noted.

Slide 22

Q1 mid single-digit sales and high single-digit Core OpInc growth

Group[1] USD million	Q1 2022	Change vs. PY % USD	Change vs. PY %cc
Net sales	**12,531**	1	5
Core operating income	**4,083**	3	9
Operating income	**2,852**	18	26
Net income	**2,219**	8	15
Growth ex. prior year Roche income		*23*	*32*
Core EPS (USD)	**1.46**	-4	2
Growth ex. prior year Roche income		*6*	*12*
EPS (USD)	**1.00**	10	17
Growth ex. prior year Roche income		*25*	*34*
Free cash flow	**920**	-42	
Growth ex. prior year Roche dividend		*-14*	

1. Constant currencies (cc), core results and free cash flow are non-IFRS measures. An explanation of non-IFRS measures can be found on page 35 of the Condensed Interim Financial Report. A reconciliation of 2021 IFRS results and non-IFRS measures core results and free cash flow to exclude the impacts of the 2021 divestment of our Roche investment can be found on page 40 of the Condensed Interim Financial Report. The free cash flow impact represents the dividend received in Q1 2021 from Roche in relation to the distribution of its 2020 net income.

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So on the next slide, we present our results for the quarter. Overall, as Vas mentioned, we delivered solid sales and profit growth. I think it's also important to keep in mind that this quarter's results with prior year comparisons are affected by the divestment of our Roche investment and the corresponding loss of income from associated companies, which you see here in the lines below operating income.

To aid the comparisons, we have published a reconciliation of our 2021 results excluding those impacts on our website, and we have also shown here the growth excluding prior year Roche investment income.

In quarter 1, sales and core operating income grew 5% and 9%, respectively, now with the sales benefiting from the strong performance of our in-market brands and core operating income driven by higher sales and increased productivity. Net income grew 15%, mainly driven by higher core operating income. And core EPS grew 2%. However, as you can see, if we exclude the impact of the prior year Roche income, net income would have grown 32% and core EPS 12%. Of course, we expect these impacts on EPS and core EPS to be offset over time by our ongoing USD 15 billion share buyback program which we expect to conclude in the second half of 2023. Free cash flow was negatively impacted by USD 0.5 billion due to the loss of gross annual dividend share paid out last year in March. However, important to note, underlying free cash flow is in line with expectations. And operationally, we are on track to reach our full year free cash flow objectives.

In summary, it has been a solid start to the year with the strength of our in-market growth drivers, Vas laid out earlier Entresto®, Kesimpta®, Cosentyx®, Zolgensma® and Kisqali® and our new launches, including Leqvio® and Pluvicto®, reinforcing our confidence in our midterm growth expectations.

Slide 23

Q1 Group core margin increased by 110bps to 32.6%

driven by Sandoz which benefitted from low PY base

	Q1 2022			
	Net sales change vs PY[1]	Core operating income change vs. PY[1]	Core margin[1]	Core margin change vs. PY[1]
	% cc	% cc	%	%pts cc
Innovative Medicines	4	5	35.9	0.2
Sandoz	8	26	22.8	3.3
Group	**5**	**9**	**32.6**	**1.1**

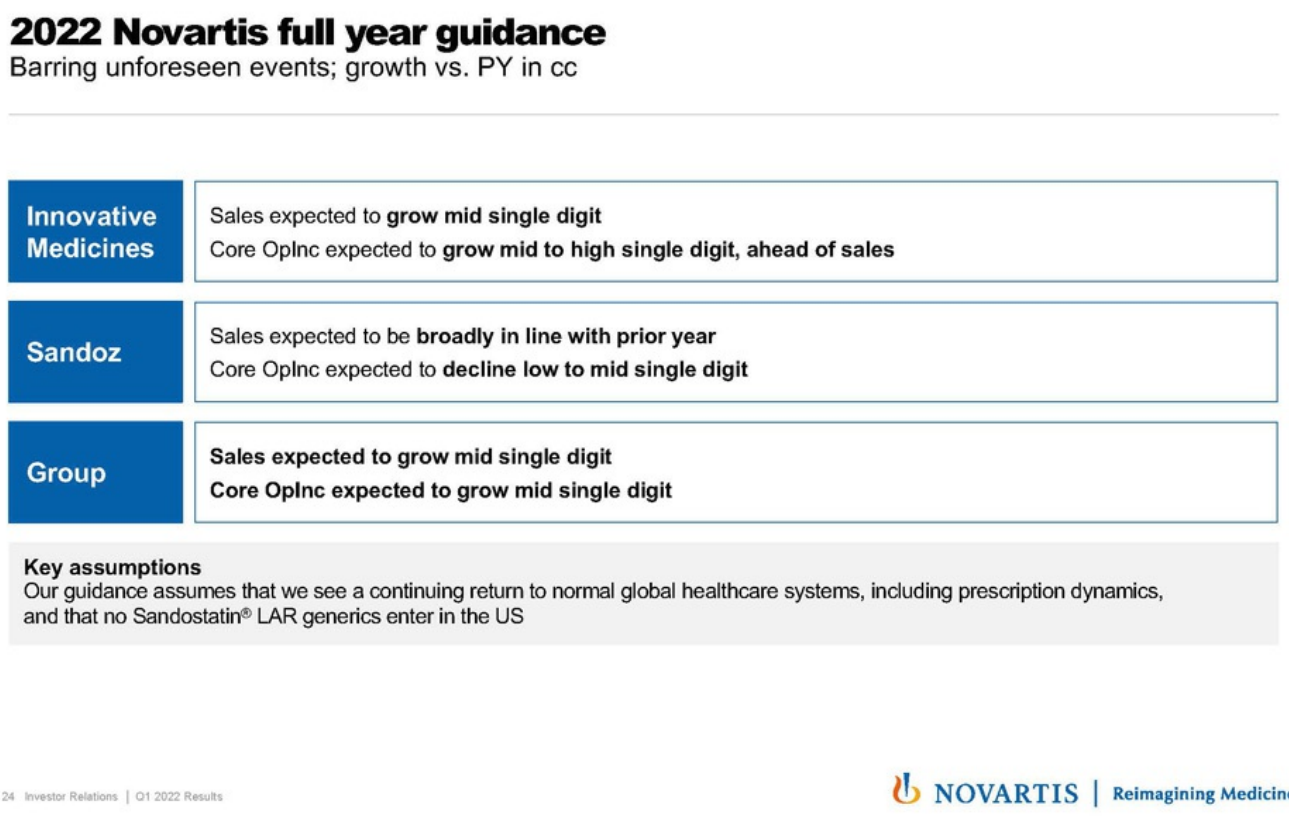
1. Constant currencies (cc), core results are non-IFRS measures. An explanation of non-IFRS measures can be found on page 35 of the Condensed Interim Financial Report .

As you can see on the next slide, Innovative Medicines sales grew 4%, benefiting from the strong performance of the in-market brands, partly offset by generic erosion, especially in the Oncology portfolio.

Innovative Medicines bottom line grew 5% and core margin reached 35.9%, up slightly from the prior year in constant currencies.

Sandoz numbers benefited this year due to a significantly lower prior year base with business dynamics continuing to return to normal with net sales up 8% and core operating income up 20%. And the margin is improving 330 basis points to 22.8% of sales. Overall, the group core margin increased by 111 basis points to 32.6% mainly driven by Sandoz' performance for the quarter.

