AstraZeneca PLC (NASDAQ:AZN) Q2 2024 Earnings Conference Call July 25, 2024 6:45 AM ET

Company Participants

Andy Barnett - Head, IR
Pascal Soriot - Executive Director & CEO
Aradhana Sarin - Executive Director & CFO
David Fredrickson - EVP, Oncology Business
Susan Galbraith - EVP, Oncology Research and Development
Ruud Dobber - EVP & President, BioPharmaceuticals
Sharon Barr - EVP, BioPharmaceuticals Research and Development
Marc Dunoyer - CEO, Alexion and Chief Strategy Officer, AstraZeneca
Dave Fredrickson - EVP, Oncology Business
Leon Wang - EVP, International and President, China

Conference Call Participants

Mark Purcell - Morgan Stanley
James Gordon - JPMorgan
Gonzalo Artiach - Danske Bank
Rajan Sharma - Goldman Sachs
Sachin Jain - Bank of America Merrill Lynch
Tim Anderson - Wolfe
Emmanuel Papadakis - Deutsche Bank
Peter Welford - Jefferies
Seamus Fernandez - Analyst
Matthew Weston - UBS
Mattias Haggblom - Handelsbanken
Pete Verdult - Citi
Luisa Hector - Berenberg Capital Markets

Operator

Welcome to AstraZeneca's Half Year and Q2 Results 2024 Webinar for Investors and Analysts.

Before I hand over to AstraZeneca, I'd like to read the safe harbor statement. The company intends to utilize the safe harbor provisions of the United States Private Securities Litigation Reform Act of 1995. Participants on this call may make forward-looking statements with respect to the operations and financial performance of AstraZeneca. Although we believe our expectations are based on reasonable assumptions, by their very nature, forward-looking statements involve risks and uncertainties and may be influenced by factors that could cause actual results to differ materially from those expressed or implied by these forward-looking statements.

Any forward-looking statements made on this call reflect the knowledge and information available at the time of this call. The company undertakes no obligation to update forward-looking statements. Please also carefully review the forward-looking statements disclaimer in the slide deck that accompanies this presentation. [Operator instructions] And with that, I would now like to hand the conference over to the company.

Andy Barnett

A warm welcome to AstraZeneca's half-year and second-quarter 2024 presentation conference call and webcast for investors and analysts. I'm Andy Barnett, head of investor relations. And before I hand over to Pascal and other members of our executive team, I would like to cover some important housekeeping points. Firstly, all the materials presented today as additional and additional resources including updated epidemiology tables and our recent Investor Day materials are available on our Investor Relations website.

This slide contains our safe harbor statement, which I'd encourage you to take time to read we will be making comments on our performance using constant exchange rates, or CER, core financial numbers, and other non-GAAP measures. A non-GAAP to GAAP reconciliation is contained within the results announcement and all

numbers quoted are in millions of U.S. dollars unless otherwise stated. This slide shows the agenda for today's call.

And following our prepared remarks, we'll open the line for questions. We will try and address as many questions as we can during the allotted time, although I did ask the participants to limit the number of questions you ask to allow others a fair chance to participate in the Q&A. And with that, Pascal, I'll hand the floor over to you.

Pascal Soriot

Thank you very much, Andy. Good morning, good afternoon, good evening, everybody. In the first half of the year, total revenue grew by 18%, driven predominantly by strong underlying demand for our medicines across key therapy areas and geographies. We recorded a record second quarter with almost $13 billion of revenue.

Core operating profit increased to $8.4 billion, while core EPS increased 5% to $4.03. On both measures, it is important to recall that in the first half of 2023, the company benefited from onetime -- other core operating income totaling $1.1 billion. Adjusting for other operating income, growth in core operating profit and core EPS in the first half would have been higher. And this shows that we continue to work on leverage with faster operating margin growth and revenue.

With the strength of our underlying business, I'm pleased to announce we've upgraded our full year guidance we now expect both total revenue and core EPS to increase by mid-teens percentages. It is a strong upgrade. They rely on our underlying -- the underlying strength of our business. Collaborative revenue, as you've not probably noted, are not growing.

Aradhana will provide you with additional detail shortly in our prepared remarks. Please move to the next slide. Taking a closer look at our total revenue performance in the first half, we continued to benefit from our diverse broad-based business. We delivered double-digit growth in the U.S., in Europe, in emerging markets, ex China, and in China, we delivered a growth of 15%, nearly 30% ex China.

Oncology biopharmaceuticals and rare disease all delivered double-digit growth in the first half of the year, supported by increasing demand for our leading medicines. Please move to the next slide. We saw continued pipeline momentum in the first half of the year, delivering several potentially transformative phase 3 trials readout and new approvals across our therapy areas. Since our Investor Day in May, we reported positive results for the phase 3 NIAGARA trial of Imfinzi which marks an important step toward building our presence in bladder cancer.

