2022 Q3 results presentation and transcript

2022 Q3 results presentation

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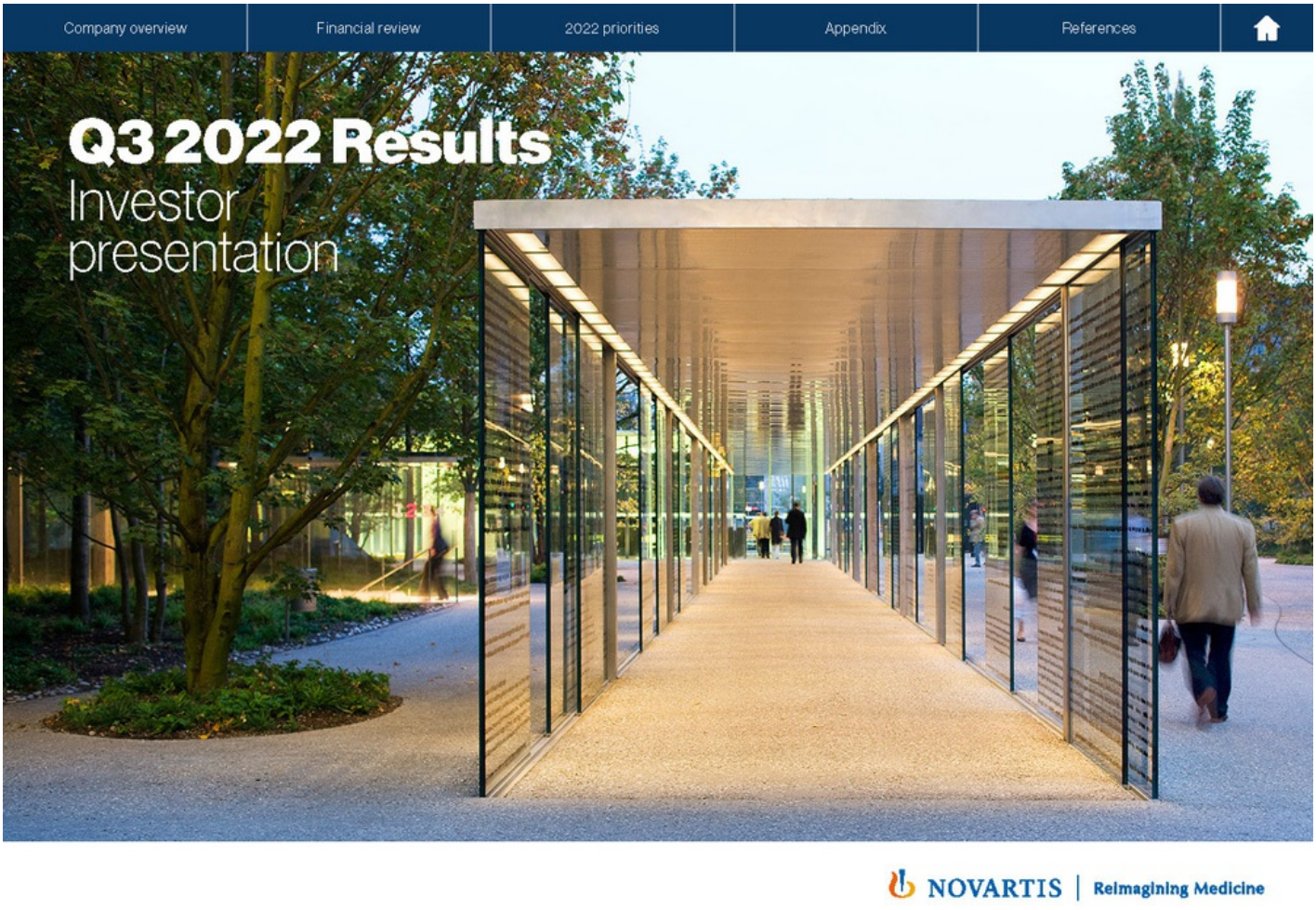
Transcript

View the 2022 Q3 results presentation and read the transcript slide by slide

Slide 1 – Samir Shah, Global Head Investor Relations



Thank you very much, and good morning and good afternoon, everybody. Thank you again for taking the time to participate in Novartis' quarter 3 conference call.

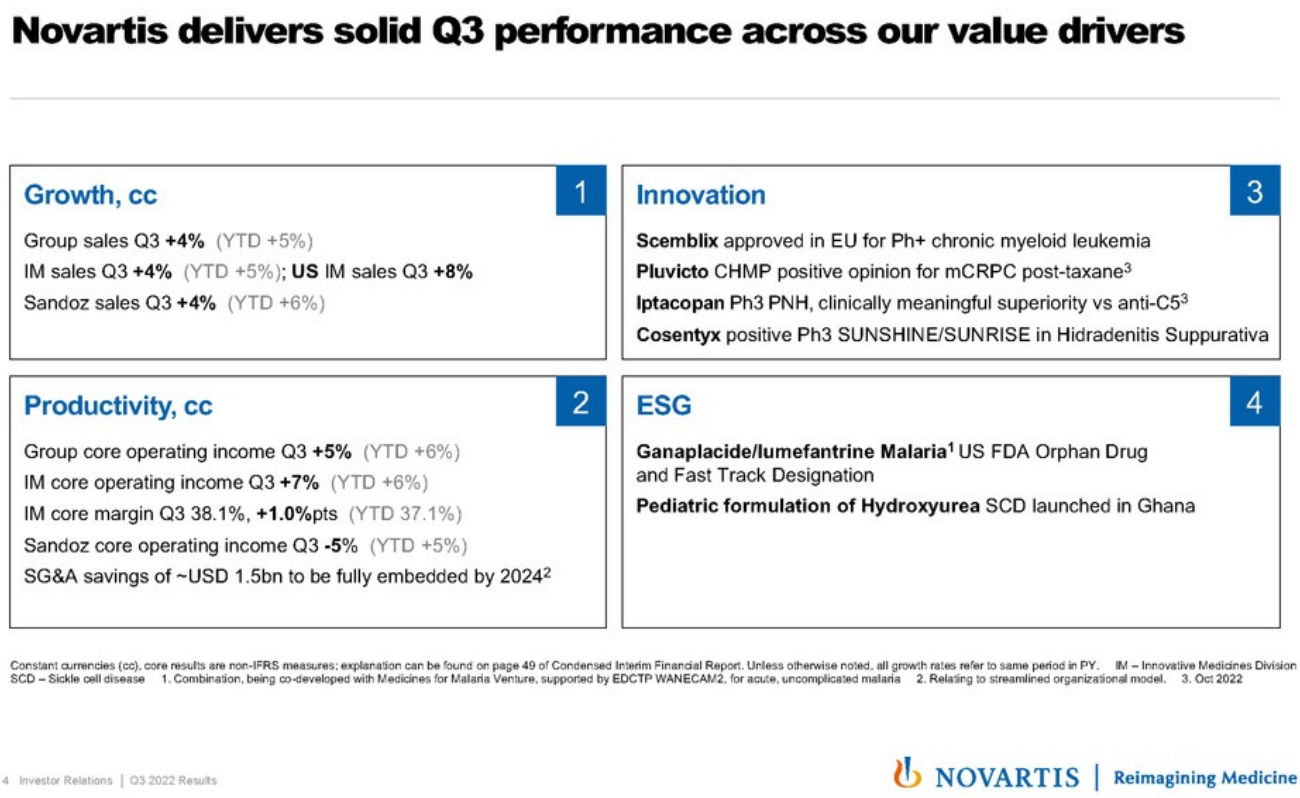
Slide 2

Before we start, just a quick reminder of the safe harbor. 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, 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

Thank you, Samir, and thanks, everyone, for joining on today's conference call.

Slide 4



Moving to the first slide, we take a couple of slides forward. Novartis delivered solid quarter 3 performance really across all of our core value drivers. From a growth standpoint, group sales were up 4% in constant currencies. That was driven both by solid performance in IM at 4% as well as in Sandoz. US IM sales were up 8%, consistent with our strategy to continue to improve our position in the US market.

From a productivity standpoint, group core operating income was up 5%, again driven by IM, which was up 7%. We also had continued our margin progression with a 1 percentage point improvement. Our savings from our SG&A program are on track, and Harry will cover that in a bit more detail.

From an innovation standpoint, we had some important events, particularly the approval of Pluvicto® with a positive opinion in Europe from the CHMP. And the readout we had and announced earlier this week of Iptacopan in PNH across two superiority endpoints versus anti-C5, and I'll go through that in a bit more detail.

Lastly, on an ESG front, we had an important announcement with respect to our work with the Medicines Patent Pool as well as two additional important milestones for two development programs with hydroxyurea in sickle cell disease as well as in malaria.

Slide 5

1 GROWTH

Strong performance of Entresto®, Kesimpta®, Kisqali®, Pluvicto®

Q3 sales[1]

	Sales USD million	Growth vs. PY USD million	Growth vs. PY cc
Entresto	1,135	211	31%
Kesimpta	289	180	172%
KISQALI	327	95	49%
PLUVICTO	80	80	nm
SCEMBLIX	41	41	nm
Tafinlar + Mekinist	450	33	16%
LEQVIO	34	29	nm
Cosentyx	1,274	27	7%
PIQRAY	103	21	26%
MAYZENT	94	18	29%
LUTATHERA	132	12	15%

Constant currencies (cc) is a non-IFRS measure; explanation of non-IFRS measures can be found on page 49 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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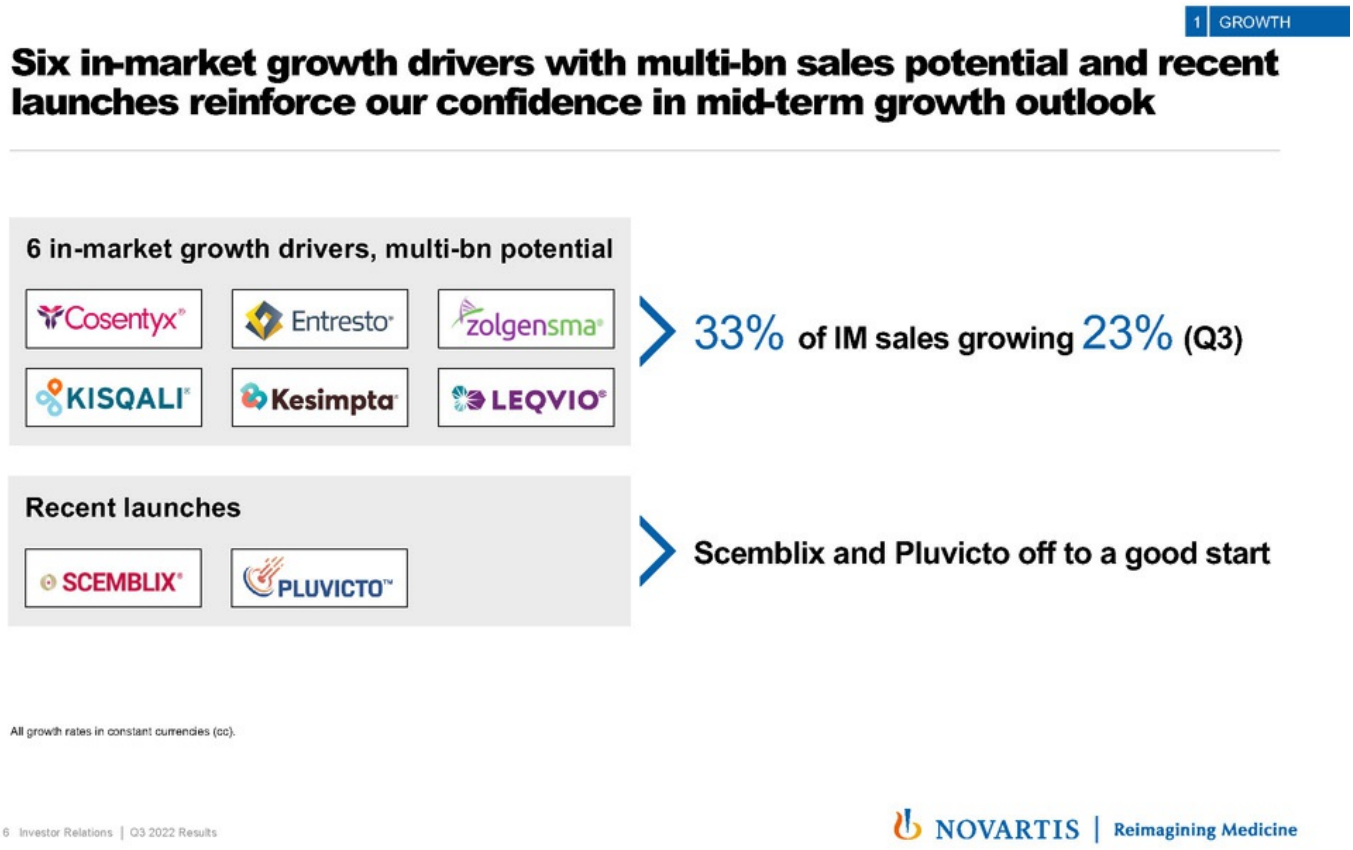
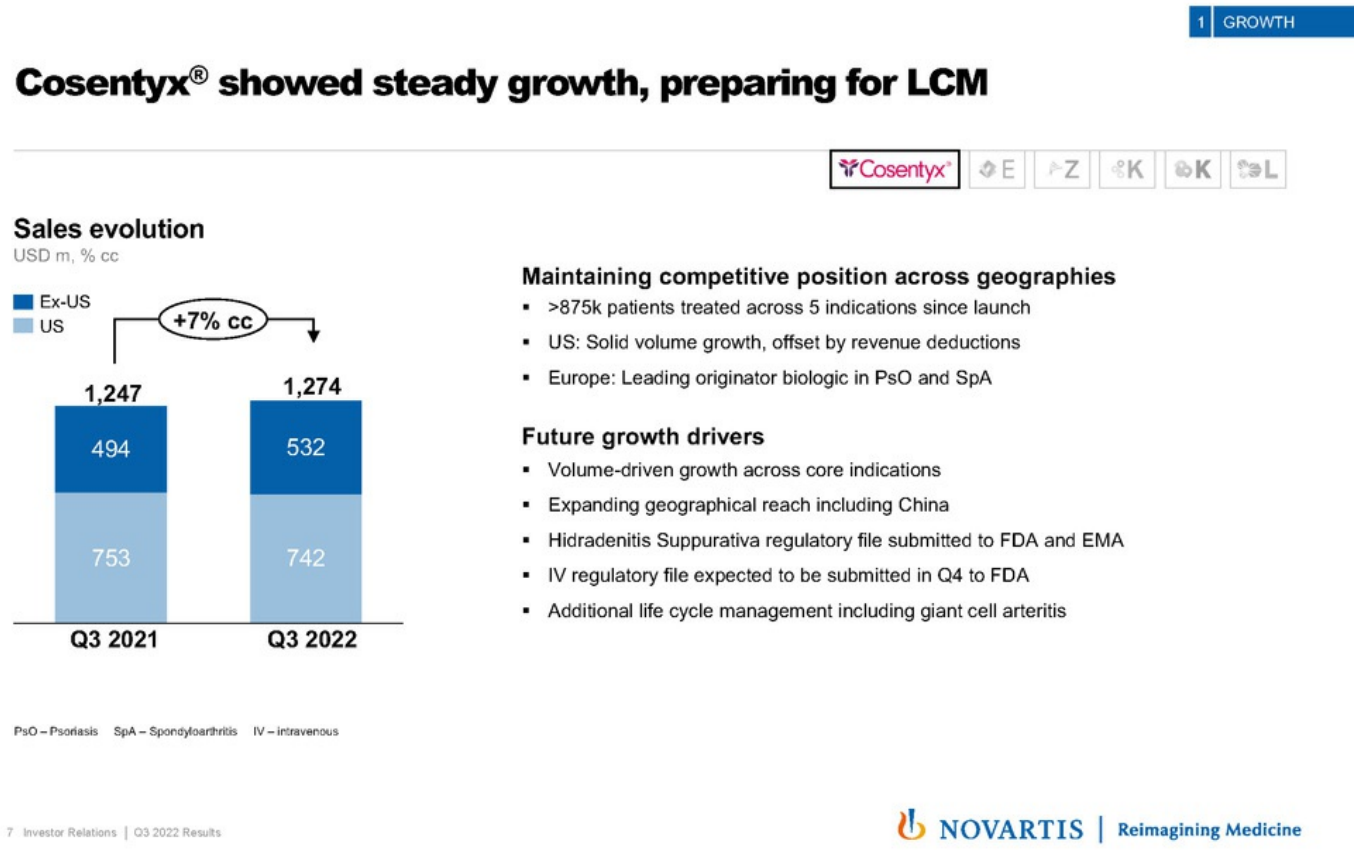
Moving to the next slide. The performance in the quarter was really driven by Entresto®, Kesimpta®, Kisqali® and Pluvicto®. And you can see the growth here for each of these brands. Entresto® continues its strong trajectory. Kesimpta® and Kisqali® performing well. And Pluvicto® in its first full quarter in the launch, also performing very well in its early days. We also saw good performance across some of the other brands, and we'll come to that brand by brand in the upcoming section.