Slide 24



Turning now to our guidance slide on Slide 24. We are confirming our guidance for the full year. And as a reminder, within the divisions, we expect another year of Innovative Medicines sales growing mid-single digit and core operating income to grow mids- to high-single digit ahead of sales.

The expected Innovative Medicines core margin increase will be driven by good top line momentum and continuation of productivity programs, including the recently announced new organizational structure. These drivers are expected to more than offset the anticipated higher energy cost and inflation pressures in our supply chain.

And for Sandoz, it's important to note that the very low quarter 1 prior year base with a weak cough and cold season to COVID and the uncertainty related to currency political – current geopolitical events.

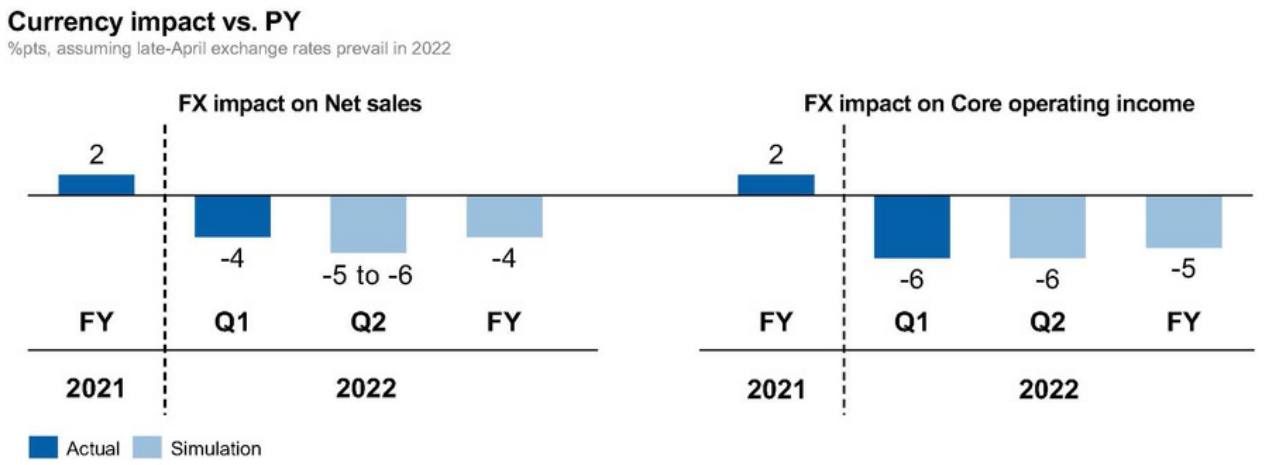
Therefore, we continue to expect the top line to be broadly in line with the prior year and core operating income to decline low to mid-single digit. Of course, we will be monitoring during quarter 2 and given the strong quarter 1 performance to see if we can give an update here.

But for now, given that the geopolitical events are likely to hit a bit harder Sandoz, if you will, we remain cautious here. This will be mainly driven by the expected gross margin pressures because also pricing and inflation coming in. And of course, we will have got a clearer picture later in the year.

For the group, we expect both the top and the bottom line to grow mid-single digit. The key assumption for this guidance is that we see continued return to normal global health care systems, including prescribing dynamics and that no Sandostatin® LAR generics enter in the US in 2022.

Slide 25

Expected currency impact for full year 2022



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And then finally, on Slide 25, given the strengthening US dollar and as currencies are constantly changing, I want to bring to your attention the estimated currency impact on our results using current exchange rates. In quarter 1, currency had a negative 4% point impact on net sales and a negative 6% point impact on core operating income. Looking forward, if late April rates prevail for the remainder of '22, we expect the full year impact of currencies on top line to be a negative 4% points and on bottom line a negative 5% points. In quarter 2, the impact on sales would be negative 5% to negative 6% points and on bottom line negative 6% points. And as a reminder, we update these currency impact estimates monthly on our website. And with that, I hand it back to Vas.

Slide 26 – Vasant Narasimhan – CEO of Novartis

Vas Narasimhan
Chief Executive Officer

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Thank you, Harry.

Slide 27

Novartis appoints Aharon (Ronny) Gal, Ph.D. as Chief Strategy & Growth Officer

- Effective no later than August 1, 2022
- Leads the newly created Strategy & Growth function that combines corporate strategy, R&D portfolio strategy and business development
- Reports to CEO and joins Executive Committee of Novartis
- Brings over 20 years of life-sciences industry experience including financial research and analytics, management consulting and business development

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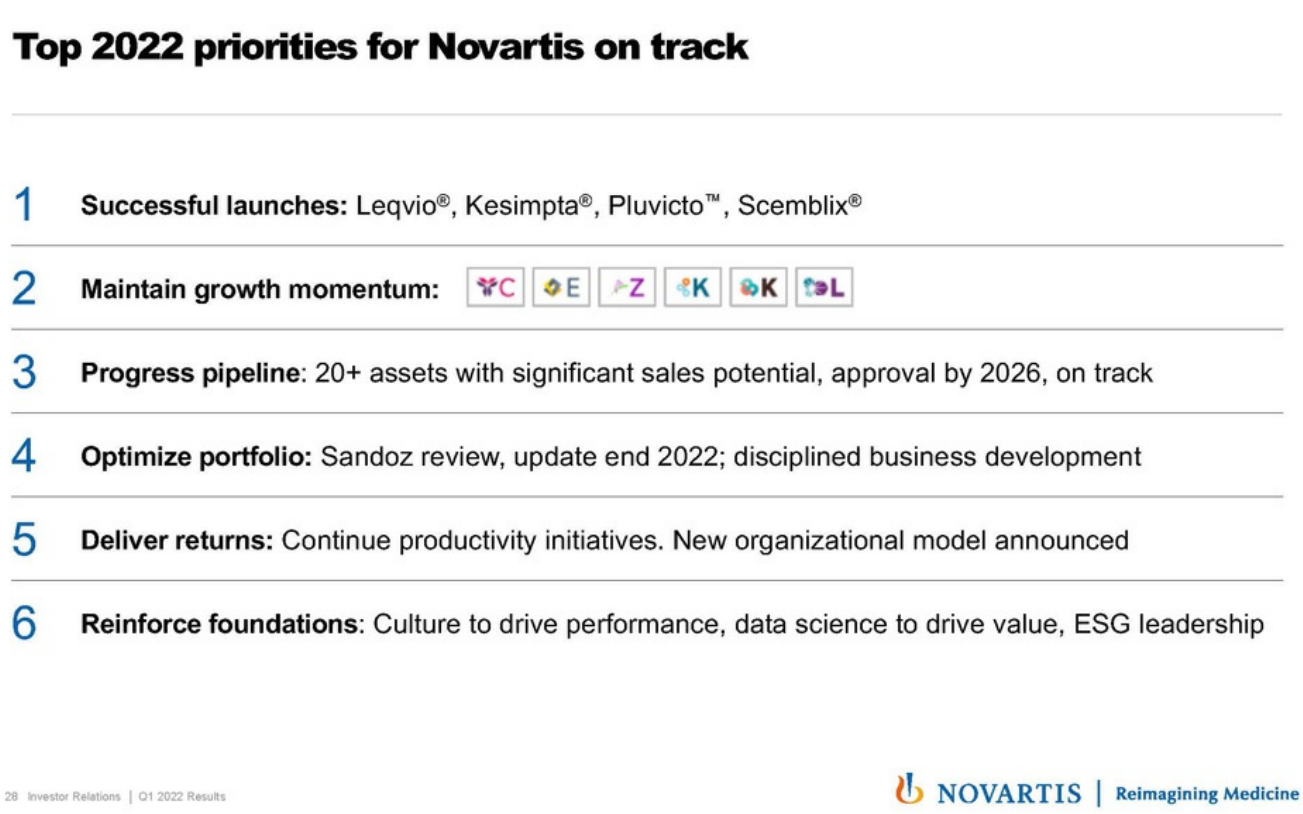
So if we go to Slide 27. Also today, we announced the appointment of Ronny Gal as our Chief Strategy and Growth Officer. As a reminder, we created the strategy and growth function to enable us to combine corporate strategy, R&D portfolio management and external business development into a single unit to help us drive the near, mid- and long-term growth of the company. So Ronny will report to me as he sits on the executive committee. He brings over 20 years of life sciences experience, both on the analytical side of things, but also deep understanding of the science in the US commercial environment.