We received FDA approval for Imfinzi in endometrial cancer based on the DUO trial, and we received breakthrough designation for ADRIATIC in limited stage cell lung cancer, small cell lung cancer. Additionally, breakthrough designations were granted for Tezspire in COPD, following the encouraging results from the phase 2b course trial and enibroparatide in high-property design with phase 3 results expected in the first half of next year. Taken together, the collection of phase 3 readouts and new launches listed on this slide will support underlying momentum in the future growth potential of our business. With that, please advance to the next slide, and I will hand over to Aradhana, who will take you through our financials.

Aradhana Sarin

Thank you Pascal, and hello, everyone. Next slide, please. As usual, I will start with our reported P&L. As Pascal just highlighted, we have had a very strong start to the year with total revenue increasing 18%.

This was driven largely by substantial product sales growth across the portfolio. Alliance revenue also increased by 50% in the first half, mainly driven by an increase in HER2 sales in regions where Daiichi Sankyo record revenue. Please turn to the next slide. This is our core P&L.

In the first half, total revenue grew 18%, as I just mentioned, and our core product sales gross margin was 82.4%. We've previously said that we anticipate a slightly lower core product sales gross margin for the full year versus 2023, and we expect downward pressure in the second half driven by the usual seasonal impact of medicines such as FluMist, as well as increased before supply, which comes at a lower gross margin. In the first half, both SG&A and R&D costs increased 15%. We expect R&D expense for the full year to be toward the

upper end of our indicated low 20s percentage range due to accelerated trials and the inclusion of expenses following closure of various business development transactions, including Gracell, Fusion and Amolyt.

All operating profit in the first half increased by 7% despite a significant decline in other operating income. Recall that in the first half of 2023, other operating income was $1.1 billion related to the gains by the disposal of the U.S. rights of Pulmicort Flexhaler and the amended before this agreement. Reflecting the aforementioned substantial decline in other operating income, core EPS grew 5% at CER to $4.03.

Please turn to the next slide. In the first half, net cash inflow from operations grew by around 15% to $700 million. Net debt increased by $3.8 billion to $26.3 billion, driven by the recent acquisitions, which created a total cash outflow of over $5 billion. We also made the final payment to the former shareholders of Acerta and paid the second interim dividend in the first quarter.

We continue to expect a roughly 50% increase in tangible capex in 2024 as we invest in both increased capacity and new capabilities. Tangible capex of $799 million in the first half included maintenance capex as well as investments in our new API facility in Ireland, a new inhaled manufacturing site in Qingdao, China, and our new cell therapy manufacturing site in Rockville, Maryland. In May, we announced plans to build a new end-to-end ADC manufacturing site in Singapore. As previously communicated, we anticipate deal payments related to past transactions to be in the same range as last year or at around $2 billion.

Finally, our current net debt to adjusted EBITDA ratio is now at 1.8 times. Please move to the next slide. As you can see on this slide, strong performance of our leading medicines across key therapy areas supports our full year guidance upgrade. In the first half, eight of our medicines delivered total revenue above $1 billion.

Next slide, please. We now anticipate total revenue and core EPS to increase by a mid-teens percentage at constant exchange rates, up from our previous guidance of a low double-digit to low teens percentage. Importantly, this upgrade does not include any increase in collaboration revenue. Last year, we booked $594 million in collaboration revenue which reinforces this upgrade is entirely driven by an improvement in underlying performance from our product sales and alliance revenues.

Based on average June FX rates, we continue to anticipate a low single-digit adverse FX impact on total revenue and a mid-single-digit adverse impact on core EPS. With that, please advance to the next slide, and I will hand over to Dave, who will take you through our oncology performance.

David Fredrickson

Thank you, Aradhana. Next slide, please. Oncology total revenues grew 22% to $10.4 billion in the first half, driven by strong demand for our key medicines and building on momentum gained from the first quarter. Tagrisso Global revenues grew 12% in the quarter, reflecting further global demand for ADAURA, initial launch uptake for FLAURA2 in some of our markets and continued expansion of treatment duration in the frontline setting.

Calquence's total revenues increased 22% in the second quarter with sequential growth of 10%, driven by sustained BTK inhibitor leadership in frontline CLL and continued international expansion. Imfinzi total revenues grew 18%. As expected, growth was impacted by the 25% price reduction in Japan, and we anticipate a second mandatory price reduction of 11% in Japan, which reflects the shift from weight-based to fixed dosing to take effect from August. We continue to see strong demand for Imjudo in combination with Imfinzi in both liver and non-small cell lung cancers, demonstrating total revenue growth of 19% in the quarter.

Lynparza remains the leading PARP inhibitor globally across all tumor types, delivering sales growth of 7%. On in HER2, total revenues increased 49% in the second quarter with sustained market share leadership in second-line HER2-positive breast cancer. We also received positive feedback from the medical community following the presentation of DESTINY-Breast06 data last month, which we believe support continued expansion in HER2 low. Following in HER2's tumor-agnostic approval in April, we saw encouragingly early launch signals in the quarter with 13 NCCN guidelines updated and a rapid increase in physician awareness.