Slide 6



Moving to Slide 6. One important element of our story is our ability to make our six key in-market growth drivers into multibillion-dollar medicines. And we stayed on track with respect to that, to really continue our confidence in our midterm growth outlook. Those six brands now account for 33% of IM sales, and they were growing 23% in the quarter. And as noted, both Scemblix® and Pluvicto® now are off to a good start and could one day be added to that list of six brands to also be potential multibillion dollar brands in the future, depending on how readouts go in the earlier lines.

Slide 7



Moving to the next slide. Now we'll just take a walk through each of the individual brands, and I'll give you some of the key highlights from the quarter.

Cosentyx® showed steady growth in the quarter. You can see 7% growth in quarter 3. We were maintaining our competitive position in our three core geographies. We have over 875,000 patients now treated. In the US, we saw solid volume growth, but we also saw the impact of increased revenue deductions, particularly in Medicaid and 340B segments, relative to a previous uplift we saw in revenue deductions in the previous year. That's something we'll continue – we expect to continue in quarter 4.

Now with respect to Europe, we maintain our leadership position amongst originator biologics in psoriasis and spondyloarthritis.
Future growth drivers for Cosentyx® to get to that USD 7 billion peak sales will be driven by our continued expansion in China. Notably, in China, at the moment, we do face headwinds with the ongoing lockdowns, but we continue to expect China to be an important part of our story.

Hidradenitis suppurativa has now been filed – submitted, filed in both FDA and EMA. I'll tell you a little bit more about why we feel like we have a good opportunity with this indication.

We expect to submit our IV regulatory file in quarter 4. And we also continue to advance our life cycle management program across additional indications, including giant cell arteritis where we saw pretty solid Phase IIb data.

Slide 8

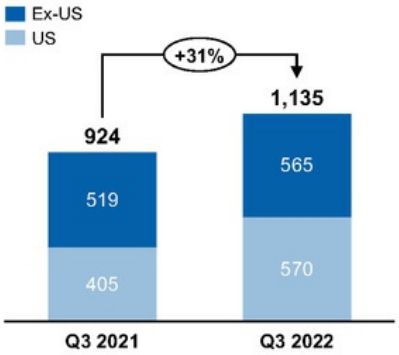
1 GROWTH

Entresto® +31% cc, growing strongly across geographies

Entresto

Sales evolution

USD m, % cc



US weekly TRx[1]

Total prescriptions (000)

Strong quarter performance

- WW: Increased to >8m patients on treatment[7]
- US: Accelerated momentum, ~1.1m TRx in Q3
- Europe: Strong demand growth continues

Future growth drivers

- Only 1/3 of eligible HFrEF population on treatment in G7[2]
- Strong profile in clinical and RW settings in HF[3,4]
- Guidelines (AHA/ACC/HFSA) support Entresto as 1st choice in HFrEF, expand support in HFpEF[5,6]
- Hypertension: High unmet need in Asia Pacific[6]

See last page for references TRx – Total Prescriptions WW – Worldwide HFrEF – heart failure with reduced ejection fraction RW – Real world AHA – American Heart Association ACC – American College of Cardiology HFSA – Heart Failure Society of America HFpEF – heart failure with preserved ejection fraction

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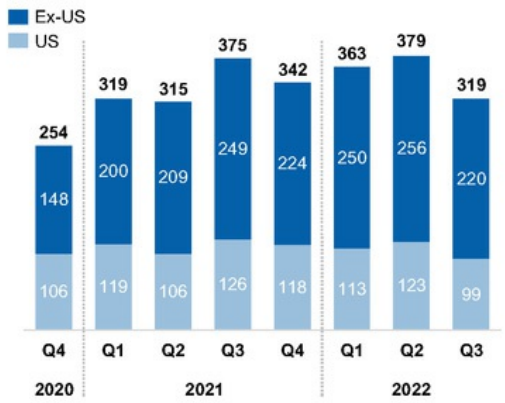
Now moving to Slide 8. Entresto® continues strongly across all geographies, 31% growth in the quarter. You can see here the weekly TRx has continued to set record after record, really strong performance in the US, but also around the world. We now have over 8 million patients on therapy. Accelerating momentum in the US, strong demand in Europe.

When you look at the future growth drivers of the brand, it's worth noting that only 1/3 of eligible HFrEF patients are currently on treatment in the G7. And there's a strong profile we continue to build in clinical and real-world settings in heart failure. We have guidelines that continue to support the use of Entresto® and HFrEF and also support its use in HFpEF. And we're also seeing good demand from the hypertension indications we were able to secure in Japan and in China.

Slide 9

Zolgensma® sales now predominantly incident patient population



- Both US and ex-US market now mainly incident patient population
- YTD double digit growth in incident patients treated
- 2500+ patients treated worldwide[1]

Future growth drivers

- Foundational treatment for SMA type 1 newborns
- Now approved in 45 countries with access pathways in place in 30+
  - Access negotiations ongoing in 10+ countries (e.g. Brazil, Argentina)
- Efforts ongoing to increase newborn screening (35% in Europe; 98% in US)

IT data: STEER enrolling continues; STRENGTH to start in Q4 2022

1. Across clinical trials, managed access programs and in the commercial setting.

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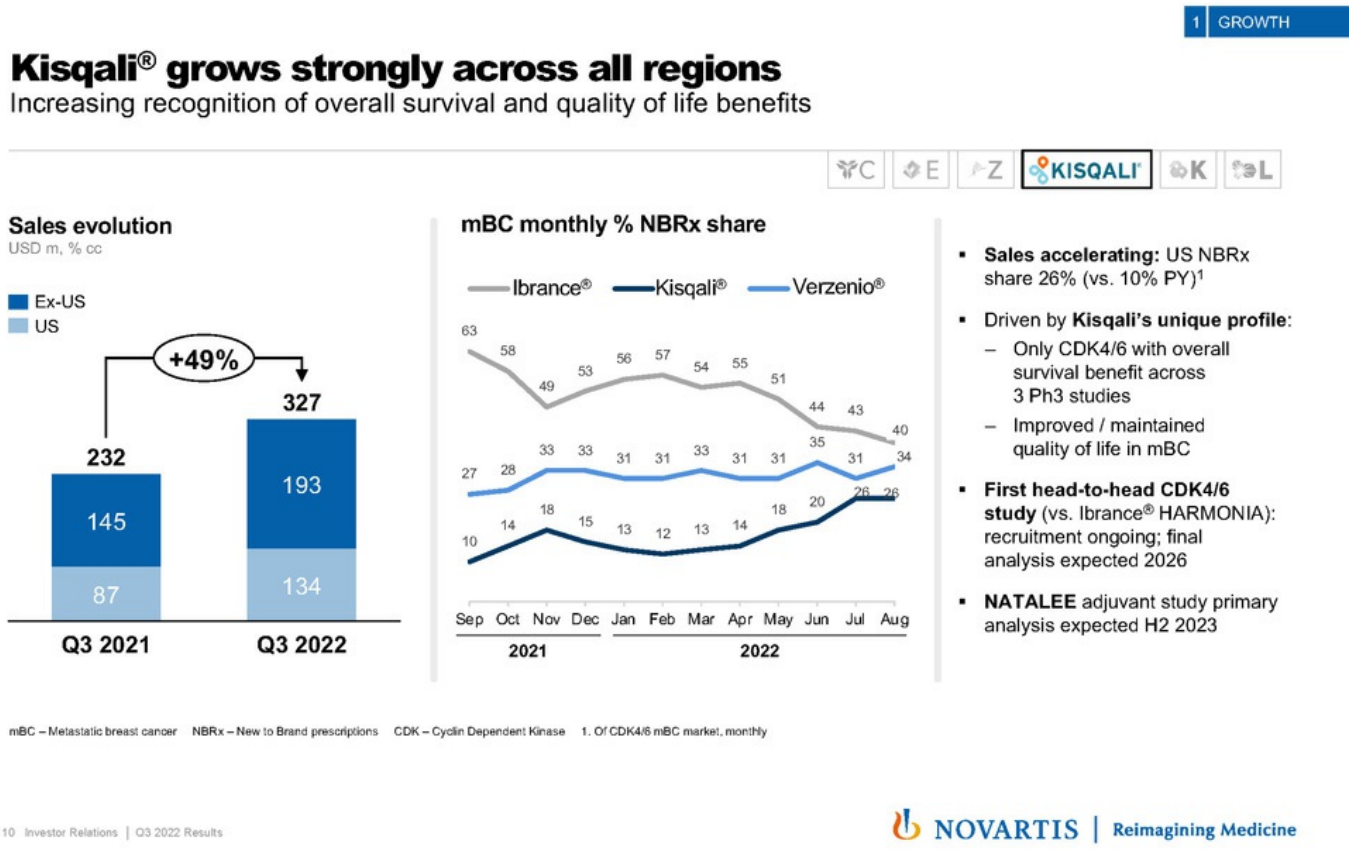
Now moving to Slide 9. Zolgensma® had a little bit of a challenged quarter. We now are predominantly seeing – we're seeing demand from the incident population. Both US and ex US have shifted to an incident patient population. Year-to-date, we still have double-digit growth in incident patients treated, and we've exceeded 2,500 patients treated worldwide.

Going forward, what will be key for us is to continue to expand into new markets. It's a foundational treatment, as you all know, for Type 1 in newborns. We are approved in 45 countries, and we have access negotiations ongoing now in 10-plus markets, including some important markets, such as Brazil. We also continue to work to increase newborn screening rates to 35 – above 35% in Europe and hopefully get over time to the rates that we see in the US, where we're close to 98% of newborn screened.

Taken together, we expect Zolgensma® to – we continue to expect Zolgensma® to reach the USD 1.5 billion to USD 2 billion sales level in the IV indication alone. But getting beyond that sales level will require expansion into the intrathecal indication in the 2- to 18-year-old patient segment, where the STEER study is continuing to enroll, and we also have the STRENGTH study looking at the IV utilization in that indication starting in Q4 2022.

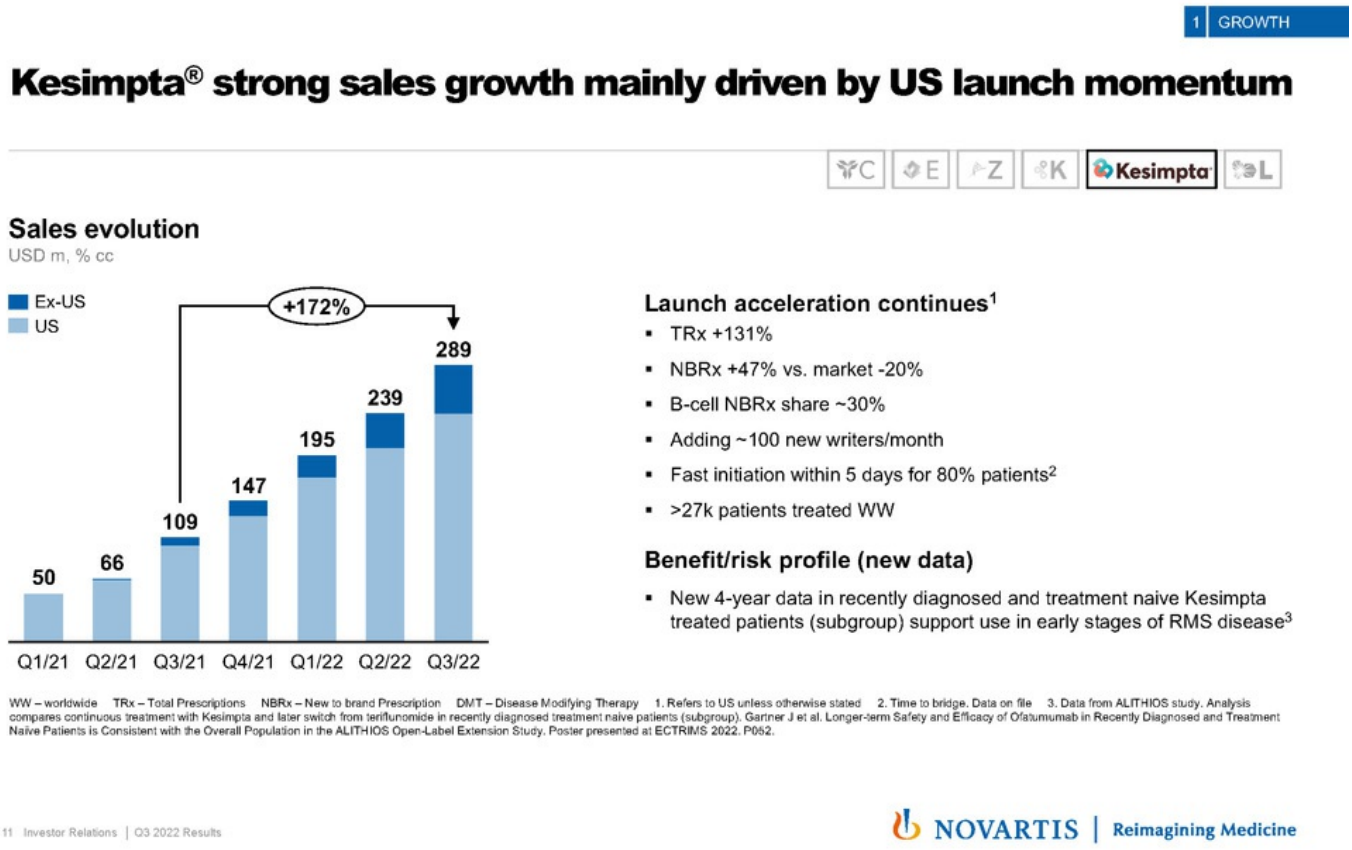
Slide 10



Now moving to Slide 10. Kisqali® had a really strong quarter across all regions, with 49% growth on the quarter. You can see, importantly, in the middle panel of the slide, the trend break we've had with respect to NBRx share in the US in the metastatic population, where we've been able to climb over the course of this year from 12% to 13% to now 26% exiting in August. That's really on the back of the strong data that we have with respect to OS across all of the metastatic lines. It's the only CDK4/6 with overall survival benefit across three Phase III studies. We also have a strong data with respect to quality of life.

We've launched a head-to-head study, the HARMONIA study versus Ibrance® to further solidify that profile. And the NATALEE study continues. We have not had any feedback yet from the steering committee with respect to the first interim analysis. And when that feedback becomes available, if it indicates any action on our part, we'll, of course, inform the market.