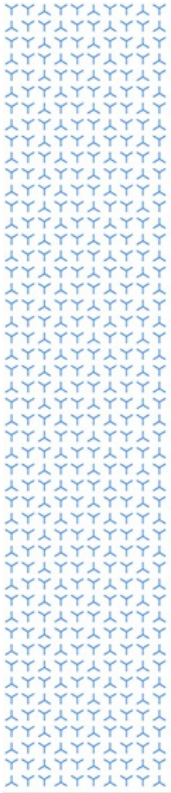
Previously worked at management consulting as well as business development. So very excited to welcome Ronny to the team no later than August 1 of this year.

Slide 28



So moving to the last slide, 6 key priorities we outlined in January, and they remain on track, successfully launching our key – driving our key launches Leqvio®, Kesimpta®, Pluvicto® and Scemblix®; maintaining the growth momentum across our 6 key growth drivers; progressing our pipeline of over 20 potential significant assets that had the potential to be approved by 2026; optimizing our portfolio with our Sandoz review on track but also remaining disciplined on M&A and business development; delivering returns, and so the recent reorganization with a potential of USD 1 billion plus productivity that we're committing to has been announced, and we'll continue to work through that over the course of this year; and of course, maintaining the foundations of culture, data science and ESG. So with that, I'll close and open the line for questions. Operator? Sorry, one note I forgot to mention. Please limit yourself to one question and we'll try to do multiple rounds if we have time. Thank you. (Operator Instructions)

Q & A



Q&A

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- Operator

Your first question today comes from the line of Graham Parry from Bank of America.

- Graham Glyn Charles Parry - BofA Securities, Research Division

Q. So it's a follow-up on NATALEE. The original trial design, I think, only had two interim. So one was a futility at 40% of events. And then there was a stop for outstanding efficacy at 70% of events. And I think the total event number you're looking for there was just over 300. But you're highlighting now that you have two efficacy interims as well as the futility that's already passed. So can you just help us understand the trial design. So what percentage of events was that futility analysis performed at? And then at what percentage of events are the two upcoming efficacy analyses? And just to confirm, those have the potential with the stop for efficacy in them.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Graham. So as you know, we amended the study protocol that increased to 500 events along the way. And with that, we added – we updated as well the various readouts. So the – I don't have in front of me the readout for the futility endpoint. But I can say that our interim analyses for efficacy are at the 70% and 85% information fractions. So that's when we would expect to have those interim analyses. But of course, it's difficult to predict based on an event-driven study as to when exactly those would occur. And so we'll continue to keep you up to date. And as a reminder, we don't guide to specific time lines on interim analyses, and we'll only provide updates if material information is provided by the DMC. Next question operator.

- Operator

Your next question comes from the line of Simon Baker from Redburn.

- Simon P. Baker - Redburn (Europe) Limited, Research Division

Q. It's a broader question on multiple sclerosis. It was flagged up on a call yesterday that traditionally Russia and Ukraine is disproportionately involved in MS studies. Since you have, I think, about 30 ongoing MS trials

around the order, I just wonder if you could give us an update on the current situation, any potential exposure you have two trials in Russia and Ukraine and any effect that could have on trial time lines.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Simon. So overall, again, we feel like our trials are manageable in Russia – in Russia and the Ukraine. We are in the single-digit percentages in terms of the percentage of Russia and Ukraine patients in our – in our global studies. Now specifically in multiple sclerosis, we're in the roughly low to mid-teens on the studies in terms of the percent of the global patients for our BTK inhibitor multiple sclerosis studies, but we already have plans in place to offset those. And so at the moment, we believe we can fully mitigate the patients required from those two countries. No patients in our multiple sclerosis BTK study or LOU studies were – have been enrolled so far. And so we'll simply reallocate to other markets and we expect to remain on track. We'll, of course, keep you updated if anything were to change in that regard. Next question operator.

- Operator

Your next question comes from the line of Matthew Weston from Credit Suisse.

- Matthew Weston - Crédit Suisse AG, Research Division

Q. It's another Russian question, one for Harry, please. The annual report for last year shows that you have just under USD 0.5 billion of Russian ruble receivables. I'd be interested to understand, how is cash collection today? Are you limiting deliveries to only people who pay you upfront? And then how should we think about impairment testing on that quite sizable amount of money? And then finally, Harry, if you were to have to write some down, would it go through core? Or would it not?

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Matthew. Harry?

- Harry Kirsch – CFO of Novartis

A. Yes. So Matthew, overall, our cash collections and shipments actually are very normal. Cash collections are very good, actually. Now over the past years and, in this role, almost over 9 years, we always had here or there some difficulties with the wholesaler and then we put these wholesaler in the question on a payment plan or potentially prepayment plan. But that's not the case yet with any of them. Of course, we monitor on a daily basis. And the receivables are in ruble. You have seen also ruble returning back, if you were, to strength, and we have not seen difficulties to pay.
Now in terms of impairments, we would have to see, but I don't expect actually impairments on it. We are highly insured. A significant part of these are insured. And from that standpoint, we carefully monitor. We are insured and we don't see issues yet. Again, we monitor should that change, we would inform you. But I see a very stable product flow and a very stable cash collection.

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Harry. And just one update to Graham's first question. The futility analysis was done at a 40% information fraction. I would also note, it does take us a couple of months between a lot for one of these to actually have the DMC read the data. So next question operator.

- Operator

Your next question comes from the line of Wimal Kapadia from Bernstein.

- Wimal Kapadia - Sanford C. Bernstein & Co., LLC., Research Division

Q. So can I just please ask about Kesimpta® life cycle management. So I appreciate you're still early – in the early stages for the product. But one of your key competitors has started a 6-month subcu trial earlier this year and they also have a high-dose trial ongoing. So do you have any plans to extend the dosing frequency and/or change the dose for Kesimpta® in an attempt to really ensure durable share gains? I appreciate it's a bit further down the line, but just curious to hear your thoughts.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Wimal. So first, I think the key benefit of Kesimpta® is that the patient doesn't have to go into the center and have to deal with pretreatment with steroids and additional observation. So our understanding of competitor life cycle management activities would still involve the patient ultimately coming in to the center and of course then going into the various elements involved with that. So our focus remains on providing that flexibility for patients. We find it to be a key value driver, both to outstanding safety, excellent efficacy, but also monthly at-home administration. In terms of total time in the patient's lives, it's significantly, significantly lower. We are evaluating various life cycle management activities. But at this point in time, we haven't actually instigated, I guess, any new studies. We'll continue to evaluate, and we'll keep you posted. Next, operator? – Question operator?

- Operator

Your next question comes from the line of Andrew Baum from Citi.