Taken together, we expect to see a return to sequential growth into the third quarter for HER2. Finally, our recently launched novel AKT inhibitor, Truqap, delivered $92 million in the second quarter for total revenues, reflecting strong adoption in the biomarker altered population. Looking ahead, we're pleased with the U.S. approval of DOE expanding Imfinzi into the endometrial setting.

Additionally, we look forward to bringing the benefit of FLAURA2 to more patients globally following approvals in Europe, Japan and China and further cementing Tagrisso as a backbone standard of care in EGFR-mutated non-small cell lung cancer. And finally, the recent approval of CAPItello-291 in Europe will help to build additional launch momentum for Truqap. With that, please advance to the next slide, and I'll hand over to Susan to cover key R&D highlights from the quarter.

Susan Galbraith

Thank you, Dave. Over the past quarter, we've presented several practice-changing data sets. At ASCO, we had two back-to-back plenary sessions for LAURA and ADRIATIC, demonstrating our leadership in early stage lung cancer. The strength of these data were reinforced by the inclusion of LAURA as a Category 1 recommendation in the NCCN guidelines within 12 days of data presentation and its acceptance for priority review in the United States.

We also presented the data for DESTINY-Breast06 in a special oral session at ASCO. DESTINY-Breast06 is the first phase 3 trial of a HER2-directed therapy or an antibody drug conjugate to show benefit across both the HER2 low and HER2 ultra-low breast cancer population. And this data set represents the opportunity both for more patients to receive on HER2 and for them to receive it earlier prior to chemotherapy. Finally, at EHA, we shared the results from Echo, extending the reach of Calquence earlier into mantle cell lymphoma.

These data show that Calquence in addition to standard of care chemo immunotherapy improved progression-free survival and had an early trend for improved overall survival, the first BTK inhibitor to show an overall survival trend in this setting. The positive high-level results from Niagara are trial for Imfinzi plus chemotherapy, followed by Imfinzi maintenance in the muscle invasive bladder cancer setting, signals our potential expansion into bladder cancers. There are approximately 120,000 patients with muscle-invasive bladder cancer globally. And even after cystectomy, patients still experience high rates of recurrence and a poor prognosis.

This makes the positive event-free survival and overall survival results from Niagara incredibly important, and we look forward to sharing these data at an upcoming congress. Beyond Niagra, our broader program targets all stages of bladder cancer as we look to redefine the outcomes for patients with this challenging disease. And with that, please advance to the next slide, and I'll pass over to Ruud to cover biopharmaceuticals performance.

Ruud Dobber

Thank you so much, Susan. Next slide, please. Our Biopharmaceuticals medicines delivered total revenue of $10.4 billion in the first half of 2024, representing growth of 17%. Total revenue growth for both CVRM and R&I was 22%, and we were very pleased to see Farxiga had $1 billion of revenue versus the first half of 2023, further strengthening our franchise in cardiorenal diseases.

In the second quarter, Farxiga delivered 49% growth in Europe and 38% growth in the emerging markets. We saw 16% growth in the U.S. compared to prior year, though sequential growth was impacted by inventory movements following the launch of North line generic in the first quarter. Following Wainua's approval in ATTR polyneuropathy at the end of 2023, we have seen encouraging launch uptake for this ultra-rare disease, which can be fatal if left untreated.

Wainua starts includes a mix of patients who are new to treatment, some who have switched from other medicines and some who are using Wainua as an add-on to their existing medication. In the second quarter, R&I was our fastest-growing therapy area, up 26%. We saw strong growth across the portfolio with global sales from the Tezspire alliance on track to achieve blockbuster status this year. Equally, Brezstri saw strong growth of 51% in the first 6 months, and like Tezspire is on track to achieve blockbuster status.

Finally, it has been another strong quarter for Symbicort in the United States and emerging markets. And Airsupra continues to see strong volume uptake following its launch at the start of the year. with revenues reflecting introductory discounts as access builds. Next slide, please.

I will now hand over to Sharon to discuss the latest developments from the biopharmaceutical pipeline.

Sharon Barr

Thank you, Ruud. We have had several exciting data presentations in the first half across our biopharmaceuticals R&D portfolio. In the second quarter, we presented two key data sets from our CVRM portfolio that support our confidence in their multi-blockbuster potential. At EAS, we presented the phase 1 data for AZD0780, our oral PCSK9 inhibitor for hyperlipidemia.

In this trial, AZD0780 delivered a statistically significant LDL-C reduction of 52% on top of standard-of-care statin resulting in a 78% reduction from baseline. This efficacy, combined with the excellent bioavailability of the compound means that we can dose once daily with no food effect or need for fasting. Nearly 70% of patients with cardiovascular disease are not meeting their guideline-directed LDL-C target despite high-intensity statin use. This potential best-in-class profile may offer patients a convenient option to achieve LDL-C targets.