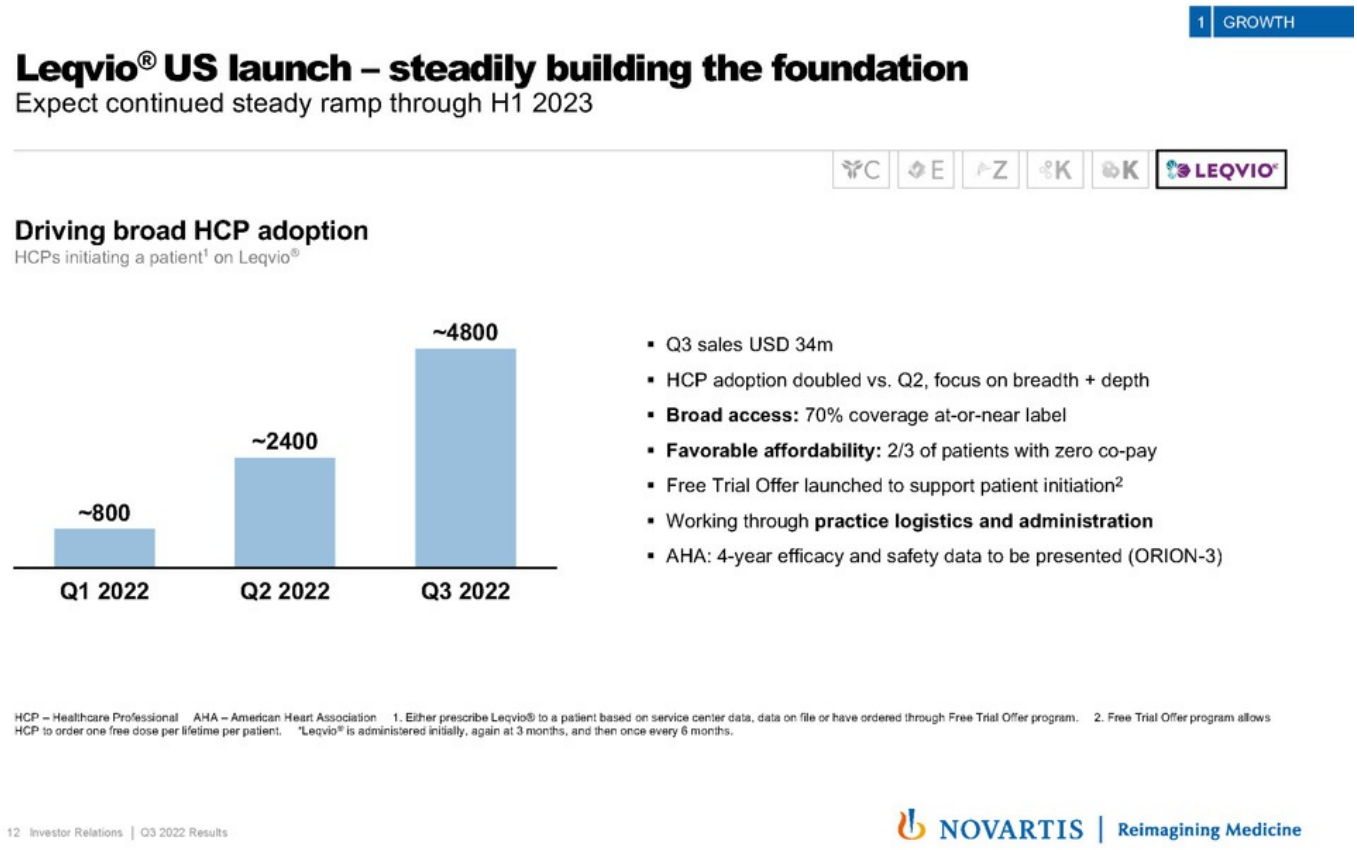
Slide 11



Moving to Slide 11. Now Kesimpta® had strong sales growth as well in the quarter, driven by its US launch momentum, 172% you can see here on its launch trajectory. Really, all of the key metrics are trending in a favorable direction. TRx, 131%. NBRx, 47% versus a market notably that's declining 20%. We are up to 30% NBRx share in B-cell – amongst B-cell therapies in MS in the US with a goal to reach 50% share. We're adding 100 new writers per month. Our initiation programs with our patient hub are performing extremely well.

And we also released new 4-year data in recently diagnosed and treatment-naive Kesimpta® patients that support its use in earlier stages in RMS disease. So really good trajectory here and an opportunity for us now to also accelerate our efforts outside of the United States to bring this medicine to more multiple sclerosis patients around the world.

Slide 12

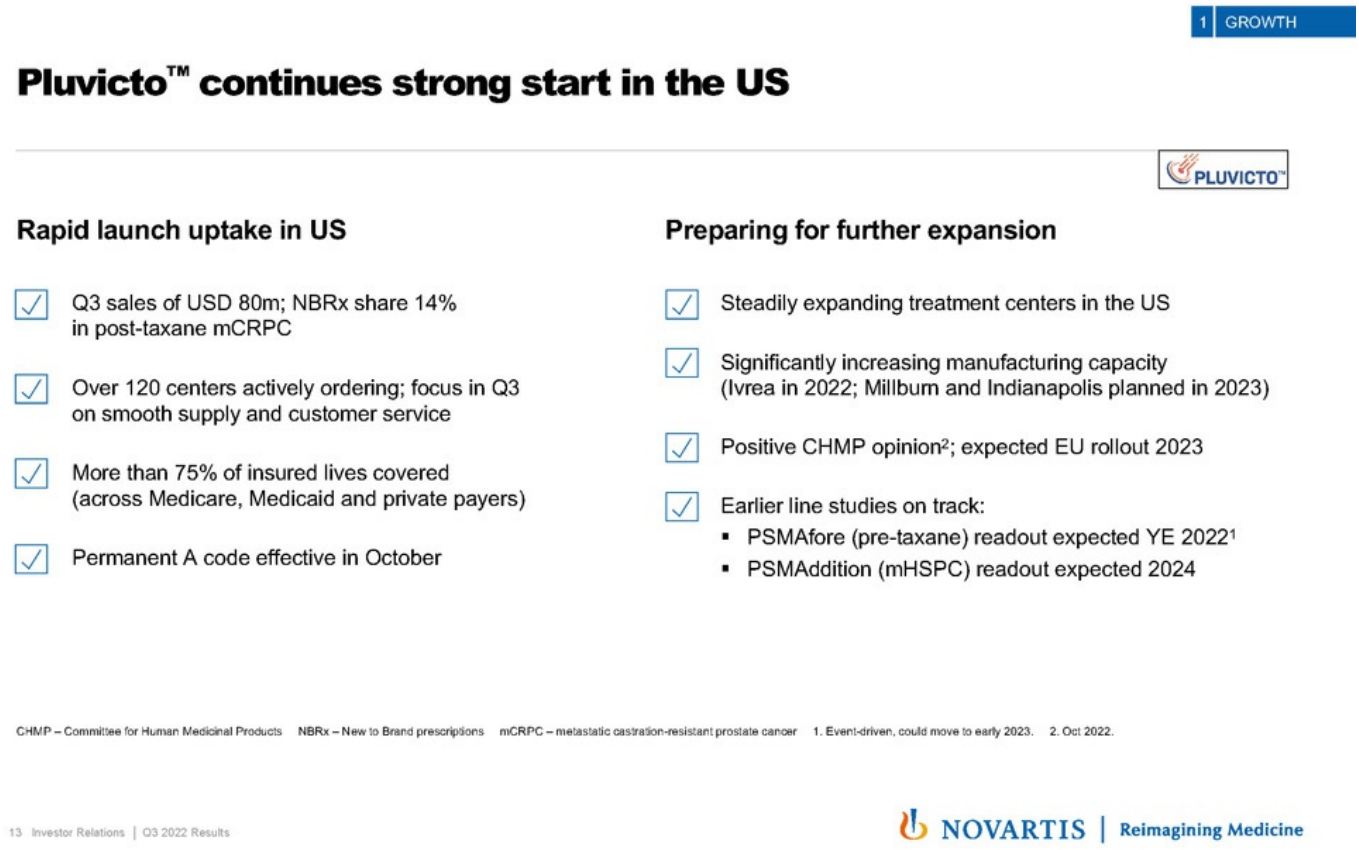


Now moving to the next slide. Now with Leqvio®, as we've noted, this is a steady build over the course of 2023 and the first half of 2024. Last quarter, we highlighted that we have good data or good positioning right now with respect to market access with 70% of lives covered at or near the full label. The vast majority of patients are able to access the medicine with a low co-pay. And now what we're doing is step-by-step expanding HCP adoption with now 4,800 or so physicians that have been able to initiate a patient on Leqvio®. What is critical now for us is to guide these physicians through the process so that they're able to get their patients on board, they're able to see how buy and bill work. And importantly, they're also able to see the impact of the medicine on lowering LDL for their patients.

What we find is in physicians that have gone through that process and have ultimately seen the impact on their patients, over 80% of physicians are pleased by the process and are pleased by the clinical and safety profile of the medicine. We just need to get more physicians through that process. So you can see some of the other data on the right-hand side. We have a free trial offer as well that's launched has seen strong uptake.

So we'll continue to work through the hurdle step-by-step. I think the right things are happening. But again, this is going to take time. And we really think it's midyear next year before you would expect to see any further acceleration beyond the linear path that we're on at the moment.

Slide 13

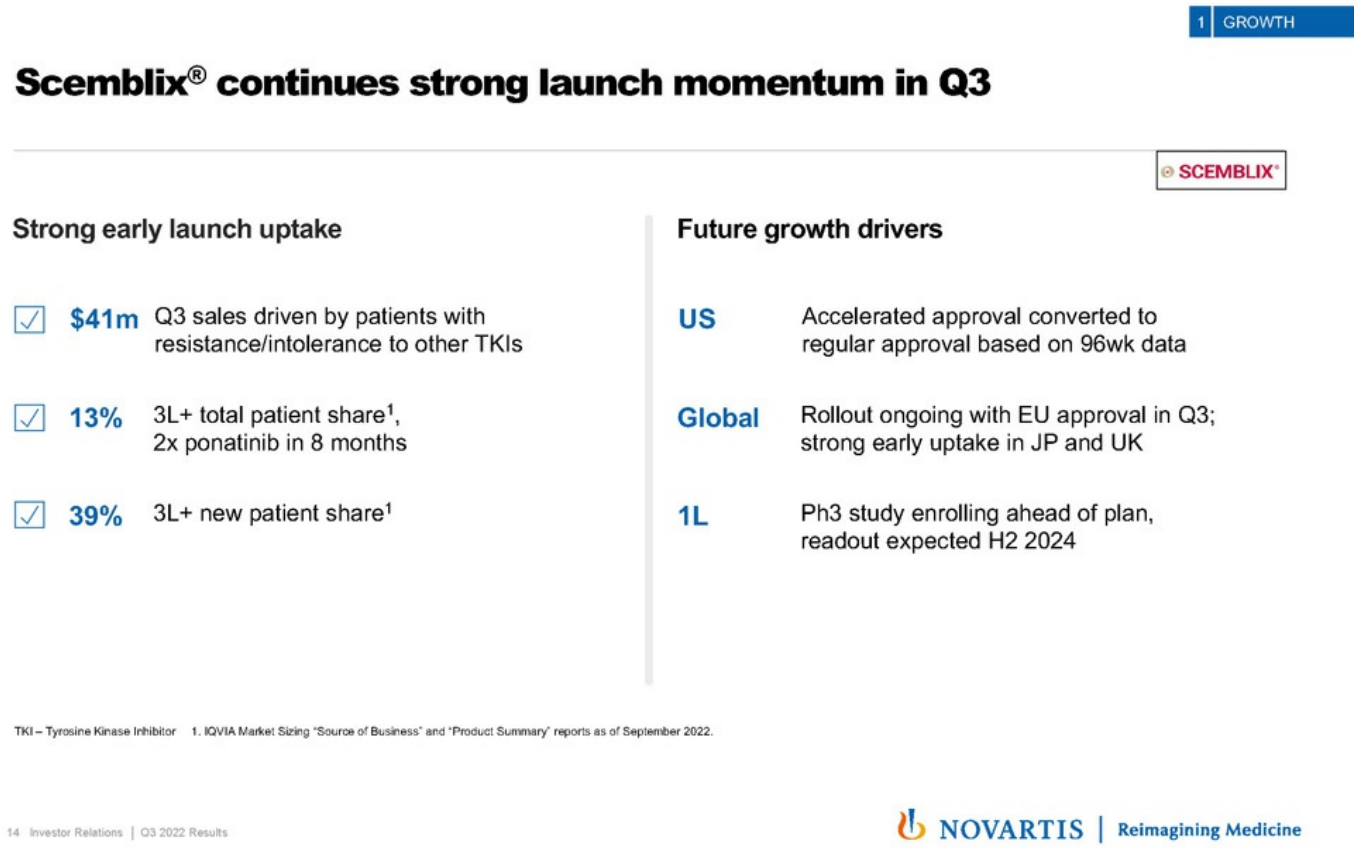


Now moving to the next slide. Pluvicto®, as I noted in my opening comments, is off to a strong start in the US. We're seeing very rapid launch uptake for this brand in the third, fourth line castrate-resistant prostate cancer, metastatic prostate cancer segment. USD 80 million in share, we're already up to 14% NBRx share in the post-taxane setting. We have 120 centers actively ordering, and we're really focused on servicing those centers in an outstanding way. 75% of insured lives are covered, and we have a permanent A code now in effect as of October.

Now looking ahead, as we prepare for additional data and potential expansion of the indications for this medicine, we're expanding the number of treatment centers. We expect to, over time, get to 350 to 400 centers. We're significantly increasing our manufacturing capacity. And we have our Italian site at Ivrea online and Millburn and Indianapolis are planned for 2023.

I mentioned already the positive CHMP opinion, and we're on track for the readout of PSMAfore before the end of this year and PSMAddition. And of note, PSMAfore, our current assessment is this would cover all pre-taxane metastatic patients, eliminating the need for one of the additional studies we had previously expected to be running in that setting. And in PSMAddition, in the hormone sensitive setting, we would expect to read out in 2024. So more to come, but overall, a solid launch so far with Pluvicto®.