- Andrew Simon Baum - Citigroup Inc., Research Division

Q. Unusually, across the industry, Novartis has built and is building a large cardiovascular presence. I'm just curious whether you see any role for a Factor XI inhibitor within that space. There's at least a couple of partnered agents (inaudible), Abelacimab which I can barely pronounce but you're familiar with given it came from your own portfolio? And then second, potentially partnering with Bayer on the Factor XI. I wonder if you had any comments.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Andrew. So in terms of Factor XI, we developed a very attractive Factor XI agent that we ultimately determined at the end of Phase II that it would be better to move forward in other people's hands. So we struck a partnership with Blackstone Life Sciences. They have taken the medicine forward and continue to develop it.

So we continue to monitor the progress of the medicine. At the moment, our view is that the focus we have on heart failure and on the various contributors to ASCVD between, of course, PCSK9, Lp(a) as well as other factors, is enough at the moment to take on. But we certainly are monitoring the space with a keen eye to what is the size of studies and the amount of investment that will be required to differentiate on safety given that NOACs will ultimately go generic in the coming years and that will be the standard that we'd have to go up against. But we'll keep you posted if anything were to change. Next question operator.

- Operator

Your next question comes from the line of Richard Vosser from JPMorgan.

- Richard Vosser - JPMorgan Chase & Co, Research Division

Q. Just looking at the oncology franchise in general, there seems to be a number of destockings in Q1. So

should we anticipate this to reverse in Q2? And also, should we think for the rest of the year about an acceleration as diagnosis improves as we come out of the pandemic? Just thoughts on the overall franchise there.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Richard. In quarter 1, we saw a few dynamics. One, we continue to see in certain cancers that we have a focus, in such as breast cancer, lower diagnosis rates than pre-COVID levels and lower NBRx, as I mentioned, with Kisqali®. That combined is we also did see destocking and impacts on some of our, let's call it, more mature brands or mature promoted brands as well as off-patent brands.

At the moment, we do expect the trend to stabilize and we expect in the remainder of the year the performance in Oncology to be driven by our newer medicines, of course, Kisqali® as well as Pluvicto®, Scemblix®, et cetera. But of course, continued performance from Promacta®/Revolade® and Jakavi®. And so I think we'll have to monitor it closely, but we're optimistic that things will start to get back to normal over the course of Q2. Next question operator.

- Operator

Your next question comes from the line of Emmanuel Papadakis from Deutsche Bank.

- Emmanuel Douglas Papadakis - Deutsche Bank AG, Research Division

Q. Perhaps one on JDQ. Congratulations on the impressive AACR update. Just curious in your strategy to differentiate or catch up there given you're a little late behind the two leaders in that space. I'm particularly interested on the latest perspective as regard to the SHP2 combination. I see you started an internal combination program. Does that signal deprioritization of the Mirati collaboration and when indeed might be seen update of – clinical update of the combination days from either Mirati study or indeed your own internal efforts?

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Emmanuel. One of the things we've observed thus far in very early clinical data is in order to have a good combination agent, we need a pretty clean profile from the G12C agents. So one of the advantages we hope we will have, is given the absence of Grade 3/4 AEs in our studies, but it is a kind of combination agent of choice so that despite us being late we would have the opportunity to combine the medicine with other attractive agents.

With our SHP2, I think that's part of the story. We do have studies ongoing with Mirati and Amgen, but we believe our JDQ molecule is optimized for combination with our SHP2 to really allow us to get to the optimal dosing with limited AEs and hopefully maximize the benefit for patients in our studies.

So the key to our strategy is having a medicine that can be the combination agent of choice from a G12C standpoint and then hopefully demonstrate, despite us being late in mono, that we'll be able to win the battle in the long run with combinations, PD-1, SHP2 and perhaps others. Important to note, we still need to do larger studies. I don't want us to overextend our interpretation of a relatively small clinical study, but at least the early signals are promising. Next question operator.

- Operator

Your next question comes from the line of Emily Field from Barclays.

- Emily Field - Barclays Bank PLC, Research Division

Q. I just wanted to ask on the business in China. I know you had a – Innovative Medicines had a very strong quarter in first quarter. But just if you are seeing any impact as we get into second quarter from lockdowns in some of the major cities or just any impact on the broader business.

- Vasant Narasimhan – CEO of Novartis

A. Maybe I'll give the China question to Harry. Harry on China.

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you, Emily. So overall, we have seen very limited impact in China, as you say, in quarter 1, not at all. And in quarter 2, of course, we are daily monitoring. When there is a city or an area with a risk of lockdown, usually then wholesalers ship a bit earlier to ensure that pharmacies and hospitals on the ground have product. So we don't see really impact, very marginal only. And of course, we continue to monitor that. I mean it's one of the reasons why we also kept our forecast assumptions. Should this spread bigger, there would be likely some impact. But we have kept the forecast assumption that we need to see continuation to return to modern prescribing behaviors and China certainly is one of the focus areas for that forecast assumption. But again, so far, we don't see or very limited impact of this. And we will continue to monitor and provide you an update in quarter 2.

- Vasant Narasimhan – CEO of Novartis

A. Thanks Harry. Next question operator?

- Operator

Your next question comes from the line of Tim Anderson from Wolfe Research.

- Timothy Minton Anderson - Wolfe Research, LLC

Q. A couple of questions on Cosentyx®. Q1 in the US was a little bit weaker versus what we're expecting and I'm wondering why? And then also, just wondering how to think about that product in 2023 as Humira faces biosimilars and as AbbVie tries to lock in formulary placement for that product for Humira. And then Skyrizi, their goal is to preserve volume with Humira. They'll do that through stepped-up rebating. And I'm imagining that puts a fair amount of new pressure on products like Cosentyx® and other brands in the category. Is that a fair assessment? And does that kick in only in 2023 and beyond? And does that at all pose a risk to the USD 7 billion peak sales guidance?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Tim. I mean we remain confident in the USD 7 billion-plus peak sales guidance. When you look at the dynamics in quarter 1, this is pretty standard for us when we look at reverifications as well as the other elements in the US to get patients confirmed for the remainder of the year. Within the, I would say, dynamics we've historically seen for the brand, we saw good volume growth overall with Cosentyx®, particularly in rheumatology. That said, in the US, we would expect to be growing in the single-digit range in the next two years until we get our new indications and new formulations online, which we then think will give us the next wave of acceleration. Cosentyx®' additional growth will be driven by our strength in Europe as well as the China NRDL listing and launches elsewhere around the world. So it's a combination of those factors that will drive the growth in the next two years. And then the new indications, new formulations, et cetera, will give us the next boost which we believe to get us over that USD 7 billion mark.

And in terms of the specifics on the Humira dynamics, et cetera, again, I think that's all built into the forecasted

numbers that I gave you right there. We feel confident in our overall contracting position given the volumes we currently have with Cosentyx® and the positions we have with the relevant formularies. Next question operator.

- Operator

Your next question comes from the line of Peter Welford from Jefferies.

- Peter James Welford - Jefferies LLC, Research Division

Q. I wanted to come back to Sandoz. You flagged that there were certain onetimers in the quarter that boosted 1Q. I wonder if you could just talk a little bit about those and what the impact of them was? And also, if you look at the margin of Sandoz, obviously, a lot of that was boosted by some of these onetime effects presumably in the easy comp. But can you give us any sort of idea of that sort of significant year-on-year gross – sorry, core operating income margin improvement? How much of that do you think is actually sustainable and due to some of the efficiency measures within? And how much of it, on the other hand, is just something we should assume is a 1Q onetime effect to help us guide think about the quarters coming forward.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Peter. I'll give that one to Harry. Harry?