We are now moving at pace with AZD0780 into the next stage of development with a phase 2b trial ongoing and data expected in the first half of 2025. In May, we presented data from the phase 2b MIRACLE trial of balcinrenone with dapagliflozin for heart failure and CKD. This is one of three novel combinations we are developing that leverage dapagliflozin as a foundational treatment. The combination offers the benefit of SGLT2 therapy and leverages the unique mechanism of action and selectivity profile of balcinrenone, an MR modulator that has been shown to retain the organ protective effects of MR antagonists without increasing hyperkalemia.

The MIRACLE trial showed this combination resulted in a numerical decrease in UACR compared to dapagliflozin alone. And importantly, did not increase hyperkalemia at the doses selected for phase 3. These data inform the ongoing Balance HF phase 3 trial in heart failure patients with kidney disease. Currently, only 25% of patients with heart failure and CKD, Stage 2b or an MR antagonist as standard of care due to the risk of hyperkalemia.

By combining balcinrenone and dapagliflozin, we aim to deliver an innovative mechanism to treat a broader population with heart failure and CKD. Let's move to the next slide, and I will now hand over to Marc, who will cover our rare disease portfolio.

Marc Dunoyer

Thank you, Sharon. Can we go to the next slide, please? Rare disease grew 15% to $4.2 billion in the first half, driven by growth in neurology indications, increased patient demand and continued global expansion. As per the previous quarter, the growth rate at CER includes a small benefit from countries with high inflation. In the second quarter, Ultomiris revenue grew 36% with the vast majority of growth coming from neurology indications, generalized myasthenia gravis and NMOSD.

In PNH, we achieved over 80% conversion to Ultomiris across major markets. and the recent launch of VOYAGER is progressing well, providing benefits for the PNH patients, we experienced clinically significant extravascular hemolysis. Beyond complement, Strensiq and Koselugo grew 14% and 45%, respectively, driven by continued patient demand and new launches. Please advance to the next slide.

In July, we closed our acquisition of Amolyt Pharma, which expands our rare endocrinology portfolio with the addition of eneboparatide, currently in phase 3 for patients with hypoparathyroidism. Hypoparathyroidism is characterized by the deficiency in paratoid hormone production, which results in significant disregulation of calcium and phosphate. This can lead to life-altering symptoms and potentially chronic kidney disease. Hypoparathyroidism most commonly occurs post next surgery, often related to thyroid disease.

Many of these patients are women and over half of the patient with hypoparathyroidism are peri or post menopausal women who are at greater risk of osteoporosis. It is one of the largest known rare disease with over 250,000 patients across the U.S., EU and Japan. Clinical priorities for hypoparathyroidism include a normalization of serum and urine calcium level, a reduction of dependence on delicalcium, and vitamin D supplement as well as restoring normal bone turnover and preserving bone mineral density. In May 2024, eneboparatide received fast track designation from the FDA, reflecting the seriousness of the disease and the potential for eneboparatide to address the urgent unmet need.

We anticipate data from the phase 3 CALYPSO trial in the first half of 2025. And as a reminder, we expect eneboparatide to be a blockbuster opportunity. With that, please advance to the next slide, and I will hand back to Pascal for closing remarks.

Pascal Soriot

Thank you, Marc. Next slide, please. At our recent Investor Day, we outlined a new ambition for our company to deliver $80 billion in total revenue by 2030. While this target is ambition -- ambitious, it is risk-adjusted, meaning we did not assume all of our programs would be successful.

Importantly, this ambition doesn't assume future M&A. We also reaffirmed our ambition to achieve a mid-30s percentage core operating margin by 2026, and we are on track to achieve this. Beyond 2026, we will target at least a mid-30s percentage core operating margin. Further progression there will depend on our pipeline and our portfolio evolution.

Finally, given our ongoing pipeline momentum, we upgraded our previous ambition, and we now expect to launch at least 20 -- 20 [indiscernible] by the end of the decade and are already well on our way. Next slide, please. Illustrated on these slides are the medicines, compounds, and RAIs that we believe have peaker revenue potential greater than $5 billion. Importantly, a large number of these are already on the market.

and the majority of those still in development are in registrational trials. In addition, we believe that by 2030, we will have over 25 medicines delivering at least $1 billion in annual revenue almost doubled the number of blockbusters today. Turn to the next slide, please. In the first half of the year, we delivered five positive phase 3 trials and several important new approvals and launches.

Looking ahead, we anticipate readouts from over 40 phase 3 trials before the end of 2025, mainly for assets that we believe have greater than $5 billion peak revenue potential. Importantly, we will be sharing data later this year from multiple early stage trials that support investment in potentially high-value disruptive technologies. This includes data for our bispecific antibodies an in-house antibody-drug conjugates as we seek to extend our lead in this important innovative areas of oncology as well as emerging data for our portfolio of medicines to address weight management and we look forward to sharing data from our oral GLP1 -- GLP-1/glucagon and long-acting Amarin phase 1 trials. These are a few of the important investments that will fuel growth in 2030 and beyond.