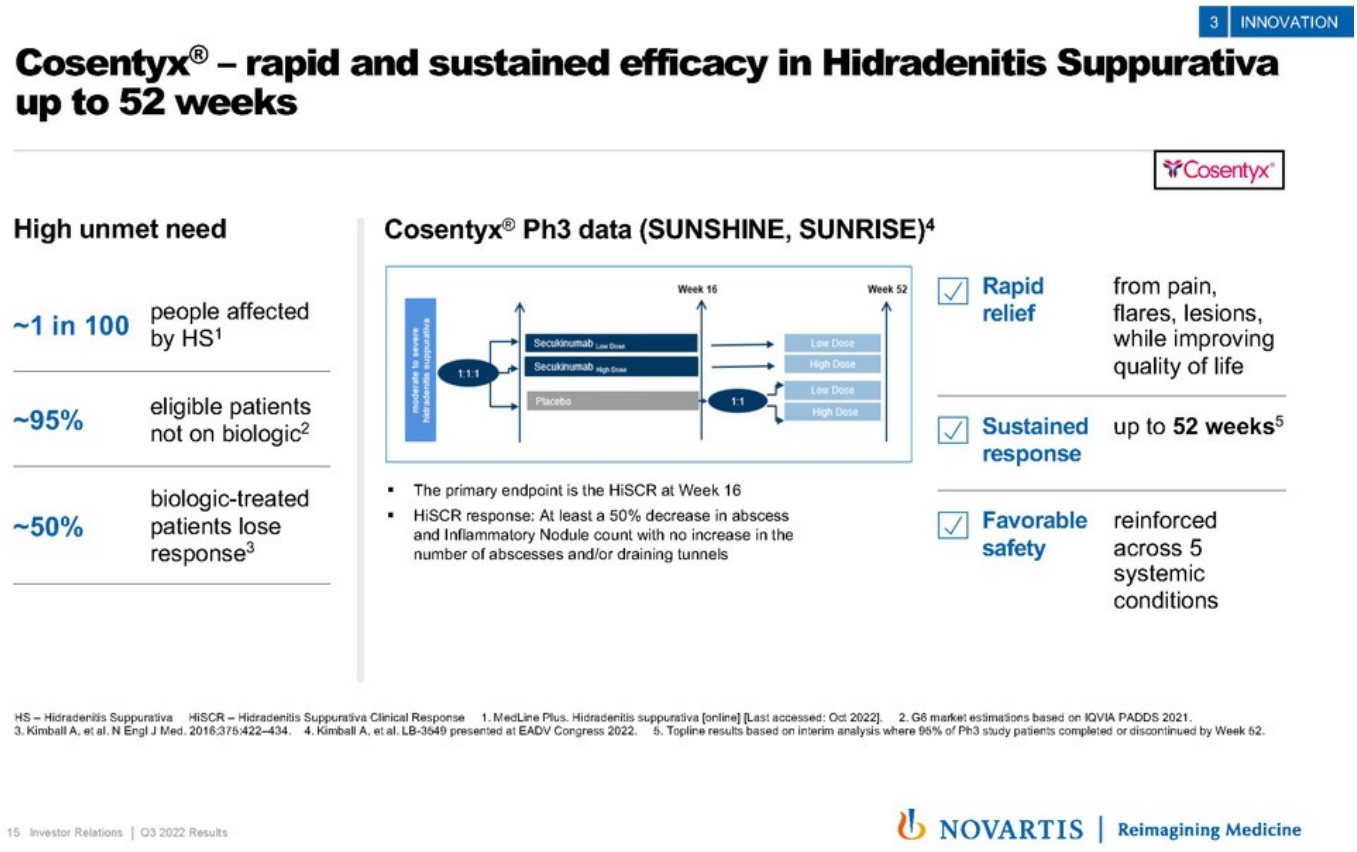
Slide 14



Now moving to the next slide, looking at Scemblix®. Scemblix®, also continuing a solid launch momentum through quarter 3. You can see USD 41 million in sales, 13% total overall patient share in the third-line setting and 39% third line new patient share. That new patient share growth has slowed a bit, as we would have expected, as we need patients to switch off of therapies that they're currently in line to be typically moved to Scemblix®.

Looking ahead, we've had the accelerated approval converted to a regular approval based on 96-week data. The global rollout is ongoing. And importantly, our Phase III study is enrolling ahead of plan. We continue to see strong launch momentum where we have Q3 sales driven in part by – Q3 sales were USD 41 million, and we had a 13% patient share in the third-line setting. NBRx share is at 39%. And overall, we expect Scemblix®, the critical element now, will be moving forward our ability to move into the earlier line. The study is enrolling ahead of plan, and we'll provide further updates. But right now, we forecast the second half 2024 outlook for Scemblix®.

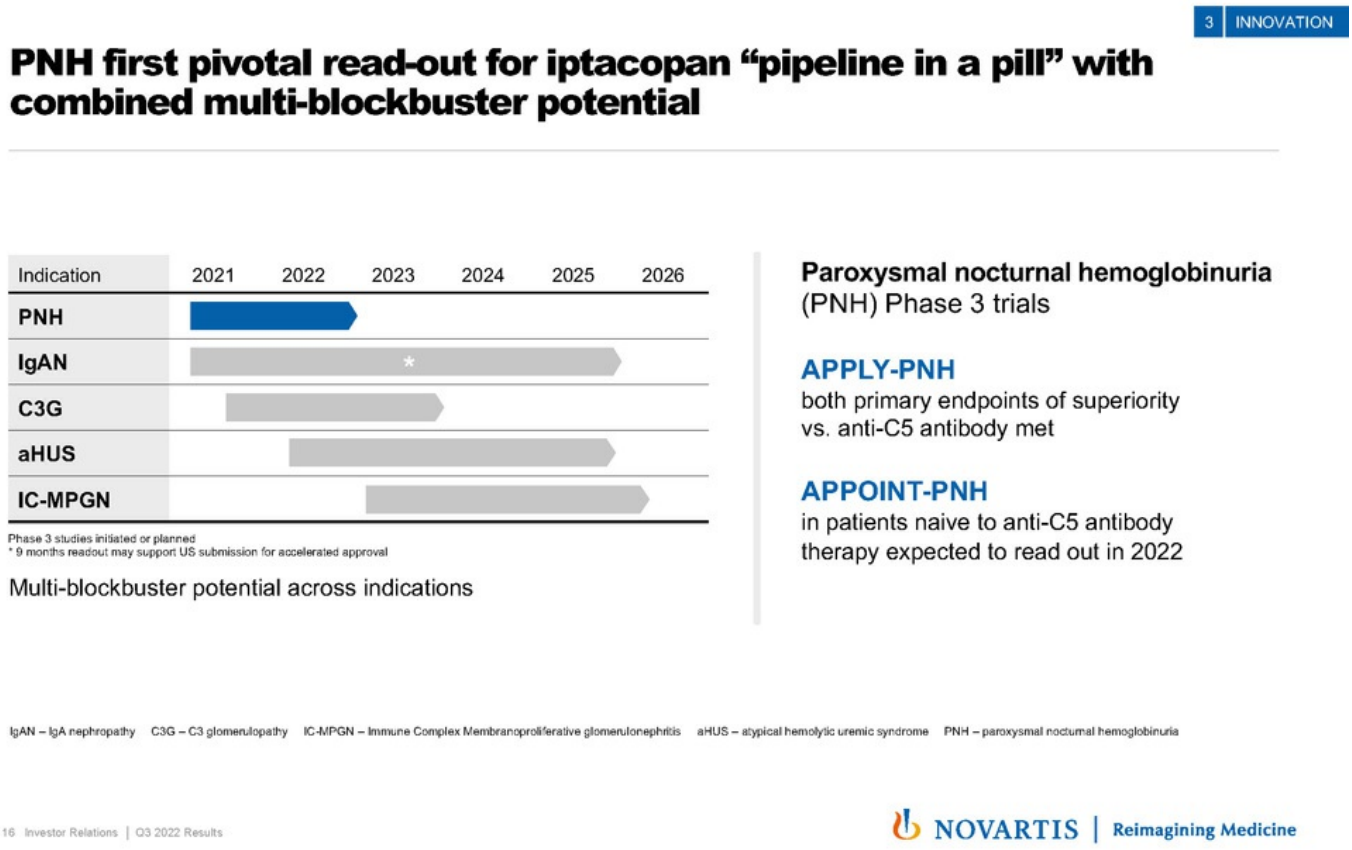
Slide 15



Now turning to some of the clinical data we had in the quarter. Cosentyx®, we had previously top line data, 16-week data in hidradenitis suppurativa. Now we have the 52-week data in-house. And just to remind everyone that it's a high unmet need patient population, one of the more common dermatological conditions that dermatologists see. 95% of eligible patients are not on a biologic today and 50% of biologic-treated patients lose the response over time. So there's definitely a need for a better therapy that can sustain its efficacy over time.

With the SUNSHINE and SUNRISE data set, we were able to collect data both at the 16-week and 52-week time period. We've already demonstrated data that showed a rapid relief from pain flares and lesion, but now we have data in-house to suggest that we have a unique benefit to sustain the response over 52 weeks, along with a favorable safety profile. So we look forward to sharing that data. We have filed, as I mentioned already, with the regulators. And overall, we're hopeful that this can be a key growth driver for Cosentyx® over the coming years.

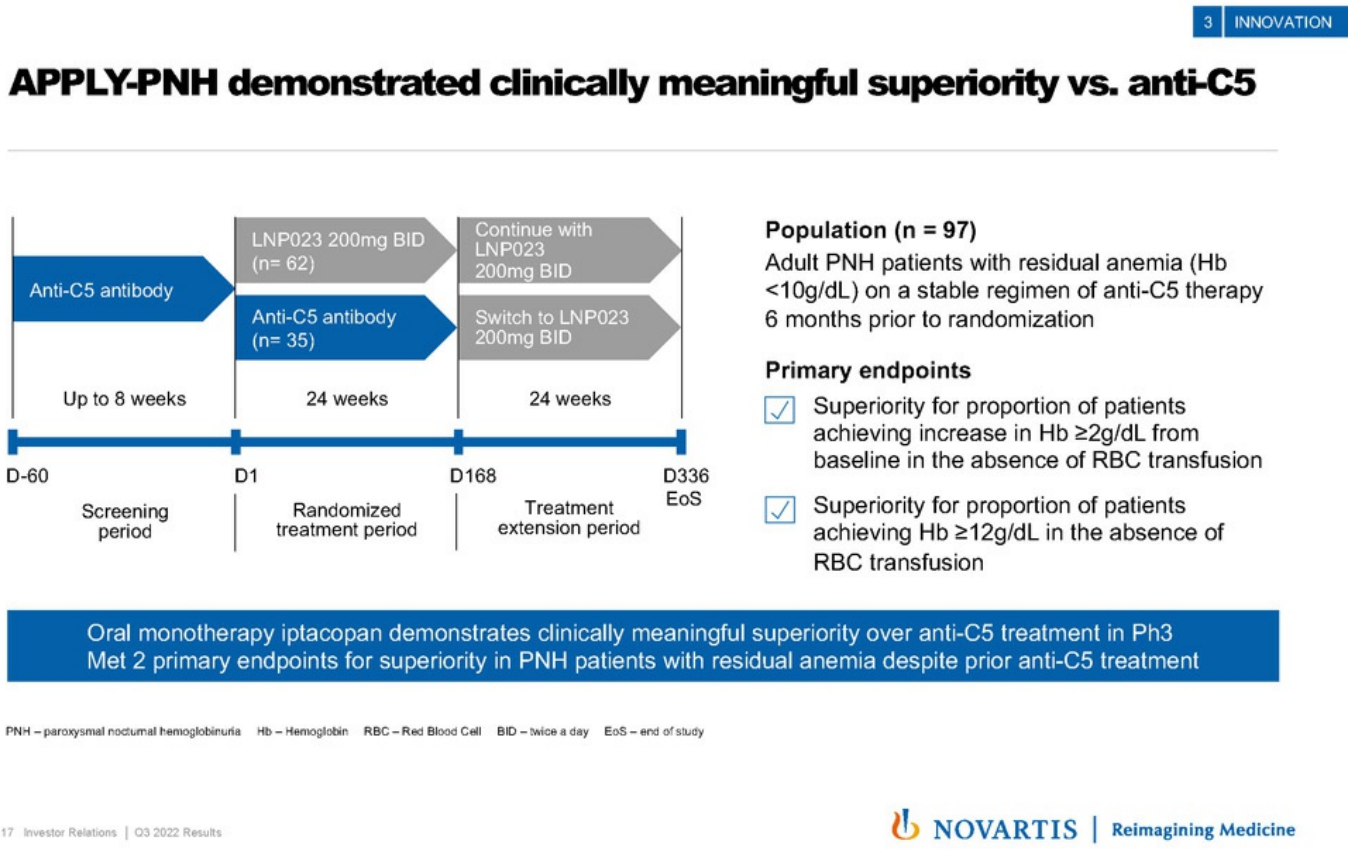
Slide 16



Now moving to the next slide. Earlier this week, we announced the release of the Iptacopan Phase III data in PNH, and this is a medicine we believe can become a pipeline in a pill over time with the range of indications we're currently developing the medicine for. As a reminder, we are in – we read out the PNH Phase III with an additional Phase III upcoming, the APPOINT-PNH study. We're in Phase III studies in IgAN, C3G and atypical hemolytic uremic syndrome. And we have a range of additional indications currently ongoing.

As a reminder, the APPLY-PNH study related to the treatment of patients who had refractory anemia after treatment with an anti-C5 and the APPOINT study is in treatment-naive patients to anti-C5 antibodies, also expected to read out in 2022.

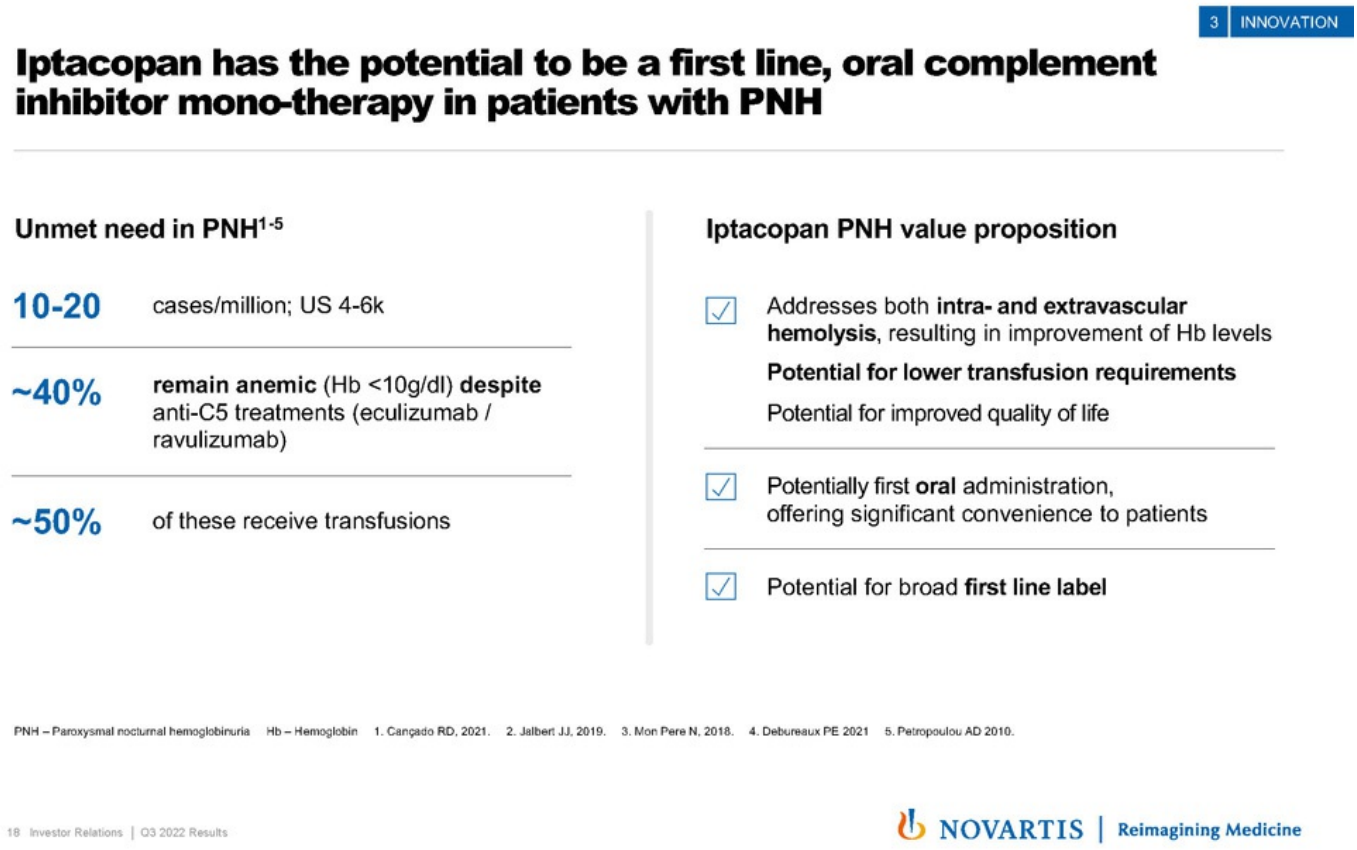
Slide 17



Now looking on the next slide, Slide 17, to the APPLY-PNH study specifically. This is a study, as I mentioned, patients were on C5 therapy for up to 8 weeks. They then switched to – if they had refractory anemia that demonstrated hemoglobin levels of less than 10 grams per deciliter, they were randomized to either receive Iptacopan or an anti-C5 therapy for 24 weeks. And after that period of time, they would continue on Iptacopan for the extension period. We demonstrated superiority for both endpoints, and I would say clinically meaningful superiority on both endpoints in terms of proportion of patients at greater than 2 grams and greater than 12 grams per dl.