- Harry Kirsch – CFO of Novartis

A. Yes, Peter, thank you. As you have seen, Sandoz has improved. The margin was a low base prior year by basically 330 basis points, call it 3 margin points to close to 22.84%. Now roughly 2 points of those come from cost of goods, a little under 1% from SG&A and then 0.6% from OIE, where we would have these little divestment gains. As you know, everything above USD 25 million divestment gains, we would always co-adjust. Sometimes not too often, we have little divestment gains that are below USD 25 million and then they would stay within OIE. But the overall OIE bucket went from – we call, correctly, from a minus USD 11 million OIE effect, total OIE, prior year quarter 1 to plus USD 7 million OIE number in '22. So the absolute numbers are small, it's USD 18 million total OIE impact, which is that 0.6% of margin or 4 points of a 26% improvement.

So the core margin, if you take that little OIE effect out, it's like 22%. So overall, not significant. But of course, we mention it, when the OIE contributes to the overall improvement. So if you take that out, that is not a bad representation, also a very good representation of the underlying profitability.

And then we have to see over the next quarters how pricing will do and, of course, how much the cough and cold season will be back to fully normal. And the other thing is, of course, given the larger cost of goods, percent of sales, the energy cost and some of the supply price inflation, how much we offset from productivity. Overall for the company, I'm very confident we do that. Within Sandoz, we have to watch that given the bigger part of the P&L was Innovative Medicines.

- Vasant Narasimhan – CEO of Novartis

A. Terrific. Thanks, Harry. Next question operator.

- Operator

Your next question comes from the line of Keyur Parekh from Goldman Sachs.

- Keyur Parekh - Goldman Sachs Group, Inc., Research Division

Q. Vas, if I look at the last 6 months since you reported the third quarter on October 27 – 26, you've announced the strategic review for Sandoz, you've done the Roche stake sale, you've reorganized the Innovative Medicines business and today announced this new kind of initiative on kind of big growth kind of a new seat on the ECN. Just wondering kind of – is there a common theme across these 4 initiatives? It seems that you're doing a lot on a very short period of time. So just trying to get a sense for what's driving these measures.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Keyur. Look, our goal is to drive outstanding company performance for the benefit of our shareholders and benefit of patients and society. And I think all of these moves on the first order are creating value for our shareholders. Clearly, evaluating if Sandoz fits within the group or is better as a stand-alone company, and we've demonstrated with Alcon, we do that in a thoughtful way. In the case of Alcon, we created an outstanding stand-alone company. We'll evaluate the same with Sandoz.

The sale of the Roche stake and buying back our own shares in a place where we view our shares are undervalued relative to the potential of the company and the growth that we have confidence in and that our Board has confidence in, again, a value-creating move.

Reorganizing so that we become much more agile, efficient, take out costs out of the system, improve our overall operating performance both on the top and bottom line generate differential growth. Again, I think a very logical thing to do to increase shareholder returns and value and improve the performance of the company.

And then lastly, you referenced, it was kind of part of the reorganization, but the creation of the strategy and growth function is to create a consistent top-level view of do what is the right things we need actions we need to take on our internal pipeline versus the external opportunities that we have before us in order to keep a consistent growth as we've guided of the mid-single 4% to 5% range in the coming years and then above peer median in the back half of the decade. So it's about performance, it's about creating shareholder returns. And it's about driving more impact of the company on medicine. Thank you, Keyur. Next question operator.

- Operator

Your next question comes from the line of Florent Cespedes from Societe Generale.

- Florent Cespedes - Societe Generale Cross Asset Research

Q. A quick follow-up on Sandoz, please. Could you elaborate on the performance of the different businesses, if you see any inflection point, especially in the US where you used to be under pressure from – strong pricing pressure there. So if you start to see any inflection point could be very helpful.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Florent. So overall, Sandoz had – is now getting back to growth globally, but particularly, I would say Europe has had strong underlying performance, driven both by biosimilars and small molecules. Also good performance in our international, as we call it, emerging markets plus Japan.
The US still declined in the single-digit range, but we currently have an outlook that we expect in – over the course of '22 and the first part of '23 to really bottom out on the US oral solids business which will then allow us to build on biosimilars and new launches to get back to growth. And we expect coming out of '23 and then into the mid-2020s, '24, '25, et cetera, for the US business to really grow on the back of biosimilar launches as well as more first to files in the overall injectable and small molecule pipeline.

So that's the dynamic we see. But certainly still some ways to go – a little bit more to go in the US to get to the bottom, but that should be coming and then we get back to growth. Europe is a very solid footing. And in international markets, we generally tend to do well. Next question operator.

- Operator

Your next question comes from Sarita Kapila from Morgan Stanley.

- Sarita Kapila - Morgan Stanley, Research Division

Q. How should we think about the Lu-PSMA opportunity, particularly given there's been a restriction to a Gallium imaging agent versus Gallium and [FAT] that could just limit the number of accessible patients in the overall commercial opportunity.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks. For Lu-PSMA, we have currently worked very hard on [locameto], our Gallium agent, where we are – we've already secured agreements to have this agent distributed widely amongst diagnostic centers. So we expect over the coming months to be able to relieve any constraint on imaging these patients to enable uptake of the medicine. And as I mentioned, we're leveraging the Lutathera® footprint, but also beginning to work already in bringing additional centers online in order to fully capture the earlier-line opportunities. We're going to need to move from roughly 250 centers where we currently service RLTs to get to over 500 centers, roughly 550 centers. That's part of a multiyear effort.

As a reminder, we expect Pluvicto® in this later-line, third, fourth line prostate – metastatic prostate cancer setting to be around USD 0.5 billion to USD 750 million opportunity. And really the more significant opportunity would come from the very large patient populations in the earlier-line settings where we have a readout in the second half of this year as well as a readout next year within – current evaluation ongoing to expand into additional lines of therapy to see if the medicine can be more broadly used.

- Operator

Your next question comes from the line of Steve Scala from Cowen.

- Stephen Michael Scala - Cowen and Company, LLC, Research Division

Q. My recollection is that NATALEE readout initially was 2023 but that was moved up to 2022. That may have been announced as early as 2019 due to confidence in an interim look. So what changed since 2019 when things were apparently progressing very quickly? And if the current slow event accumulation is due to delayed visits and therefore delayed event detection as a result of the pandemic, how would that impact the final analysis?
Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Steve; so since 2019, we increased the sample, if my recollection is correct, we increased the sample size of the study up. We certainly increased our overall time line. I don't recall exactly, but I'll look into the point you raised around what we said previously on interim, certainly a very fair challenge. But with the revised 5,000 patients in the study and 500 events, we've been forecasting on an ongoing basis.

One thing that is important to note is we did a very detailed look over quarter 1 to ensure that we've collected all events. And to our best assessment, we don't believe this is – our current event rate is due to delayed reporting of events or over COVID impacts. We believe now we have a clean look at the study and that the event rate is below our projected event rate. Unrelated to operational concerns, but just related to the events

accrual rate in the study.

And of course, we'll keep you updated, but I think our team did a pretty rigorous job over the recent months to really ensure we have all of the best data on hands to provide you this update. Next question operator.

- Operator

Your next question comes from the line of Laura Sutcliffe with UBS.