And as I've said before, by the end of 2025, it will be clear to investors that we are on track for the 2030 goal we've set ourselves. And of course, I realize on the assumption many of those trials, not necessarily all of them, but many will succeed. With that, please advance to the next slide, and we will go to the Q&A.

Question-and-Answer Session

Operator

[Operator instructions] And with that, let's move to the first question, which is from Mark Purcell at Morgan Stanley.

Over to you, Mark.

Mark Purcell

Two questions. Could you help us understand what you perceive the sustainability is of growth in the legacy products that did incredibly well in the second quarter? So I guess I'm talking Symbicort, Pulmicort, Crestor, Brilinta, Zoladex, and Forxiga. So that's a sort of a mix of different drivers there, but emerging market revenue growth was strong in all of these. And so hopefully, you could help us gain some perspective there.

And then secondly, a question for Susan. For Imfinzi in bladder cancer, obviously, you'll weigh on NIAGARA data. Can you help us understand the opportunity in the two other trials that I can read out in the next 12 months to focus that in NIPC but also the non-muscle-invasive bladder cancer trial, Protomatic, which looks very interesting.

Pascal Soriot

Thank you, Mark. Two great questions, and I'll ask Susan to answer the second one, maybe let me try to address the first one, which really allows me to make maybe a broader comment on our upgraded guidance. You've seen our upgraded guidance for the whole year. I think it's important to keep in mind that in this upgraded guidance,

we expect -- in the second half, we expect continued strength and the same momentum of growth in our core strategic products.

Many of our older products, we also expect to continue growing. There is an area of uncertainty around two products, Symbicort and Farxiga, Farxiga in particular in China because we -- I'm not yet sure of the timing of the VBP process. And Symbicort, Ruud could comment on this a little later if necessary. But in the U.S., in particular, there's some uncertainty around the durability of the ongoing -- the ongoing trend.

Now those uncertainties could resolve to the positive, in which case we would definitely have an upside versus what we expect today. But this is important to keep in mind that the core strategic products are very much on track in the second half, a good trend, and the area of uncertainty, which we've reflected in our guidance for the year, mostly related to those two products in Symbicort and Farxiga. With this, Susan?

Susan Galbraith

Yes. Thank you. So I appreciate the question, Mark. The opportunity for I-O in bladder cancer, I think, is actually significant. And we've obviously seen other trials that are positive, but I'm excited by the NIAGARA data, not just because we've hit on EFS but OS. And I think this bodes well for the VOLGA study. Obviously, EV, enfortumab vedotin has shown activity both as monotherapy also exciting data in combination with pembro in the first line of bladder cancer. And I think the opportunity for that combination with durvalumab and with chemo in the VOLGA study in the perioperative setting is really exciting.

The non-muscle invasive bladder cancer is also a really important indication. And again, given the NIAGARA data, I think that has to increase the probability that there's a good opportunity there also for Imfinzi. So we're excited about all of this in totality coming together and seeing what the opportunity is to further improve on the outcomes of patients with bladder cancer at all stages of the disease.

Pascal Soriot

Thanks, Susan. Maybe, Dave, you could add some further insights on this indication and -- and then Ruud, if you want to comment on Symbicort in particular, I think Farxiga have covered it, but if there is anything you want to add on Symbicort, over to you, Dave.

David Fredrickson

Thanks. So just Mark building off Susan's commentary on the studies and the unmet need and the opportunity. If we take a look at bladder cancer in aggregate. So NIAGARA, VOLGA together with atomic I think -- and obviously, we need to see positive study results, but this is a blockbuster plus opportunity in aggregate from these.

And I think that NIAGARA, as Susan says, gives good reason to believe in Imfinzi within this bladder cancer setting. I'd also say that importantly, these are catalysts that are coming within the '24, '25 period in terms of the news flow. So we don't have to wait a long time to understand whether those opportunities will materialize or not. Ruud?

Ruud Dobber

Yes. Thank you, Dave. So three remarks regarding the Symbicort performance. So first of all, the brand remains doing very well, not only in the United States, as you have seen, but also in the emerging markets. Clearly, emerging markets, there's no reason to believe that, that will slow down anytime soon. There's a lot of loyalty across the markets and the brands United States is slightly more complex. We saw generic competition entering in the market in 2023. We have launched our own authorized generic some years ago.

And equally -- and I think that's an important event. We have reduced our list price in the beginning of this year. And we -- as a result of all those 3 factors, we have seen a very substantial increase of the volumes, but also regarding our price. Whether that is sustainable, time will tell.

But at least in the short term, we still hope that Symbicort will remain a very strong brand in the United States.

Pascal Soriot

Thank you, Ruud. So as you can see, there is, of course, uncertainty on Farxiga and Symbicort. As I said before, if those uncertainties resolve positively over the next few months, then there is certainly upside. But for now, that's how we see the trend.

James Gordon, JPM. James, over to you.

James Gordon

Hello. James Gordon, J.P. Morgan. A question about collaboration revenues because I noticed within the guidance that it's no longer expected to increase this year.