We have submitted this data or plan to submit this data to an upcoming medical congress, where we would share not only the magnitude of the effect in the primary endpoint, but also secondary endpoints, which cover – secondary endpoints, including transfusion independence, quality of life, overall response rate as well as other measures.

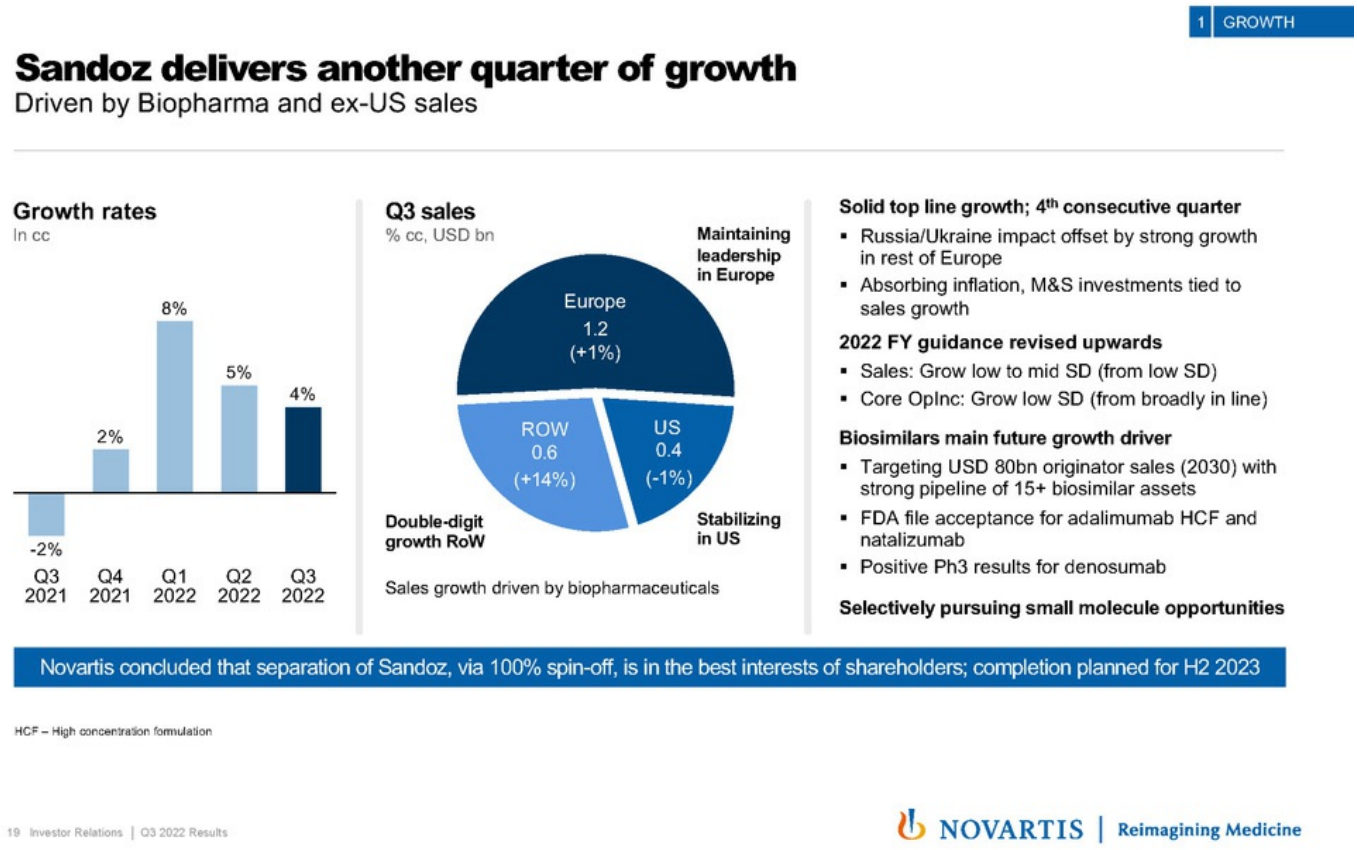
Slide 18



So moving to the next slide. Just as a reminder, our goal with this medicine is to be a first-line therapy for all patients with PNH. And that is the positioning that we plan to achieve both through our labeling and through the launch process. 10 to 20 cases per million is the current estimate of PNH with a current prevalence in the United States of 4,000 to 6,000. In the population of the current study that we just read out, about 40% of patients remain anemic with hemoglobin less than 10 grams per deciliter on anti-C5 therapies.

It's also worth noting that a higher proportion of patients have some level of anemia, some level of fatigue or other clinical manifestations of the disease. So the unmet need is significant even in the case of anti-C5 treatments. And 50% of patients – of these patients receive transfusions. We believe Iptacopan presents a unique opportunity to address both intra and extravascular hemolysis, potential for lower transfusion requirements and improvements in the quality of life. We think the oral administration in this setting makes a lot of sense, and then we can talk more about that in the Q&A. And we believe that this – there is a potential for this medicine to have a broad first-line label.

Slide 19



Moving to the next slide. Lastly, before handing it over to Harry, Sandoz has delivered another solid quarter of growth. And you can see the growth rates here where we once again had a 4% sales growth. This was driven in part by Europe, but particularly by our performance in the rest of world markets, where we had double-digit growth. This is the fourth consecutive quarter of solid top line growth for Sandoz despite having to overcome the impact of Russia and Ukraine and absorbing inflation and other headwinds. We've revised the full year guidance upwards, and Harry will speak more about that.

And we want to just remind again that biosimilars are the key future growth driver of the business. We had the file acceptance of adalimumab high concentration and natalizumab in the quarter as well as a positive Phase III result for denosumab as well from the biosimilars unit. So with that, I will – and we're on track, I should say, as well for the spin – planned spin in the second half of next year. So with that, I'll hand it over to Harry.

Slide 20 – 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 for the third quarter and the first nine months of the year. And as always, my comments refer to growth rates in constant currencies. This is, of course, particularly important given the significant currency fluctuations we all see, and so we believe it offers a better view of the underlying operational performance.

Slide 21

Solid Q3 and YTD performance

Group[1] USD million	Q3 2022	Change vs. PY % USD	Change vs. PY % cc	9M 2022	Change vs. PY % USD	Change vs. PY % cc
Net Sales	12,543	-4	4	37,855	-1	5
Core Operating income	4,282	-4	5	12,635	-1	6
Operating income	2,168	-33	-23	7,248	-21	-13
Net Income	1,575	-43	-33	5,489	-29	-20
Growth ex. prior year Roche income		*-38*	*-27*		*-21*	*-12*
Core EPS (USD)	1.58	-8	1	4.60	-6	2
Growth ex. prior year Roche income		*1*	*10*		*3*	*11*
EPS (USD)	0.73	-41	-31	2.50	-27	-19
Growth ex. prior year Roche income		*-35*	*-25*		*-20*	*-10*
Free Cash Flow	4,169	-6		8,393	-18	
Growth ex. prior year Roche dividend		*-6*			*-14*	

1. Core results, constant currencies and free cash flow are non-IFRS measures. Further details regarding non-IFRS measures can be found starting on page 49 of the Condensed Financial Report. A table showing the Q3 2022 and 9M 2022 key figures excluding Roche can be found on page 9 and a reconciliation of 2021 IFRS results and non-IFRS measures core results to exclude the impacts of the 2021 divestment of our Roche investment can be found on page 57 of the Condensed Interim Financial Report.

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On Slide 21, this shows the usual summary of our operational performance for the third quarter and the first nine months. We have also provided growth rates with and without the impact of the prior year Roche income to allow a better understanding of the underlying business. As you can see, we maintained our growth momentum in the quarter, with quarter 3 sales growing plus 4% and core operating income plus 5%, with sales growth driven by our major Innovative Medicines brands, in particular Entresto®, Kesimpta® and Kisqali®. Higher sales were also reflected in higher core operating income growth and inflationary headwinds have been offset by productivity efforts.

Operating and net income declined in the quarter, mainly due to higher impairments of about USD 0.5 billion and higher restructuring costs of about USD 0.4 billion versus prior year, which were mainly due to the implementation of our previously announced streamlined organizational model. Core EPS grew 1%. However, if you exclude the impact of the prior year Roche income, core EPS would have grown 10%. Free cash flow in the quarter was strong with USD 4.2 billion, but declined 6% in US dollars versus prior year with a significant impact from currencies.

Turning to the first nine months. We delivered a stronger – a slightly stronger growth year-to-date, with sales growing 5% and core operating income growing 6%. Core EPS in the first nine months grew 11%, excluding the Roche stake impact.

Slide 22

Continuing core margin improvements for Group driven by IM

	Q3 2022				9M 2022			
	Net sales change vs. PY (in % cc)[1]	Core operating income change vs. PY (in % cc)[1]	Core margin[1] (%)	Core margin change vs. PY (%pts cc)[1]	Net sales change vs. PY (in % cc)[1]	Core operating income change vs. PY (in % cc)[1]	Core margin[1] (%)	Core margin change vs. PY (%pts cc)[1]
Innovative Medicines	4	7	38.1	1.0	5	6	37.1	0.5
Sandoz	4	-5	22.3	-2.2	6	5	21.9	-0.2
Group	4	5	34.1	0.2	5	6	33.4	0.5

IM – Innovative Medicines 1. Constant currencies (cc), core results are non-IFRS measures. An explanation of non-IFRS measures can be found on page 49 of the Condensed Interim Financial Report.

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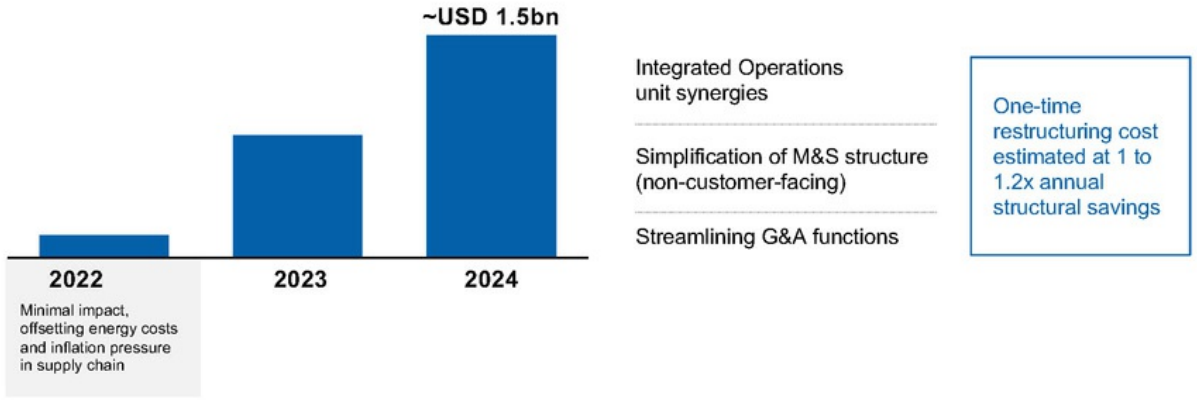
On the next slide, I would like to drill down, as usual, into the performance by division. So for Q3, Innovative Medicines top line grew 4%, and the bottom line, 7%, resulting in an improvement of the core margin of 100 basis points to 38.1%. Sandoz net sales also grew 4%, although core operating income decreased 5%, mainly due to increased M&S investments versus a quite low prior year base and prior year small divestment gains. This was reflected in the core margin, which decreased to approximately 22% of sales, which is also in line with the year-to-date core margin for Sandoz.

Overall, for the first nine months, we saw a slightly stronger sales performance for both divisions. IM sales grew 5% and core operating income, 6%. And for Sandoz, sales grew 6% and 5% on the bottom line, benefiting from a strong cough and cold season, return towards normal business dynamics and a low prior year base in the first half of the year. Our year-to-date core margin improved by 50 basis points for IM, which drove then also the 50 basis points improvement for the group.

Slide 23

On track to deliver operational efficiencies

Savings of ~USD 1.5bn to be fully embedded by 2024



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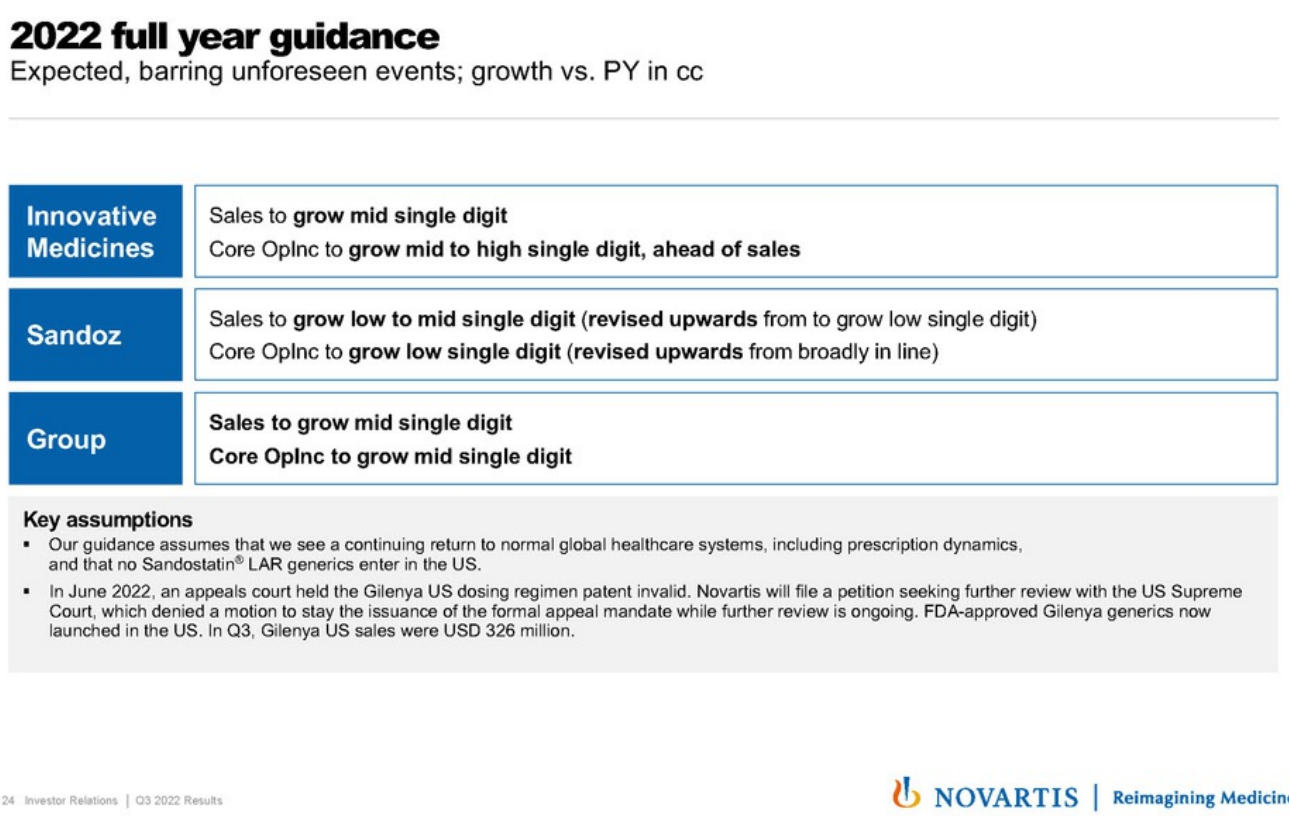
Now on to Slide 23. On the next slide, a reminder of the cost impacts of our simplified organizational model. We continue to expect to deliver USD 1.5 billion in structural cost savings to be fully embedded by 2024. And as a reminder, we also expect onetime restructuring costs to be 1 to 1.2x this annual structural savings. And for year-to-date this year, we have around USD 0.8 billion in restructuring costs related to the new streamlined model and expect approximately a total of USD 1 billion for the full year of restructuring costs on this topic. The rest of the onetime restructuring costs we anticipate will largely fall into 2023.