- Laura Sutcliffe - UBS Investment Bank, Research Division

Q. Just perhaps in the light of your Chief Strategy and Growth Officer appointment, maybe you could touch on some comments you made on your recent call when you announced your business reorg on the idea that you're good at getting your pipeline to market but maybe need to get better at getting very big drugs to market. So as not too many steps to remove from saying that you might want to think about reprioritizing your Innovative Medicines pipeline. So could you maybe just talk about your process for deciding when not to pursue projects and whether you think there's such a thing as too big of a pipeline. And specifically, maybe you could talk about how your colleagues are incentivized to shut projects down rather than keeping them alive.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Laura. A big question there. So a few points – few points I'd raise, kind of going step by step. First, we do have, I think, a rigorous approach to prioritizing our pipeline, particularly after proof-of-concept readout, through submission. We not only look at scientific factors, scientific tractability but also look at, of course, NPV, ENPV, peak sales, return on capital employed, probablized return on capital employed. But I think it's important that we have very good analytics to back up those assessments of those molecules and then make sure that, also versus the competitive set, we've looked at them with silver eyes. So I think that's one thing we want to upskill in the organization, to have really outstanding information with which to make those decisions and also evaluate against other external opportunities.

Then on top of that, I've previously stated that we've increased the thresholds that we're putting in place at an asset level, not necessarily at an indication level. But we want assets that have the potential to be multibillion-dollar assets. That will mean that by exception we might go after some others when they are strategically – have a good strategic fit, but it's certainly our goal to find multibillion-dollar assets. And then to have the discipline to say no when assets don't meet those thresholds.

We've also endeavored over the recent years to focus down on therapeutic areas that we really believe we can build scale in for the long term. Clearly, as Andrew mentioned earlier on the call, cardiovascular is a top priority. Immunology, given all of the various medicines we have in the pipeline on top of Cosentyx®, of course, we have our BTK inhibitor. We have VAY as well as other assets now progressing through also a priority.

Neuroscience, given our presence in multiple sclerosis but also emerging assets we have in neuroscience. And of course, solid tumors and hematology.

So 5 kind of pillar of TAs. Of course, we have some medicines in areas like ophthalmology and respiratory. But we want to have our focus be to build scale in those 5 priority TAs and again have the discipline always to chase anything else that might be around in other therapeutic areas.

So I think with those factors in place, we can, over time, really ensure we have the right pipeline to drive growth for our company. As I mentioned, over 20-plus multibillion dollar assets to our current assessment. But

certainly, we'll ask Ronny to reassess that and give us an honest look and to honestly tell us where we're at and what do we need to do and where does the external environment give us opportunity and where maybe doubling down on other internal assets give us an opportunity as well.

So a lot of, of course, ongoing work, but I think we're on the right track. And we're hopeful and optimistic that with Ronny coming onboard, we can even accelerate on that journey. Next question operator.

- Operator

Your next question comes from the line of Seamus Fernandez from Guggenheim Securities.

- Seamus Christopher Fernandez - Guggenheim Securities, LLC, Research Division

Q. So, Vas, maybe first question is just how you see the PCSK9 environment evolving in the context of Merck's oral PCSK9 where we're seeing some pretty robust data. I'd love to just kind of get your thoughts there and then the evolution of the market as we see it for an injectable therapy.
And then second, just wanted to get a better sense of the impact of inflation and how – what levers Novartis has the capability to pull to keep up with inflation? Do you see a pricing environment in the United States that can actually facilitate price increases? Because it appears that, that won't necessarily be available in international markets. But maybe you can just correct us where our thinking might be wrong as it relates to the ability for Novartis and the rest of the pharmaceutical industry to keep up with inflation.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Seamus. I think on the PCSK9, first, it's important to take a step back and look at the global unmet need. I mean there's an estimated 16 million-plus patients around the world who have ASCVD that are not adequately controlled with current agents. So big, big opportunity. In the US alone, 18 million to 20 million patients. So there is plenty of space here for many agents. And even if we capture a fraction of that with Leqvio®, we have a very sizable – sizable medicine. That I think, first, is important as context.

It's also important to note with Leqvio®, our goal is to access that broader market. I mean if you look at current PCSK9 monoclonal antibodies, they're accessing a fraction of this market. So our goal is to grow the market. And with bringing forward a twice-a-year Part B medicine and then setting up the infrastructure in cardiovascular care with Part B clinics but then also with population health agreements around the world, we think it's a pretty unique value proposition for an asymptomatic disease to have a twice a year therapeutic versus having chronic therapies where we know that patients generally don't comply with their statins or ezetimibe or related therapies.

So that's the broad strategy. So when I think about orals or monthly injectables, I don't think it changes our strategy and our belief that in the long run, the ability to provide twice-a-year medicines through the physician buy-and-bill and Part B model in the US and population health around the world is a long-term opportunity to address this relatively vast market opportunity. And I mean, let's see what happens. Of course, as you know, in cardiovascular disease, it's a long journey to get from early clinical data ultimately to the patients at the other side of the long journey. Now in terms of inflation, Harry?

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you. And thank you, Seamus, for the question. Very important, of course, in the geopolitical environment we are living. I think I would start with that usually also my experience and given our cost structures, inflationary pressures can be usually well balanced with productivity measures. And so we are not very energy-intensive.
On the other hand, of course, if inflationary measures get into the personnel cost side which over time will

happen here or there, I think we have very good productivity programs in place to offset that.

And of course, also our move transformation for growth which combines, for example, our shared service, together with our manufacturing supply chain, there, our leader, (inaudible) and his team will further strengthen the impact of our procurement organization across our complete external spend. So that's one element. And overall, I think we are very well positioned to fight any potential bottom line effect off with increased productivity measures.

In terms of pricing power, I mean, as you described, it's mainly in the US given our portfolio and business. We have been, within our pricing policies on key brands, increasing in the mid-single to mid- to high single-digit range in list prices. (inaudible) depending on the rebates, we have to get a plus or minus low single-digit environment. Of course, we look at that also from a competitive standpoint. But of course, we would always price with our commitments.

And ex-US, there is some limited pricing increases potential, but much less and usually more for Sandoz. We have also some OTC elements in the Sandoz business.
But I think key is for us that we do not only try to offset pricing, but with significant productivity measures as well as via procurement, ensuring that our suppliers do the same in their productivity efforts and offset inflation as much as possible.

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Harry. Next question operator.

- Operator

Your next question comes from the line of Kerry Holford from Berenberg.

- Kerry Ann Holford - Joh. Berenberg, Gossler & Co. KG, Research Division

Q. A question on M&A. Given the recent pullback in valuations and seemingly tough IPO markets, I wonder, Vas, if you can give us your latest perspective on the environment. In the context of the broader market moves, are you noting more external interest, greater willingness to discuss potential collaborations and M&A opportunities?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Kerry. When you look at, of course, the pullback in the XBI and I think I've heard various data points but many companies trading below their even the cash they have on hand, I think it certainly points to doing the disciplined look. But I think first and foremost, we have to be science-driven and really ask is there science and good data to support an acquisition? And I think there, as we're seeing in the broader biotech market, it's been challenging. And then I think a lot of data readouts have pointed to the fact that it is hard to find novel drugs effectively.

So we continue to look. Our focus remains, as I've guided in recent quarters, into the sub USD 2 billion space to see if there are attractive methods. And when there are good deals out there, we're, of course, looking to do them.

I do think over the course of this year as well, expectations amongst sellers, so to speak, will adjust. And there may be more openness to think about how partnerships and M&A and business development could be conducted. So there could be more activity certainly in the sector second half of the year. And we'll, of course, be doing our part to diligently keep screening and see what's out there that could be attractive. Next question

operator.