And I can see two elements that look that might have changed. So firstly, for PARP1 and a potential partnership, it looked like the previous guidance may be allowed for a contribution for that. But you've now started phase 3 for prostate and breast, and you're doing that so low. So is that fair that you're now assuming that you are going to end up doing this product by itself? And how should we read that? Is that a lack of interest from external partners? Does that mean the asset doesn't look as exciting? Or are you still as excited about [indiscernible] as a product even if it's just you doing it by yourself? And the other element, I think, could be that you could have got a milestone from Merck on Lynparza passing through a sales threshold.

So is that right that, that could be Lynparza getting just pushed out a year for hitting $3 billion? Or could it be that Lynparza is not talking out? Because I don't think you gave a peak sales for Lynparza at the Investor Day. Is that because there's some other things to be where we of, like, for instance, the pattern might go in China at the end of this year? Or do you think it's just you get there but just a year later to get that milestone? Thanks.

Pascal Soriot

A couple of very quick comments, actually, James, great questions. But quick comments before I hand over to Susan in terms of our confidence in the PARP1, which is very strong. No question about it. And maybe Dave in terms of Lynparza trend.

Very quickly, Lynparza, in China, you really get impacted when you go VBP, not necessarily when you lose patent protection as you know very well. So I don't think that's really a factor. A general comment on collaboration revenue. It's not visible from the outside, of course, but I can tell you any deal we do, whether it's a licensing in or a partnership deal.

Typically, we work one year, sometimes two years on those deals before we conclude them. And the reason is basically, we want to make sure that we set up a partnership that is both strategically valuable and also creates value for our shareholders, but also is structured in a way that enables the partnership to be successful. We don't want really to get into partnership when we I cannot operate successfully together with our partners and all our partnerships, quite frankly, are extremely successful. We have great relationship with our partners, whether it's Merck, whether it's Amgen, Daiichi Sankyo, And each time we really make a special effort to make sure that the whole thing is operationally structured.

So this is going to be successful. So the consequence of this is the timing of these partnerships is a little bit unpredictable. And so we don't guide specifically on the content of the collaboration revenue line, just like we don't guide specifically on the individual product sales. But at this point in our guidance, we concluded the best is to assume a relatively stable collaboration revenue overall and things can always change, of course, as we go through the year.

But that we thought was the best reflection of where we are at this point. Dave, do you want to cover the Lynparza specific -- specific question? And then Susan, you could talk about the confidence we have in the PARP1.

David Fredrickson

Sure. So I was pleased in the second quarter with Lynparza to see that sequentially, we saw 7% growth in Q2 versus Q1. And I think that -- what's important to note there is we know that in the U.S., in particular, we've seen some real negative class pressure, particularly as second-line label modifications were made just in terms of all of the class going through those elements. And so I think that in the U.S., Q1 marks the bottom of where we were and that you see sequential U.S. growth coming into the quarter. And I think that's coming from

strength that we're seeing on driving within breast cancer, continued strength in the areas of frontline ovarian cancer and I'm optimistic that we'll continue to see sequential growth in the U.S. moving forward. As we take a look at Europe and Japan, we also saw sequential growth in those regions.

And I think that, that's really, really important as well. On Lynparza, international, for the quarter, there's some stocking dynamics in both Brazil. And within Russia, those happen to be our two largest international markets as we kind of take a look at Lynparza performance. But I'm optimistic that Lynparza has a good solid second half sequentially in front of us, and we continue to focus on our areas.

And I look forward to driving DOE and the opportunities that we have to do that. And I think that that's my outlook for the medicine.

Susan Galbraith

Yes. Thank you. And just to add, I'm really very pleased with the development of sipavibart, first of all, because in terms of the discovery, it's come from our understanding of how we can improve on the great medicine that Lynparza is. And secondly, as the data maturing in both our PETRA and [indiscernible] trials, and we have presented most recent updates earlier this year.

As the data mature, both the efficacy and safety data look really very encouraging to deliver on what we're hoping for from this medicine. And we do have a broad clinical development plan. You've got two trials that already posted, the EvaPARprostate01 and the initial breast cancer study, but there's multiple other opportunities that are being developed, and I think there's going to be a great opportunity for this to be a very important medicine moving forward.

Pascal Soriot

Thank you, Susan. So I think the key message here in the end is, it's very good to see that we are actually able to upgrade substantially the guidance while considering collaboration revenue will remain stable. So that really reflects a strong momentum in our core business, in particular, our core strategic products. But also our more traditional products in the emerging markets.

And as I said, uncertainty around Symbicort and Farxiga, those may resolve positively. We'll have to see over the next two to three months. And the collaboration revenue, of course, as always, like for products, there's always movements and noise in this total forecast, but could also vary around what we are forecasting today. Let's move to the next one, which is a question from Gonzalo Artiach, Danske.

Gonzalo, over to you.

Gonzalo Artiach

Hi. Good afternoon. Can you hear me?

Pascal Soriot

Yep.