This year, we do expect to see some savings. As you can see here illustrative on the chart. But the overall impact will be minimal as this will offset higher energy cost inflationary pressures. All of these elements are, of course, part of our 2022 guidance. As a reminder, part of the USD 1.5 billion savings we expect to be reinvested into our pipeline and a significant part will contribute to achieve our approximately 40% plus margin target in the 2027 plus time frame.

Slide 24

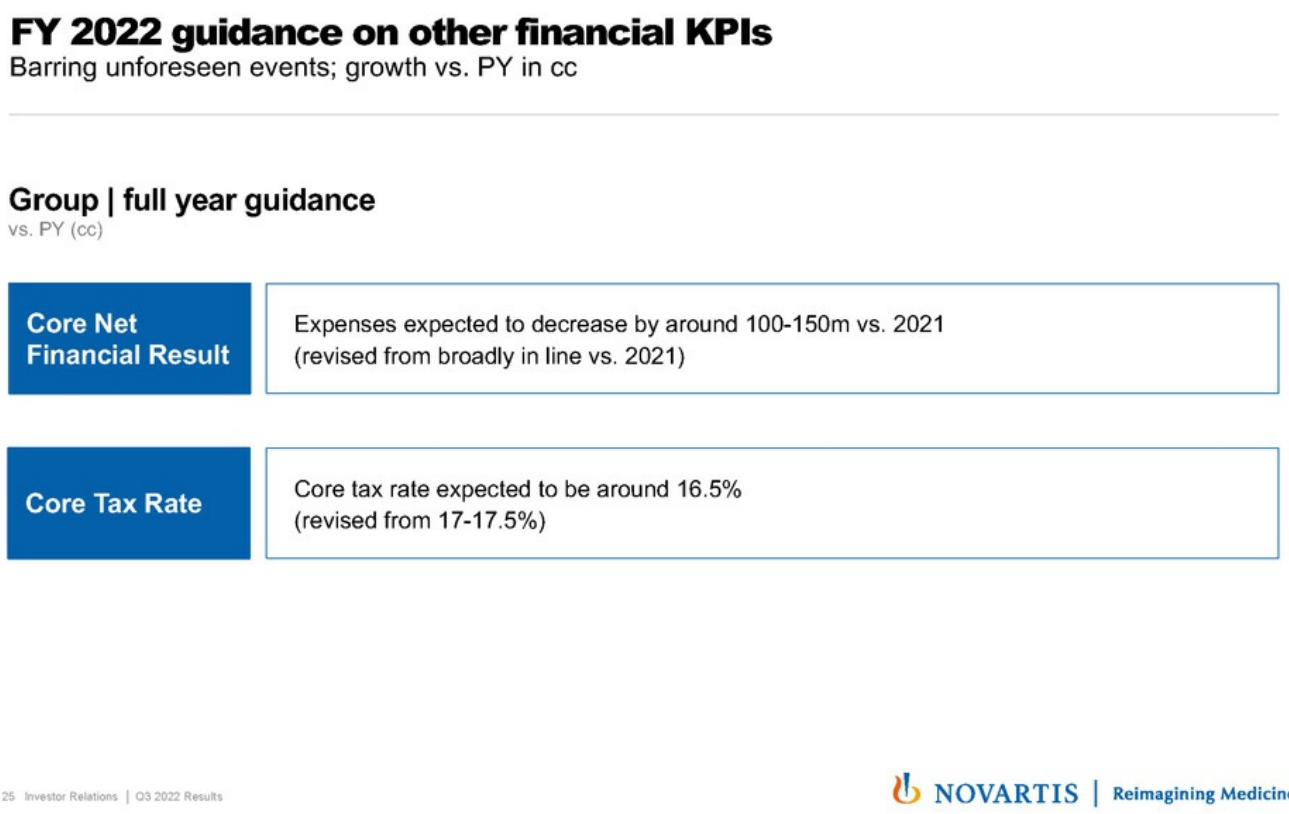


Now turning to Page 24. Within the divisions, we expect Innovative Medicine sales growing mid-single digit and core operating income growing mid- to high single digits ahead of sales. The anticipated Innovative Medicines' core margin increase should be driven by the expected continued good top line momentum and the continuation of our productivity programs, including the new streamlined organization model.

For Sandoz, the performance year-to-date allows us to upgrade sales and core operating income guidance, and sales are now expected to grow low to mid-single digit, revised upward from low single digit. And core operating income is now expected to grow low single digit, revised upward from broadly in line.

For the group, we confirm our overall guidance. We continue to expect both top and bottom line to grow mid-single digit in 2022. And as you have seen from our year-to-date results, we are quite on track – very much on track to deliver on that guidance. The key assumption for this guidance is that we see continuing return to normal global prescribing behavior and health care systems and that no Sandostatin® LAR generics would enter in the US in 2022. The guidance also takes into account the entry of Gilenya® generics that have now launched in the US. For your information, Gilenya® US sales in quarter 3 were USD 326 million.

Slide 25



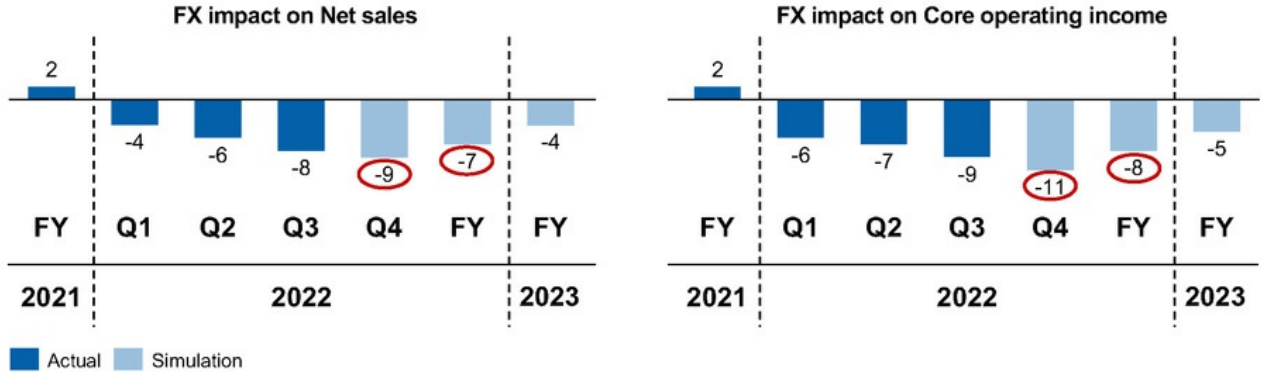
On Slide 25, I would like to provide an update on the other key financial elements of our expected core net income performance. As indicated on the Q2 call, we expect core net financial expenses to be slightly lower than in 2021, around USD 100 million to USD 150 million favorable versus 2021, revised from broadly in line versus 2021. And this change is mainly due to the higher financial income from reinvesting the proceeds of the Roche divestment and increased interest income for deposits. And the 2022 core tax rate is now expected to be around 16.5%, revised from the 17% to 17.5% range. This is mainly driven by a favorable change in the geographical profit mix.

Slide 26

Expected currency impact for full year 2022 and 2023

Currency impact vs. PY

%pts, assuming late October exchange rates prevail in 2022 and 2023



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On Slide 26, I want to provide an update on expected currency impacts if currencies stay at current levels. Obviously, currency impacts are significant this year given the strength in US dollar against many, if not all, currencies. For quarter 4, if currencies stay as they are now, we expect sales to be impacted by negative 9% and core operating income by negative 11% points. For the full year, we estimate the impact on the top line to be negative 7 points, on the bottom line, negative 8 points. Now into '23, we would expect the sales to be impacted by negative 4% and the bottom line negative 5% versus 2022. As a reminder, as currencies move quite dynamically, we update currency impacts every month on our website. And with that, I hand back to Vas.

Slide 27 – Vasant Narasimhan – CEO of Novartis

Vas Narasimhan
Chief Executive Officer

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Thank you, Harry.

Slide 28

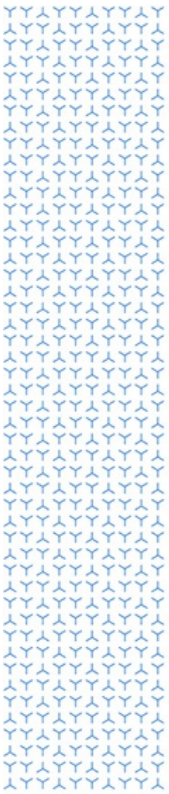
So moving to Slide 28. Just as a reminder, at our recent meet the management, we articulated our new Novartis strategy, high-value medicines, greatest disease burdens through technology, leadership in R&D and novel access approaches, a focused therapeutic area mindset across five core therapeutic areas, 2 plus 3 technology platforms in four priority geographies and a renewed focus on high-value medicines, not necessarily volume of medicines, but delivering truly high-value medicines, along with the other elements of our strategy on delivering returns and strengthening the foundation.

Slide 29

And translating that into this year's priorities on to Slide 29. We continue to maintain our growth momentum, and we confirm our 2022 guidance. Our top 22 priorities remain on track across launches and growth momentum on our six key brands. The pipeline is progressing per plan. I think the focused strategy, as I mentioned, has been executed against, and we're on track with the spin of Sandoz planned for next year. We continue our productivity plans through our new organizational model, delivering USD 1.5 billion of additional savings. And we continue to strengthen the foundations of the company, culture driving performance, data science to drive value and working towards ESG leadership.

So with that, I will open the line for questions. I would ask that questioners please limit yourself to one question, and then we'll try to move through the queue as many rounds as we can in the call. Thank you.

Q & A



Q&A

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- Operator

(Operator Instructions) We will now take our first question. And your first question comes from Graham Parry from Bank of America.

- Graham Glyn Charles Parry - BofA Securities, Research Division

Q. So it's on Pluvicto®. So very strong launch. Obviously, that's not inventory because you can't build inventory on Pluvicto®. So I was wondering actually, has this caused any capacity constraints given you're only supplying from the Italian facility at the moment? And therefore, could we expect actually sales to be flat in the quarter until you see new capacity come online? If you could just give us an update on the timing of the New Jersey and Indianapolis plants next year, are they still second quarter in the second half? Anything you can do to bring those online faster?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Graham. So with respect to Pluvicto®, we're able to supply the US demand across the 150 – 125-plus centers now we have currently set up. And we would expect demand growth to continue in quarter 4. So we're able to make that supply. What's critical for us is as we move into the period where we hope to have a positive readout in the earlier lines of PSMAfore study, we would need additional capacity to be able to service that earlier, large indication.

Right now, we hope to be able to file the Millburn facility back to the Pluvicto® file before the end of this year, and hope to have that online in the first part of next year. And we're on track for the Indianapolis facility to come online in the middle of next year. So once the Millburn facility comes online, we've invested in that facility to have additional capacity, we would be well positioned already for that new indication and the demand surge. And then once Indianapolis comes online, we would be in a position where we can service the US from two manufacturing plants in the US, dedicate our European facilities to Europe and ex US, and then look at adding additional capacity in Asia and other markets over time. Thank you, Graham.

- Operator

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

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

Q. Can I just ask about Zolgensma®, please. So some of your commentary, Vas, now suggests you've penetrated a large part of the bolus pool, and it's really about the incident population moving forward. I think it's probably fair to say, or please correct me, it's not that previously the USD 2 billion peak sales guide ex the intrathecal was a fair estimate. That's you are now saying USD 1.5 billion to USD 2 billion. So I just want to be clear, is that a change in expectations? And particularly given we're going to get close to USD 1.5 billion this year alone. And then just maybe, you mentioned Brazil, which are the key countries and maybe some timing on those countries would be great.

- Vasant Narasimhan – CEO of Novartis

A. Yes, absolutely. So the dynamics on Zolgensma®, as you all well know, we just to go through them, is that we – as we add markets, we initially penetrate a bolus of patients in the under 2 age group, and then we move back to the incident patient population. And in the incident patient population, the demand is driven by expanding newborn screening, particularly outside of the United States.

Right now, the key for us is to add those additional markets. So those markets range from Saudi Arabia and Brazil to Turkey and India. So there's a number of markets and other markets around the world where we're currently in active negotiation. And our hope is by adding those markets online, we'll be able to build that overall pool, not only of prevalent patients, which will increase sales for a period of time, but also build up the base of incident patients who are receiving Zolgensma® on an ongoing basis.

I think as we now look at the trajectory, we're ranging just because we – it's hard for us to predict exactly as we learn more when exactly these markets will come online. So we think it's prudent to say USD 1.5 billion to USD 2 billion. We certainly have the aspiration to get to USD 2 billion, but it's going to depend on how many more markets we're actually able to get on to national programs. And of course, our teams are working very hard to do that.

We're currently enrolling the intrathecal indication for a 2- to 18-year olds, as I mentioned, both to generate additional data for IV, where we do have a broader label in certain markets, including the EU, up to 5 years of age. We want to generate additional data for the IV and the pivotal study and 2 to 18 year olds.

And we remain on track. We hope to have that filing in 2024 and then approved in the first part of 2025. And that would give us the momentum to make the medicine beyond USD 2 billion over time. And I think we'll have a better sense of how large it could be depending on the magnitude of the effect we see in those indications. Thanks for the question, Wimal.

- Operator

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

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

Q. Just a question on Iptacopan in PNH. You've outlined the data for us on measures of extravascular hemolysis, but I wondered if you could give us any indication on how data on measures of intravascular hemolysis, such as LDH and rate of breakthrough hemolysis were trending. I know you'll present the data, but just wondering if you've got confidence there's at least no deterioration in those measures when switching from standard of care. And maybe you could just give us a sense of how you think about the launch uptake in that indication given we have standard of care with long-term outcomes data beyond control of anemia.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Richard. So first, I think it's worth remembering that in Phase IIb as – in the Phase IIb data sets for Iptacopan, Iptacopan demonstrated strong LDH lowering and a very favorable safety profile also with respect to breakthrough hemolysis. Given that we are in the midst of filing this data or submitting this data for congresses, I don't want to update on the secondary endpoints. We'll present all of that as soon as possible in an upcoming medical meeting. But we feel very confident about the overall safety profile of Iptacopan with respect to the various other elements that one would want to measure across intravascular and extravascular hemolysis. Importantly as well, what will be important is an upcoming data set in the frontline setting in treatment-naive patients to demonstrate that the profile holds up.

Taken together, based on everything that we've seen thus far, we – our aspiration remains to be a medicine that can be used in naive patients, in patients – to switch patients off of anti-C5s on to what we believe could be a more beneficial therapy. And then if desired, it can also be used as an add-on therapy to really cover the full range of potential indications with this medicine, a twice-a-day oral medicine, that we think can be really an attractive option, not only in the US, but would also when you consider that half of the PNH market is currently an ex US market, a twice-a-day oral could be highly, highly attractive.

So all things to work through. We look forward to presenting the data in more detail shortly. Thanks, Richard.

- Operator

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

- Emmanuel Douglas Papadakis - Deutsche Bank AG, Research Division

Q. Perhaps I could take one on Leqvio®. We don't seem to see much of an impact from the first of July J-code award. So just your latest perspective on how things are trending and what confidence on what actually drives that mid-'23 inflection? Is there something that in your view is going to capitalize a step change in the middle of next year? Or is it more really a build through the course of 2023 and your confidence that we'll still get to blockbuster status pre-outcomes data in '26?

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Emmanuel. The key here is to get enough physicians who have gone through the process of getting a patient on therapy, both then seeing the LDL reduction after the first and second dose. Second dose is at the 3-month time point, and having successfully been reimbursed in the Part B program. When those things happen, we see physicians, 80% plus of physicians, at least that we've internally surveyed, have a positive experience, both from a clinical standpoint and from a Part B reimbursement standpoint, regardless of whether they used an alternative injection center or used their own clinic.

So that's all the positive data that we have, but we need to move physicians through that process. So the reason we highlight 4,000 physicians now have initiated shows that we have that kind of – in the early part of the funnel physicians moving through the process, they probably trialed a few patients. We now had to get them through that entire process. And if they presumably have that positive overall experience, they will add additional patients on to the therapy.