- Operator

Your next question comes from the line of Naresh Chouhan from Intron Health.

- Naresh Chouhan - Intron Health

Q. Just one on the impact of inflation on cost base, following off from Seamus' question. Just a question on the phasing of the impact of inflation on the cost lines. Because I'm guessing you have a bunch of contracts that are longer term and some suppliers may yet have to raise prices. So should we be thinking about inflationary impacts on costs in H2? Or will that be pushed into next year? And then linked to that, when you formulated your guidance earlier on in the year, do you feel the inflationary pressures you're seeing now are, I mean, is fully accounted for?

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Naresh. Harry?

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you, Naresh. Yes, we have seen some in quarter 1 on energy, right, like probably most others. And – but again, we are not so energy-intensive. And when we basically forecast out the energy part as well as the supplier base, as you say, contracts a bit further out, we see roughly 1 point of OpInc as the risk around that. But we have offsetting measures to offset that and be well within our guidance.

And then of course, the other question is, of course, will this stay here, this situation, for a long time? Of course, at the moment, we assume, from a forecasting standpoint, it will remain for the rest of the year. And then beyond this year, I would say, again, we have many levers of productivity to offset that so that we are also very confident in our mid- to long-term opt margin guidance which we did together with the announcement of transforming growth initiatives. So overall, I would say, given our cost structures, manageable. But of course, we'll ask for some increased efforts to do so, but we are well prepared.

- Vasant Narasimhan – CEO of Novartis

A. Thanks Harry. Next question operator.

- Operator

Your next question comes from the line of Richard Parkes from BNP Paribas.

- Richard J. Parkes - BNP Paribas Exane, Research Division

Q. Just on your Innovative Medicines, 40% plus margin target, I'm trying to square that with some of your peers. That don't seem to feel that's a sustainable level of profitability. And given that you're a therapeutically diversified business, I would have thought that would lead to structurally slightly lower overall margins. I wondered if you could just highlight us what we're missing or what's unique about Novartis that we're overlooking?

And just following on from that, Keyur mentioned you've been demonstrated willingness to grapple challenges within the business in recent times. And I just wonder if you could update us on your thoughts of your presence in some of your more subscale therapeutic categories like respiratory and ophthalmology. Just wondering whether that might be baked into achievement as that margin target exiting those areas.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Richard. When we look at our approach longer term, and we want to maintain R&D in the 20% range as we've guided, that we're always willing – 20% of IM sales that, of course, we're always willing to go up based on opportunities if they're highly attractive. And I think you see our peer set moving around some well below that target, some well above that target, but I still think in the long run being in that 20% range is a solid investment level given the size of the company.

When you think about our SG&A, we want to be at the median or better in the sector over time. And we certainly see peers who are far more efficient than us in the SG&A areas. So when we take our current IM margin, which is in that 36% to 37% range and we see the opportunities that come with technology, with rationalizing our footprint, with the opportunity to hopefully leverage capabilities in market, we think we can get those 4 to 5 points out of SG&A to get us into that 40% range on a sustainable basis. I can't speak to how our peers look at it. Of course, it does require you to rethink your business model. And I think what we're working on right now in IM as part of this new setup is to rethink our country's footprint and our approach to go to market in country to make it much more flexibilized, much more technology-driven, and in the long-run, we hope more sustainable to enable us to launch products highly efficiently. And that's where the opportunity comes from. It's certainly not from cutting R&D and our innovation engine, it's coming from that other part of our P&L and that's how we think about it.

On the portfolio optimization, nothing new to announce other than I think it's certainly – we are looking as well as part of this transformation how to optimize our commercial footprint as well as our development footprint based on the new model of a single IM unit. As part of that, of course, we're looking at relevant TAs. And of course, in respiratory, we're largely limited to Xolair®, with a small presence in QVM inhaled therapeutics. And in ophthalmology, really Lucentis and Beovu. So it's naturally part of our thinking how to optimize these two areas. That's certainly something we'll be working on over the course of this year.

- Operator

Your next question comes from the line of Graham Parry, Bank of America.

- Graham Glyn Charles Parry - BofA Securities, Research Division

Q. So just a question on Pluvicto®. So you talked about the fact that your own gallium-based diagnostic is helping or you hope to help with the uptake. But there is some feedback that the 18x diagnostics are easier to use, easier to manufacture. I noticed that you had done a collaboration deal with an 18x diagnostic manufacturer. So can that be back applied to the label for the vision indication and/or can you add it to PSMAfore and PSMAAaddition trials? Or would this just be for a front line?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Graham. So for the current launch, we are limited to the diagnostic on label. But certainly, for the follow-up indications, we're working hard to put together the relevant data package with FDA to hopefully broaden the range of diagnostic agents that can be used. You can imagine that as part of our discussions with the FDA, we put together our best arguments to be as broad as possible on diagnostic options for physicians, but at least for now on this first indication, but we'll be limited to the Gallium agents. But over time, we hope to expand that, especially as we go into the larger market segments in the coming years.

- Operator

Your next question comes from the line of Matthew Weston, Credit Suisse.

- Matthew Weston - Crédit Suisse AG, Research Division

Q. Vas, it's a question about buy-and-bill. So since you acquired the Medicines Company, you've educated us all on the advantages of buy-and-bill and how you hope in the US it's going to help with the commercialization of Leqvio®. I'm curious how we should think about buy-and-bill when you're up against it yourself in a competitive environment. And in particular, I'm thinking of iptacopan versus Soliris/Ultomiris and other high-value infused drugs but also Kesimpta® versus Ocrevus. Does that put a meaningful barrier in the commercialization potential of those molecules?

- Vasant Narasimhan – CEO of Novartis

A. Yes, absolutely. Thanks, Matthew. So one – I think it's very situation-specific. So let's take each one of those in turn.

I think in the Cardiovascular segment, when you're trying to displace orals which have low compliance, certainly a twice-a-year injectable that can be used in a subcu setting very rapidly for patients who had previous heart attacks is very attractive to cardiologists and we think will lead to meaningful clinical benefit.

Our expectation is in the rare disease setting, that while there is certainly – it is certainly a barrier, to be clear, it is certainly a barrier that we have to overcome, that the current agents are used as infused medicines in the buy-and-bill setting, that in this population it's not a big enough driver of the economics that providing patients an oral option to avoid having to go in and out of the hospital could be highly appreciated, particularly given the opportunity to be front line and be used on top of the infused agents. So our expectation is, again, a lot of this does come to economics. And I think in that setting, the oral medicine has a very attractive profile.

And then I think in neuroscience, it is very clinic- and situation-specific. We certainly see the highest uptake in Kesimpta® in segments of the market that are not highly penetrated by buy-and-bill. And I think in those segments of the market that have high utilization of buy-and-bill, there's less interest in using Kesimpta®.

Luckily, in MS, the penetration of B-cell therapies is still relatively low given the efficacy of these B-cell therapies. So there is a vast market opportunity to displace the older agents, the BRACEs, so to speak, and that is a big opportunity, and that's 60% of our source of business. And so we have ample opportunity there to get into the market and be successful.

So you've got to look at the dynamics in each one. But certainly, in certain instances, buy-and-bill can be a formidable obstacle in our market environment. Next question operator.

- Operator

Your next question comes from the line of Andrew Baum from Citi.