Gonzalo Artiach

Hi. Gonzalo Artiach from Danske Bank. Thank you for taking my questions. I have a couple.

The first one on Dato-DXd. Is there any detail you could provide us in terms of interactions with the idea head of the PDUFA meeting on TRUPION-Lung01 potential approval, have you had any sign of a potential -- potential outcome meeting any detail here would be appreciated. And the second one on Truqap, the launch seems that it's going very good. And I was wondering if you have any hypothesis for it failing also in the biomarker population in the triple-negative cancer study? And if you have any pullbacks from your failed study here the approved indication?

Pascal Soriot

Thank you, Gonzalo. Can I suggest, Susan, you covered that, but also Truqap from a sort of a scientific viewpoint. And Dave, you could say a few words about the trend we see in the market.

Susan Galbraith

Thank you. So the TROPION-Lung01 filing remains under review. Discussions with the FDA are ongoing. And I don't have any new updates to share with you on this filing at the moment.

The -- what I would say in terms of the second half of this year is that in congresses later this year, we will -- we've already announced the TL01 high-level results, but we'll share those data at an upcoming congress. And -- just as a note, we're also finalizing and making progress on the biomarker work for TL01. And again, I think we mentioned this before, but we'll also share updated data on the biomarker as a congress later this year. In terms of Truqap, First of all, yes, it was disappointing that we didn't meet the primary end point for the data in the triple-negative breast cancer setting.

But I think the data that we've already got with CAPItello-291 and what we're looking forward to for the CAPItello-281 trial in prostate cancer is looking at the interaction of AKT and endocrine signaling both in breast cancer and prostate cancer. So in both settings, there's a kind of a reciprocal relationship between the endocrine signaling. So as ER is inhibited, you're signaling through the AKT pathway goes up and vice versa, and the same with the antigen receptor and AKT. So I think one of the things that gives us confidence in the CAPItello-281 indication, which is very significant, is the data that we've seen from the CAPItello-291 setting in the endocrine breast cancer setting.

And again, what we also know is that in the [indiscernible] group of prostate cancer, that's a group that has particularly poor prognosis and that's the group that we're focused on for CAPItello-291. So overall, I think we're very encouraged by the uptake that you've seen with the Truqap launch following the 291 results, and we look forward to seeing the full potential for this medicine as the other trials read out.

David Fredrickson

So just coming on to the performance. I mean in short summary, the uptake has been strong. the adoption of biomarker testing has been also impressive. And I think that the tolerability profile for the medicine has been really well received.

The uptake was very rapid in the prevalent population, which you see oftentimes with a late line approval, second line plus, like the one that we had. But very importantly, we see that the incident population, new starts is also strong, and that's going to be what allows us to continue to grow moving forward into the half. And just to reiterate on what Susan said, certainly is a near-term news flow. We look forward to the 281 data for CAPItello-281 opportunity to, if positive, expand into prostate cancer, which is an important opportunity for this medicine.

Pascal Soriot

Thanks, Susan and David. And let me just add that those antibody-drug conjugates are often called a smart chemo smart -- smart chemo. Smart had to be -- has to be targeted. Entirely it means you need a biomarker, and it's really good to see the progress we're making with the test that Susan was describing because that could really substantial value for data and the use of its agent in lung cancer in particular, if we could put in place targeted treatment to get a strategy.

Next question is Rajan Sharma at Goldman Sachs.

Rajan Sharma

Hi. Hopefully, you can hear me. Thanks for taking my question. So firstly, could you just maybe discuss potential implications to Wainua's cardio transform trial in ATTR-CM following some competitor data that we saw last month.

Essentially, does that positive data for [indiscernible] increase your confidence in cardio transform? And can you just remind us on time lines for that trial? I think your partner talked about potentially seeing data in 2025.

It'd be good to get your perspectives on that. And then secondly, just on automorous. Could you maybe just to the dynamics that you're seeing in myasthenia gravis.

There's been a couple of your competitors who've also reported strong market growth in assessing this morning. So some color on source of patients for automorous and how you see this evolving on the forward will be helpful.

Pascal Soriot

Thank you very much, Rajan. Sharon, do you want to cover the first question?

Sharon Barr

Thank you for the question. It's a nice opportunity to draw attention to eplontersen which is currently in an ongoing study cardio transform to evaluate the efficacy of eplontersen in ATTR cardiomyopathy. As you mentioned, the HELIOS-B trial read out earlier this year, which we view as validation of the silencing mechanism to address ATTR amyloidosis, and we are continuing to progress our own cardio transform study together with our collaborators, Ionis. This is the largest ever study run for ATTR cardiomyopathy and is powered to be able to evaluate a number of subsets within the study.

We want to be sure to give eplontersen the greatest chance to demonstrate its potential for these patients. And so with regards to the timing of trial readout, we are currently tracking toward our previously anticipated time lines and are actively in discussion with our collaborators. As we evaluate the data emerging from HELIOS-B at the upcoming ESC conference, I would also remind you that we have additional reasons for optimism. In our polyneuropathy study and a planned subset analysis, we looked at readouts of cardiac structure and function for eplontersen and demonstrated a positive benefit within that set analysis.