And so this is going to be a build. But as we build that base, we hope then to convert entire practices over to using Leqvio® over time. And that would hopefully then lead to a compounding effect and an acceleration. Overall, we remain confident that we will get to the blockbuster status ahead of outcomes data, that's for certain. And a lot of work to do, but it absolutely remains our goal. Thanks, Emmanuel.

- Operator

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

- Matthew Weston - Crédit Suisse AG, Research Division

Q. I am going on follow on with Emmanuel's question, again touching on Leqvio®. So Vas, as you pointed out, the market inflection not until 18 months into launch. As I recall, going back to Diovan and Entresto®, I thought they took four years to breakeven as products. And now we have the risk of the IRA potentially limiting small molecule life to 9 years. Can you just lay out whether or not you feel that Leqvio® will breakeven before that 4-year level we saw with large cardiovascular medicines? And if so, why?

And then I guess the other question is whether having invested so heavily in buy and bill, are there other cardiovascular assets that you hope to bring on board or have in the pipeline that you can put through the similar channel to give doctors the comfort that investing in all the practice infrastructure isn't just a single product with Leqvio®, but there's a stream of products that they can capitalize on.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Matthew. So first, on the payback period, I'll have Harry comment, and I'll come back on the second part of your question.

- Harry Kirsch – CFO of Novartis

A. Matthew, I think we – as we discussed before, these cardiovascular launches, in my experience, like GP primary care launches, and of course all of them are different depending on the product and the category and so on, but in my experience, usually then the breakeven happens roughly in year 4 plus/minus. While, of course, high-priced specialty launches sometimes have a breakeven in year 1 or at least in year 2.

So clearly, 9 years versus 13 years is not a positive, right? That's why I think also there will be initiatives to move those closer to the 13 years, both of them. But at the moment, it's 9 years. But of course, in any of these launches, one wants to have the uptake to be as fast as possible, just cardiovascular is slow. And I would expect the usually breakeven in year 4.

- Vasant Narasimhan – CEO of Novartis

A. I think, Matthew, in terms of having – it is on our mind to build a broader portfolio of medicines. So both in-house, we have efforts ongoing both in terms of life cycle management of Leqvio® as well as other novel therapeutics, which are still moving through the research pathway or research labs to try to accelerate now to make sure we have a stream of medicines. I also say broadly in the industry, there are other medicines as well that I think would also fit in terms – into the buy-and-bill model.

But on a stand-alone basis, for most practices that we've analyzed, the number of cholesterol patients in a practice, it is favorable for cardiologists once they have the setup and have it moving to do it just for Leqvio®. So I think it's an important point that it's not a requirement that you have multiple medicines. Even this one medicine alone, where you have also the certainty that you know the patient is on therapy, you see the result on the cholesterol lowering. It's highly attractive from that point clinically. And also the practice has the cost reimbursement elements as well. It's pretty attractive, we find with most practices that have gone through the process.

So we'll not only focus on Leqvio®, but also build a pipeline behind it. And as Harry mentioned, I think a top priority has to be to ensure small molecules and related technologies are not penalized relative to large

molecules. So that, of course, will take time to shape public policy. Thanks, Matthew.

- Operator

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

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

Q. And the risk of being boring, I'm going to follow Matthew and Emmanuel on Leqvio®. Vas, just on this – your expectation of a linear trend to the middle of next year, with the two drivers of more doctors being set up to administer the drug and more patients per physician, I mean that does sound a little conservative because, I mean, that in itself should – if both of those are increasing, that should drive more than linear growth. So I'm just trying to understand a little bit more about that.

And also related to that, you are running a DTC campaign with two adverts at the moment in the US for Leqvio®. Do you have any sense of how patient demand is exceeding the billing capabilities of physicians at the moment? It's not really the case of unfilled scripts, but unsatisfied patient demand. Is there any indication you can give us on that?

- Vasant Narasimhan – CEO of Novartis

A. Yes, Simon. I think on the first question, I think it's just – we've learned over the years, it's prudent on cardiovascular launches to be appropriately cautious until we see evidence that in the sales line, we see a trend break. And I think at the moment, all of the inputs look positive, as you say. We have the number of physicians that we have that have initiated some action on Leqvio®, the feedback we get from physicians going through the process. We're starting to see improvements, so we'd like to see more improvements in depth per practice that are on, that are using Leqvio® already.

So all of the things are in the right direction. Reimbursement is at higher levels than PCSK9s achieved in year 5. We've said high levels of patients don't have to pay any co-pay to access the medicine. So again, all in the right direction. But I think we would feel better if we actually saw a trend break before we start promising anything bigger than a linear trend. So that's kind of our mindset at the moment. And if it happens, that would be terrific and we, of course, share that with all of you as soon as it does.

We do have a very active DTC campaign to activate patients on the benefits of a twice-a-year therapy that can deliver up to 60% lowering on LDL cholesterol. We do see the beginnings of increased patient demand. I would note that, actually, we don't see capacity as an issue because we are able to use the AIC networks, which are continuing to expand to absorb any excess patient volume. So if a practice is not able to set a buy and bill immediately, we're able to educate practices about AICs, which are available in the community that are set up. And we've worked very closely with that expanding network of alternative injection centers to make Leqvio® available.

One of the things we've learned that we need to get much smoother at is that transition of helping a practice that send the patient to the AIC and then back to the practice. We're working on smoothing that out. But that AIC creates a pretty big surge capacity. But what we do hear from practices in general is, over time, they would like to set up the buy-and-build capacity within their own practice. It's just a matter of can they do that immediately? Or would they like to do that in the future? Thanks, Simon.

- Operator

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

- Richard Wagner - Wolfe Research, LLC

Q. This is Richard Wagner, on behalf of Tim with Wolfe Research. It's about Cosentyx®. And could we get an update on the competitive landscape in the US as AbbVie works to lock in formulary positioning for its various I&I products in 2023 onwards as Humira® biosimilars approach. What would be the impact or could be the impact on net pricing and formulary placement?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Richard. When you look at Cosentyx®, we're still in the midst of the formulary negotiations at this time. But our best belief in indication, given that formularies want to have an IL-17A available for patients, that we'll be able to maintain our formulary position at roughly equivalent position in terms of our gross to net as we have this year.

I think looking forward, what will be absolutely critical for us to continue Cosentyx®'s growth dynamics and really maximize the medicine is the approval of additional indications in hidradenitis. We have the IV indication as well. As I mentioned, we plan to file – we have a 2 ml syringe, which we're also in the midst of filing. Those would be the next big 3. And then beyond that, indications, as I mentioned, giant cell arteritis, tendinitis, amongst others. That's going to be the next wave we're going to need to maintain strong position on formularies, but also to enable the brand to continue to grow.

But for 2023, based on our negotiations to date and reviews we've had with our managed market teams, we feel comfortable with where we'll be on formularies for next year.

- Operator

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

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

Q. First, an observation, then a question. So the observation is that in response to the Pluvicto® question, it makes it sound as though Q4 sales will be appreciably above Q3. And I guess you must have some visibility since Q4 is about 1/3 over already. The question is, Vas, in the past, you have been cautious on the use of A-beta antibodies for the treatment of Alzheimer's disease. Given recent news, do you have any reason to change your view? And if yes, then how will Novartis gain a position in A-beta antibodies or some other approach in Alzheimer's?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Steve. On the A-beta antibodies, I think what's most important, particularly given the amount of investment that would need to be made by health care systems for therapies, and we of course are active in Alzheimer's disease research, is the benefit that we're seeing not only statistically significant, but clinically meaningful. And I think with the various measures that are currently used, it's hard to judge what is clinically meaningful ultimately for a patient. And I think that's going to be the question for payers, advisers, et cetera, in the US markets. Is this clinically meaningful enough? A very – the 0.4, 0.45 or whatever the number is, on the ADAS, ECOG scores.

So I think we'll have to see. That will be for others to judge. Our focus is on other mechanisms of action. I mean we think – we don't know, but certainly, our labs are working on other approaches across the full range of neurodegenerative diseases, where we have programs in the clinic, as you know, on Huntington's and Parkinson's, and continue to also look at various targets in Alzheimer's. But I wouldn't expect us to take any action on A beta, and none of the data that I've seen thus far would trigger us to make a shift at this point in

time.

- Operator

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

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

Q. Question for Harry. Just looking at the UNR844 termination, that product that you acquired by the Encore Vision acquisition. Was there an asset impairment taken in the quarter? And if not, is that coming next quarter? I wonder if you can quantify how big that might be.

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you, Kerry. Actually, the majority of our impairment recorded in quarter 3 was UNR. The potential presbyopia drops of roughly net impact of USD 0.5 billion. So we immediately, when we stopped the program, we immediately booked it. So that has happened in quarter 3.

- Vasant Narasimhan – CEO of Novartis

A. Great. Thank you, Kerry.

- Operator

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

- Richard Vosser - JPMorgan Chase & Co, Research Division

Q. Maybe we could talk about NATALEE. And maybe you could give us an update where we are in terms of the interim analysis. Is it still the case that the 70% interim should be expected at the end of the year? And then, of course, the final analysis within the second half of next year? Just some thoughts there would be great.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Richard. So we continue to expect the first interim to read out before the end of this year. But we have not heard back from the DMC at this point in time. And our approach will be that if the DMC advises us to make a change, we'll let the markets know. And if you don't hear from us, that means the DMC told us that the study should continue as planned. We expect the second interim to happen in the first half of next year and the final study should complete at the second half of next year.

Another study that – another question that often comes up is related to how we'll approach OS in these various settings. And the FDA has confirmed to us that as long as there is no detriment to OS at any of these time points, that would be sufficient for them to consider the data set as pivotal for a potential approval. Thanks, Richard.

- Operator

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

- Emily Field - Barclays Bank PLC, Research Division

Q. Just on MS. On Gilenya®, I know your prior guidance assumed no launches in the US. So good to maintain that. Just the impact on core operating margin, should we think of that as a pretty straight drop down given that

it's probably a pretty high-margin product? And then just on Kesimpta®, your share assumptions in the class going forward, do you expect those to be impacted by the potential launch of subcutaneous Ocrevus?

- Vasant Narasimhan – CEO of Novartis

A. So first on Gilenya®, Harry?

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you, Emily. Yes, this is very – it's a very high gross margin product. There's some royalty on it, but it's, of course, also small molecule, high priced. So the product margin is quite high. As you can imagine, at the end of the life cycle, there is not much M&S on it. So it's pretty much a straight drop down to the bottom line. But of course, we have mitigating actions and productivity plans, and it's fully embedded in our guidance this year.

- Vasant Narasimhan – CEO of Novartis

A. And then with respect to Kesimpta®, Kesimpta® has really been successful as a first line for switch medicine in the neurology settings that are not currently participating in infusions, as is the case with our competitor product. I think first, we need to see if a high dose subcu can be delivered without any sort of reactions and other complications. I don't think that's a given. I mean, of course, data will have to bear that out.

And then it's worth remembering our positioning will be for patients who want a monthly injection at home and don't want to go into the infusion center. Clearly, the subcu might reduce the time of the infusion center, but it remains to be seen how will steroid pretreatment need to be happened. Will it need to be continued to be IV? Can it – is it sufficient for it to be oral? What kind of monitoring requirements FDA will require?

So I think it still remains that there is a segment of the market that will want to use IV infusion or subcu infusion therapies. And there's a segment where Novartis and Kesimpta®, we hope to become the clear leader amongst patients first class – first treatment or first switch who want a very convenient, at-home, highly safe, high efficacious B-cell therapy, and that's our focus. And Harry has a point.

- Harry Kirsch – CFO of Novartis

A. Yes. Just Emily, a follow-on clarification also on Gilenya®. I mentioned that this is fully in our guidance for 2022. I just want to mention also that this has no impact to our mid- to long-term guidance. Prior to this turn of the US courts, if you will, we were expecting to lose US exclusivity, if you will, or have generic entries in the middle of '24 roughly, right? From that standpoint, our 40% plus margin goal in 2027 plus was already fully assuming that generics would have entered several years before that.

- Vasant Narasimhan – CEO of Novartis

A. Great. Thanks, Harry. And so we still have a number of questions in the queue. (Operator Instructions).

- Operator

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

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

Q. Vas, you mentioned that you would like for Iptacopan to be the therapy of choice kind of in the frontline setting. What data do you think you would need to see kind of from the frontline study to allow for Iptacopan to be in that position given the head start that the Alexion products already have in that market?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Keyur. I think what will be important is if we can demonstrate we can generate clear control of the disease. And of course, across the various parameters, LDH, safety, et cetera, that we have a compelling profile. I think when you look broadly, first, if you think first principle, the biology of this disease, this is an alternative complement pathway-driven disease. And factor B is a relatively unique component of this, in that it's not as abundant as C3 and C5, and an oral agent can get to both to extravascular and intravascular sources of factor B and inhibit those. And those include tissues that go beyond the liver, which is an important consideration when you consider ASOs and siRNAs, and oral therapy presents a unique profile in being able to reach the full broad range of tissues.

So overall, we think factor B for these alternative complement-driven diseases, including PNH, is an ideal target. And overall, the PK/PD we see for this medicine, the preclinical and clinical safety we see, has been very good. That's been borne out now in the APPLY-PNH study that we've already headlined. And we hope to continue to see that in the frontline study. And then next year in C3G, in particular, but also in IgAN. And then in other alternative complement pathway-driven diseases, including aHUS, cold agglutinin disease, MC, PGN.

So there's a range of diseases where we believe the medicine is well suited. And I think we're excited that the medicine has, so far in its first pivotal readout, borne out the clinical and preclinical hypotheses that we set forward. So we'll look forward to providing the data in an upcoming medical congress as I outlined. And then the second study as well will read out before the end of this year.

- Operator

Your next question comes from the line of Mark Purcell from Morgan Stanley.

- Mark Douglas Purcell - Morgan Stanley, Research Division

Q. First, just returning to NATALEE, the interim analysis. Is that based on all comers? Or do you need to see a significant benefit specifically in the intermediate-risk patients, which may be, I guess, as low as 25%, 30% of the events?

- Vasant Narasimhan – CEO of Novartis

A. Yes. So Mark, I think it's important to note that we're looking at both grade 2, grade 3 patients in the study. And the way we're powered is across the entire population. And we've relooked at powering many times now, and we feel very comfortable based on the study design and what we've seen from other competitors and the fact that we power it up by 1,000 additional patients. And so the results, the IDFS results, will be based on the overall population, and that's how the endpoints are designed.
As a separate point, and just to be clear, the FDA, can, at any point in time, decide that they want to take cuts between stage 2 and stage 3 patients. But our focus for our primary analysis is stage IIa, stage IIb and stage III patients as defined in the protocol, and the endpoint will be driven off of that entire patient population.

- Operator

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

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

Q. I guess one quick question just on Leqvio®. Can you just help us understand where those patients are coming from? Are they predominantly switched patients from existing PCSK9 therapy? Or is this a new patient pool? And then just very quickly, second question. Vas, as we look towards potential business development

becoming increasingly critical as the years progress, just wondering where your particular focus is given the commentary around primary care cardiovascular product launches and the ability to launch into those efficiently.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Seamus. So first, on Leqvio® source of business. Just as a reminder, the target patient population in the US is 18 million patients. And across all of the core markets, EU plus the top markets around the world, is around 70 million patients. These are patients who have had a prior cardiovascular event and are not reaching 70 milligrams per deciliter on their LDL score. And that is the guideline directed, that is the goal. So it's a big, big patient population.

Right now, I think what we can say is that the primary prescribers that we see are prescribers who also have experience with PCSK9 monoclonal antibodies. That could be low experience, it could be high experience, harder for us to say given that this is a Part B medicine, the source of business from a patient standpoint. But I presume then we're either getting switch patients on PCSK9 monoclonal antibodies, or we're at least getting a broader share of physicians that are open to the PCSK9 class.