- Andrew Simon Baum - Citigroup Inc., Research Division

Q. Just following up from the last question, but staying within the cardiovascular domain. Amgen has a mRNA-based technology which is once every 6 months. It will be buy-and-bill. Thinking about how you are building out the buy-and-bill infrastructure, I'm just thinking about with – I'm thinking about how that's going to fit in within that environment?

- Vasant Narasimhan – CEO of Novartis

A. You mean for Lp(a), Andrew?

- Andrew Simon Baum - Citigroup Inc., Research Division

Q. For Lp(a), yes, sorry if I said – yes, sorry, I misspoke.

- Vasant Narasimhan – CEO of Novartis

A. Yes, absolutely. So of course, we're watching the Lp(a) evolution as well competitive environment. Certainly, it's an siRNA, which I understood is quarterly, I'll have to double check with my team if it's quarterly or bi-yearly, But certainly, that will be able to be used through the system. And as we think about life cycle managing Leqvio®, our goal will be to, of course, also think about ways to continue to leverage the infrastructure that we're building.

To be clear, and I think that's your point, Andrew, I think our current Lp(a) pelacarsen medicine would not be able to leverage buy-and-bill. But again, the size of these markets are so large, we still think there will be a substantial market opportunity as the first-to-market subcu medicines for these patients. And then, of course, we will – we are looking, of course, to get to less frequent dosing.

We do think to be successful in cardiovascular buy-and-bill, you have to be relatively infrequent, even quarterly, we'll have to see. But certainly, twice a year is a winner, we think, in this market segment. Next question operator.

- Operator

Your next question comes from the line of Simon Baker from Redburn.

- Simon P. Baker - Redburn (Europe) Limited, Research Division

Q. It's on cell therapy. I wonder, firstly, Vas, if you could elaborate on the statement in the press release about lower demand for Kymriah®. Is that simply the nature of cell therapies in general in this environment, whether there was anything specific to Kymriah®?
And related to that, I see last week, you pushed back the time lines for your genome-edited stem cell therapy for sickle cell from late '23 to August '25. I just wonder if you could give us any color on why that was.

- Vasant Narasimhan – CEO of Novartis

A. Yes. So on the second part of your question, I'd have to get back to you, Simon, I don't know offhand on the genome editing starts. We'll come back to you on that.

Look, I think on Kymriah®, just to provide a very realistic perspective, the DLBCL second line, the failure of Kymriah® in the second-line DLBCL is beginning to hit demand and I think we will see Kymriah® to have less growth over the coming quarters and years and potentially even declines as our two competitors build out their second-line DLBCL program.

So realistically for us in cell therapies, of course, Kymriah® has the – is the only medicine indicated in pediatric ALL, has a broad label in later lines across DLBCL and FL, in the longer term, it really comes down to our next-generation T-Charge platform, which we provided data on at the end of last year at ASH, where we demonstrated pretty attractive data in both DLBCL and multiple myeloma.

And I think in the intervening years, it's really just managing Kymriah® to provide it to patients to really focus on that next-wave technology. which we expect to have materially lower COGS, hopefully much higher throughput times, better efficacy and safety and enable the overall business to be significantly more attractive and more in line with other oncology agents in the company.

- Operator

Your next question comes from the line of Steve Scala from Cowen.

- Stephen Michael Scala - Cowen and Company, LLC, Research Division

Q. Kisqali® had its first appreciably down quarter, quarter-over-quarter since launch 5 years ago. You noted the weakness in new prescriptions, but even during the pandemic, Kisqali® was, at worst, flat. I am wondering what other reasons there could be for the current weakness. It seems it could be deeper than simply new prescription trends.

- Vasant Narasimhan – CEO of Novartis

A. Yes. So we did have some stocking movements in the US. Harry, you want to say a word on Kisqali® US, maybe that would help explain Steve's questions.

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you, Vas. So in the US, Steve, there was a slightly higher year-end stocking effects in the US at the end of December. That has been worked through in quarter 1. Totally for the company, there was nothing significant. But – so there was an effect on that – and that was basically impacting the US growth in the high single-digit percent point. So that's made a bit worse than what one would expect. So – but overall, of course, we see also we would – we need to see more NBRx growth. There, we are just flat, if you will. But that was on a single-brand basis, not a small amount, if you will, that impacted, of course, quarter 1 – this one quarter 1 last year comparison.
Vasant Narasimhan – CEO of Novartis

A. And we would expect in quarter 2, still at least from where we sit today, to see a return to the historical profile of Kisqali® growth. I think we have a few more questions, operator. Next question please.

- Operator

Your next question comes from the line of Matthew Weston, Credit Suisse.

- Matthew Weston - Crédit Suisse AG, Research Division

Q. Vas, I promise it's my last. It's on ensovibep. And if you could just give us an update. Obviously, COVID is waning hopefully or certainly in everyone's hopes, but we're still seeing government is making very significant purchases to stockpile various treatment agents. So can you tell us where you are in terms of your expectations for the molecule, but specifically your plans for the subcu trial and whether or not we should expect that to start in the near future.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Matthew. As we note actually in one of the slides, we filed the EUA, and the EUA remains open with the FDA. However, at this point, given the latest feedback that in our discussions with the agency, we would expect the agency to require a Phase III study before granting an EUA approval or a general approval. We're in discussions now to understand the final study design and what the agency would expect. And then we need to make a kind of sober evaluation as to is it a doable study in light of the waning rates of COVID around the world and then we can make an appropriate decision. Certainly, we believe in the profile of the molecule and certainly our discussions with the US government, they're excited about the concept of a onetime subcu therapy.

Alongside that, we do have a once-a-day oral agent that is currently completing the various preclinical tox in early studies. We should have a read on whether it's developable over the summer. And then we have to have

a similar conversation. It's an MPro inhibitor. And we have to have a similar conversation with FDA as to what would be the clinical development requirements. And again, in the context, is it developable and how long would it take to just accrue the events required. Last question operator. I think it's Graham. Graham?

- Operator

A. Graham Parry, Bank of America.

- Graham Glyn Charles Parry - BofA Securities, Research Division

Q. Great. I'll go for round 3. So just first of all, just a quick follow-up to the first question I asked on NATALEE. I just wondered, as you're slipping into 2023, is it just slipping into 2023 or on the event rate that you're looking at, at the moment, is it a first half or second half '23 read?

And then on Cosentyx® is my actual follow-up. You've got the initial lichen planus Phase II data, I think, this year. It's a large indication, lots of patients. I just wondered if you are thinking about this as a longer-term opportunity. Because on your IP slide, it says Cosentyx® passes 2029 plus. I'm wondering, are you looking at additional IP protection strategies for Cosentyx® beyond 2029?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Graham. On NATALEE, nothing more I can really say at this point. I think we'll continue to update the event rates and provide more granularity on when we would expect a final readout over the course of this year. But I think we give you the best forecast we have now that it's now pushed into 2023.

On Cosentyx®, we do have lichen planus readout upcoming. And we are looking at, of course, the standard patent extension strategy beyond 2029, also currently to continuing to progress in NIBR efforts to develop an oral IL-17 inhibitor as well as other life cycle management strategies, biologic strategies for Cosentyx®. Nothing concrete as of yet but certainly high on our mind to get Cosentyx® to move into the 2030 alongside continuing to defend the full patent state of Entresto®. We have 10 Orange Book patents now issued and our goal continues to be to defend that, to see how – to try to keep Entresto® protected for as long as possible as well.

So thank you, everyone, for the call. I really appreciate it. Great questions from everyone. We'll look forward to speaking to everybody soon. Thank you again for your interest in Novartis.