And so our focus right now is to really say how can we get broad adoption within, let's call it, PCSK9-minded physicians. And then over time, try to expand further and further through our work with systems of care, population health agreements, et cetera, into the broader patient population of 18 million patients.

Clearly, we don't need that bigger share of that 18 million patients to reach our overall financial goals. From a public health standpoint, we would, of course, want to reach as many of those patients as possible, because right now, the odds of a patient having a subsequent event go up quite dramatically if they're not at that 70 goal. So that's kind of overall how we approach it.

There's no updates with respect to M&A and BD. We continue to focus on, let's call them, sub-USD 3 billion, USD 4 billion M&A deal, broad range licensing opportunities, focused primarily on science and does the science work? Is it fitting in our core therapeutic areas? Does it fit in our 2 plus 3 technology areas as we've outlined that to Meet the Management. And we continue to assess. Then if we find something that's attractive, where we have a differentiated view that would justify the premium and generate, we believe, value creation for our shareholders, we'll, of course, pursue it.

Other than that, we're also willing to be patient. We believe in our pipeline. We believe with our new leadership within R&D and the addition of a Strategy and Growth Officer, we can unlock the full potential of Novartis research and development and then have a steady stream of medicines going forward. And so we're going to remain disciplined as we move ahead.

- Operator

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

- Florent Cespedes - Societe Generale Cross Asset Research

Q. Vas, a quick one on China, please. As China is a key country for you, could you please elaborate on the dynamic there for your key products and if there is any, let's say, impact from lockdowns? And could you refresh our memories and please remind us the current contribution and your ambition on this country?

- Vasant Narasimhan – CEO of Novartis

A. Yes. With respect – thanks, Florent. For China, we've outlined our aspiration to become a top 3 player by

2024, which would be a player that exceeds USD 4 billion in sales in the market. We've had really a record performance in terms of number of approvals over recent years. And then also moving forward, I think, we'll lead the industry as well in terms of NRDL listings. Key drivers for us has been our oncology portfolio, Entresto®, Cosentyx®, Lucentis, amongst others.

Now we were growing in the high teens from a sales growth standpoint before the lockdowns. And I think the lockdown – we continue to grow, but we're growing more in the high single-digit frame at the moment. And we would expect that to continue until we would see a shift in the overall ability for patients to access medical care in more normal dynamics. That's part of the reason why you see the slowdown in Cosentyx® that we saw.

With Entresto®, given the strength of our overall performance globally, it doesn't really move the needle on that particular brand. So the key brand where it has an impact is Cosentyx® and, to a smaller extent, in some of the other brands.

Nonetheless, we continue to believe, given that there's over 1 billion patients – 1 billion people we can serve with our portfolio of medicines, we have to continue to find ways to continue to reach patients in the framework that is currently in place. And then also be ready that if there's a further opening up, to continue to expand our growth in the market. And importantly, we believe Leqvio® and some of our other medicines, Pluvicto®, Leqvio®, amongst others, could be significant medicines in China over time.

- Operator

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

- Andrew Simon Baum - Citigroup Inc., Research Division

Q. A question on the IRA impact on catastrophic coverage and the burden on PBMs and managed care. A significant part of Kisqali® goes through the Medicare channel. Ibrance® seems to be available at a much lower price post genericization. To what extent – to what extent, excuse me, do you see deflation of the price of Kisqali® within the Medicare segment because there'll be prior authorization, step edits within Medicare prior to gaining access to Kisqali®? And do you see any risk of spillover of that, assuming that thesis is correct, to the commercial book of business?

- Vasant Narasimhan – CEO of Novartis

A. That's a good question, Andrew. I think in general I'd say we're doing a lot of scenario planning on how the IRA could impact various brands. And I think certainly on our minds is how the increased exposure of PBMs in the catastrophic, how that will get transferred or translated into actions against some of our medicines. I think the key for us to differentiate versus a generic in a class, like in the CDK4/6, will be having a broader indication – set of indications relative to the existing medicine.

So I think that's going to be absolutely critical for us in this class to hopefully have the opportunity to expand into, as I mentioned earlier, stage IIa, stage IIb and stage III patients. Otherwise, I think there could certainly be spillover from – in the metastatic setting if there aren't broad indications for the other two players. So we'll have to see how this plays out.
I would also say, in general, in some of these cancer classes, such as the CDK4/6, you do see contracting and you do see the opportunity for commercial insurers to get rebates from branded products. So that would be the, I think, tension there in the system, is they would have to give up their commercial rebates to potentially utilize the generic. So we'll have to see ultimately how all of this plays out. Thank you, Andrew.

- Operator

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

- Peter James Welford - Jefferies LLC, Research Division

Q. I just wanted to return to Pluvicto®. I wonder if you could give us any more color at all in the centers that are currently using it. Are these generally academic centers? Are these generally centers that are using via the radiation oncologist? Or is it more nuclear medicine physicians? And particularly with regards to then the diagnostic. Just wondering, is it largely use your own Locametz®? Or are you seeing use of other diagnostics before treatment? And is that potentially a source of revenue for you in the future, the diagnostics? Or should we think of this as largely a wash for Novartis as the focus has been the therapy?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Peter. Overall, I'd say it's a mix. You have high academic centers. You also have large-scale centers, which are, in the case of prostate cancer, a combination of urology and nuclear medicine working in conjunction with medical oncology. We see that in some very large centers. And then we also see some nuclear radiology as well. That's – and we generally are focused right now on larger volume centers in this first phase of launch.

I would note that if we were able to open it up even further in terms of the number of centers, we would expect even higher volumes for this medicine given the overall demand that we're seeing. But we're taking it stepwise, making sure we can service this first level of centers absolutely fully. And now we're in the process of adding additional centers step by step.
So it's a very different situation than with Lutathera®, where because of the lower volumes and also neuroendocrine tumors being treated by certain specialists, there's a very relatively limited number of centers that were interested. Whereas here, we have more demand from centers, and then within the centers we're in very high demand that we're seeing at the moment. So those are all the dynamics we're seeing.

Overall, I would say, from a diagnostic standpoint, there is, of course, a preference for gallium, though we do see other PET ligands also used. We wouldn't view our Locametz® business as a driver for Novartis or something that can materially impact. It's kind of – as you said, kind of a wash, it's much more about identifying patients.

One of the dynamics, however, that's very important to understand, as you think about Pluvicto® in across all lines of metastatic prostate cancer with the PSMAfore study that still needs to read out, is the broadening use of PET imaging for identifying patients who have an elevated PSA and to determine the extent of the metastases for their cancer. That is a dynamic that works very much in the favor of Pluvicto® because if you identify these patients through the PET ligand, you're more likely to use a radioligand because you've seen the tumor and now you know the therapy can target what you see. And that, I think, is an important dynamic for the brand in the longer run.

- Operator

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

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

Q. Great. Thank you for the second question. Vas, you mentioned oral being quite important for Iptacopan. So I'm just curious how you think about the issue of adherence with an oral therapy in the real world setting. And then maybe you could talk here about the potential for breakthrough hemolysis as a result of potentially lower adherence.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Wimal. I mean I think there's a couple of topics that we'll have to work through. So there's always the risk of compliance and how we manage that. We can certainly share as we have more data the experience we have in clinical – in the controlled clinical trial setting. And as I mentioned earlier, we're confident in the profile we see with respect to breakthrough hemolysis.

I think for many patients, having either regular infusions, weekly infusions, biweekly, subcu infusions, all these are quite burdensome. And at least our experience has been in severe diseases that patients are highly compliant with their oral therapies given that they know these are absolutely critical for their health and well-being.

So we believe that the compliance topic can be handled in an ultrarare population that is extremely well informed about their condition, and of course, we'll take the steps necessary. And that the benefits of what we believe and hope the clinical trial data will ultimately bear out, is improved efficacy, improved safety, improved overall control, improved secondary endpoints to be highlighted in the upcoming disclosures, will motivate patients to want to get on the best therapy for the management of their disease. And that's, I think, the case we'll have to make.

Alongside that, of course, comes up the question on if you're competing against Part B medicines, how will that impact? Our assessment is that, in general, most of the hematologists who use this medicine are very low volume with respect to given that there's only 4,000 to 6,000 patients in the US. And that can be managed given that this is likely not a large cost recovery driver for those physicians.

Outside of the US, we would expect our ability to use an oral therapy to reduce the burden on health care systems as well as hopefully reach many of the patients who can't afford the currently approved therapies would allow us to, again, treat the majority, I hope, the majority of patients with these complement-driven diseases, including PNH, over time.

- 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 following up again on Pluvicto®, just to reiterate on Steve's point. So are you at capacity now though in Q3? Or should fourth quarter be higher than third quarter before you bring on next level of supply? And then in the pre-taxane setting, can you help us understand the proportion of patients in that first-line metastatic indication that goes through a large center, such as the ones you're targeting at the moment, versus community oncology and community urology centers?

And on that last group, how do you stop them from just using taxane upfront anyway? Because if they refer a patient, they'll essentially lose the income from that patient, at least for the treatment portion of the disease. And then just lastly, a question we've had a few times this morning, just why the conservatism in the guidance if Innovative Medicines is growing mid- to high-single digits and Sandoz also now growing? You've upgraded Sandoz twice now without upgrading the group guidance. So just what's sort of the difference, the bridge between IM, mid- to high, and then group guidance in mid.

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Graham. First, on supply, to reiterate, we have adequate supply to meet the demand for the post-taxane vision population for Pluvicto®. We see very high levels of demand, and we expect continued

growth of the brand in the coming quarters, in that third, fourth line – third, fourth line setting. And we allocate all capacity that is available in our network to the United States launch. If anything, we'll – if we needed, we would prioritize launches in other markets to assume that the – to ensure that the US is at full demand.

I guess what I was trying to indicate is we – even with respect to the higher demand and higher volumes we expect to see in quarter 4, those volumes could be even higher if we were to completely unconstrain the number of centers that would want to bring this medicine on board. So all on the right trajectory.

With respect to the pre-taxane setting, we would roughly expect the new data, if positive, to triple, to quadruple the number of patients that would be eligible for – so basically the broad range of patients in the metastatic setting, first, second, third line, but the full range of metastatic prostate cancer patients who have the key constrainer who have a PET scan. So once they have a PET scan, we would expect them to be eligible for our medicine. I think it's much more of PET scan availability that will drive a lot of the movement towards radioligand therapy perhaps versus taxanes or other available therapeutics.

And I guess what I'd say is it's really going to be in terms of referral patterns from community oncology to larger centers. Two dynamics there. One, how fast can we move out, because we believe that if we get to 400 or so centers, we can cover the full range of the population, the acceptability would be there. And then second, the quality of the data, so that physicians feel compelled to refer even if there's a risk that the patient has moved to another center. I think, in general, oncologists want what's best for their patients in all cases. And so I think that's going to be the other part of the story.

For more specific data, let us come back to you. We have to probably do some more work in terms of the specifics of community oncology versus large-scale centers and where the patients are in that broad metastatic population.

In terms of the guidance, Harry?

- Harry Kirsch – CFO of Novartis

A. Graham, I was expecting that question, of course. But I would say we are guiding for the total company mid-single-digit, top line and bottom line on our core sales and core opinc. We have delivered on the company for the first nine months 5% and 6%. And I expect, without getting into a very detailed quarter 4 guidance, that we are roughly in that range again in quarter 4. But of course, you have to take into account that US Gilenya® now has a generic entry, so maybe the top line a little bit less than the year-to-date, but a good mid- to high single digit on the bottom line. So overall, I think you see on the first nine months that we are very much on track for the guidance. If it's a little bit stronger on the bottom line, so be it. But I think it is roughly in line with what you have seen so far.

- Vasant Narasimhan – CEO of Novartis

A. Thanks, Graham.

- Operator

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

- Matthew Weston - Crédit Suisse AG, Research Division

Q. It's a simple question for Harry on tax. Obviously, you've changed guidance for full year '22 with a reduced tax rate and you highlighted the change in geographic mix. Harry, I wondered if that new lower tax rate is the best indication for 2023 or whether or not you see any meaningful changes that mean it's not a good indicator

for the midterm?

- Harry Kirsch – CFO of Novartis

A. Yes. Thank you, Matthew. So overall, there is always a bit of volatility on geographic profit mix. Then we adjust, if you will, to each quarter to what we believe is our full year estimate on the core and reported taxes. So basically, we moved our full year estimate from 16.9%, as we had in the first six months, to 16.5%. Now I would – again, we give detailed guidance, of course, for '23 then when we have our full year results in January or early February actually. And then – but I would expect the tax rate to be in that range of 16.5% to 17.5%. We will update you with that than early February.

- Operator

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

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

Q. A follow-up question on Pluvicto® please. Just looking at Slide 33, it highlights a change to your approach in the non-metastatic setting. So could you confirm why you're now moving to start Phase II next year rather than a Phase III this year? Can you just clarify those changes and perhaps the opportunity in that setting as well, please?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Kerry. In the non-metastatic setting, the way our previous study was designed and based on feedback from the various investigators and the FDA, we believe the PSMAfore study covers the population that we had previously believed we needed to do an additional study for. So we redesigned our program to generate additional data in a different – I don't have the detail at hand, but a different population within the non-metastatic setting. I would also say we're evaluating now Pluvicto® as well in earlier lines of therapy to see if we can delay progression as well as evaluating combination therapies as well given the overall interest we've seen on the medicine and the clinical profile that we're seeing. So that's the reason we made that switch, based on the understanding from the regulators and experts in the United States.

- Operator

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

- Richard Vosser - JPMorgan Chase & Co, Research Division

Q. When I look at the latest prescriptions for Tafinlar® and Mekinist®, they seem to have gone more into a decline in Q4. Is there anything that we should think about in terms of the dynamics you're seeing in the melanoma market, perhaps likely approval impacting those two brands that we should not think of the strong growth we've seen thus far continuing beyond for the brand?

- Vasant Narasimhan – CEO of Novartis

A. Yes. Thanks, Richard. I mean, overall, I think we didn't note any significant change, at least wasn't flagged to us any significant competitive issues with respect to Taf-Mek in the US or in our other key markets. But I think it's a good question and let us do some homework and get back to you. I don't think we have the answers straight in hand.

- Operator

Your next question comes from the line of Mark Purcell from Morgan Stanley.

- Mark Douglas Purcell - Morgan Stanley, Research Division

Q. Vas, could you help us understand the scope of the free trial offer on Leqvio® when it comes to patient initiation and what – and how that might influence increase in ACP adoption? And then secondly, on the interest of LOE in China, what's the latest situation there in terms of your best guess?

- Vasant Narasimhan – CEO of Novartis

A. So on the free trial offer, Mark, really, the idea was to – while we already provide payment terms that allow physicians to stock doses and have time to get reimbursed before they would have to ultimately pay for the doses, we also noted that for some physicians, there was a need to provide an alternative option to get them comfortable to start, to stop the medicine. So in July, we rolled out a free trial offer program that provides a dose – first dose for a patient free and then – so the physician can get comfortable, use those doses and then hopefully then pull through to follow, keep the patient on therapy as they also get comfortable with the buy and bill process.

We've had a very strong uptake of that program. And so I think over 1,000 physicians plus have signed up for the free trial offer program at the last look, which was still a month ago. So that's been a very positive step, I think, to get more physicians to stock Leqvio® in the offices so that ultimately they can provide it to patients and then hopefully get more comfortable with an ongoing procedure to start the medicine, provide the medicine and get reimbursement.

Now with respect to Entresto® in China, we currently are continuing our discussions with the – our, I guess, our litigations with the – in China against the various generics. I mean at this point in time, we would expect Entresto® to be fully on – protected through '23 and '24 and then impacts in '25 and beyond. But that's something we'll have to continue to look at because it's an evolving landscape with respect to data protection and the ongoing litigations that we have in the country. So we'll keep you updated accordingly.

And I believe with that, we've cleared the entire question queue. I want to thank everyone, and apologies for the two technical disruptions. And we'll look forward to keep you up to date over the course of the remainder of this year.