So we look forward to the full readout of cardio transform.

Pascal Soriot

Thank you, Sharon.

Marc Dunoyer

From the beginning of 2023, the growth of the branded market in myasthenia gravis in the United States, but also around the world has been very dynamic. And this is accelerating with the arrival of new clinical options for patients. So we have mentioned in my prepared remarks that the growth of Ultomiris for the second quarter was -- is 36%. And I also said that predominantly, this growth came from myasthenia gravis and the launch in NMO in the United States.

So we are continuing to have a very sustained growth on neurology indications, both of them. And obviously, that of myasthenia gravis together. We anticipate the growth rate of branded medicine in the myasthenia gravis to remain very solid and robust in the months and years to come with the arrival of many clinical options.

Pascal Soriot

Thank you very much, Marc. Next question is from Sachin Jain at Bank of America. Sachin, over to you.

Sachin Jain

Thanks for taking the question. Thanks for your questions. Just a couple on upcoming pipeline data. So one for Sharon and then one for Susan.

So firstly, for Sharon on obesity, given the moves in the sector there's obviously a lot of focus ahead of you presenting days later in year. So I wonder if you could just comment first on Eccogene and remind us why you think it's best-in-class. And how would you think about data relative to the 6% weight loss we saw from Roche. And then on Amylin, I wonder if you could just touch on the commentary on mechanism around calcitonin potentially better safety relative to the Zealand data, which looked very tolerable.

And then for Susan, just a follow-on on TL01. As we look today for a guess at World Lung, I wonder if you could comment on the importance of the non-squam subset being normally significant and where the FDA is focused there at all in your recent interactions. Thank you.

Pascal Soriot

So thank you, Sachin. Should we start with Dato and Tier 1, Susan?

Susan Galbraith

So obviously, the FDA I'm interested in seeing the OS data and following the readout that we shared the OS data with the FDA. And as I've said, we will share the OS data at an upcoming congress in the second half. So I think we can answer the questions once we share the data really on that point.

Pascal Soriot

Thank you, Susan. Sharon, obesity, two subquestions. Sachin lacks the sub questions. So one is Eccogene best-in-class; and the second is Amilyn and the safety profile and in particular the calcitonin dimension to this.

Sharon Barr

Yes. Thank you, Sachin, for the questions. And thank you for the focus on our weight management portfolio. So your first question was about AZD5004 the molecule that we in-license from Eccogene and together are bringing forward with our collaborators at Eccogene.

So I'll remind everyone that this is an orally bioavailable GLP-1 receptor agonist that is suitable for once-daily dosing and has demonstrated a very positive PK/PD profile. We move forward into a phase 1 study, which read out earlier this year. That was a highly controlled inpatient four-week study. in monotherapy.

And we look forward to sharing the full results of that study at a major medical conference later this year. That study, like all phase 1s, was designed to demonstrate safety and target engagement. We saw no red flags in that study, and we are encouraged to move forward with two phase 2b studies, launching later this year, one in type 2 diabetes and one in obesity. I would note that 5004 is not our only focus in weight management.

that we are exploring both incretin and non-incretin pathways. And you referred to this when you asked about our Amylin molecule. So AZD6234 is a long-acting Amylin agonist. And we, like others in the field are aware that balancing selectivity between Amylin and calcitonin is a really important feature for these molecules.

We know that Amylin itself promotes satiety and protects lean muscle mass, and we think that selectivity for Amylin over calcitonin offers a better tolerability profile. Now as a field, we're trying to understand how exactly to dial in that selectivity, but to date, the profile that we have generated with AZD6234 looks very positive. And we will be sharing updates on phase 1 progress for AZD6234 as well as AZD9550, which is our dual GLP-1 glucagon agonist at an upcoming meeting.

Pascal Soriot

Thank you, Sharon. Next question is from Tim Anderson at Wolfe. Jim, over to you.

Tim Anderson

Thank you. A couple of questions. On data, you have a phase 3 TROPION-Breast02 front-line triple-negative data coming out this year and it's on a similar time line of is Gilead phase 3 ASCENT 3 trial. These are fairly similar in design.

So that means we should be able to do reasonably like-for-like comparison of your drug to delve which will help test whether your drug is better as far often claims it is. So can you just frame out what you think we'll see and whether in side-by-side comparison, are we likely to conclude that your drug is better? And then second question on emerging markets, notable because in aggregate, they are higher in sales than what your European sales are and the growth is high. My question is on margins in emerging markets. you had, at one point, given some metrics on operating margins.

How do those compare today margin dilutive are they going forward?

Pascal Soriot

Thank you, Tim. Maybe a quick comment on the first one. We said before that the emerging markets, they're not uniform. It varies by subregion to subregion.

But if you look at them in aggregate, you don't get there the level of operating margin you typically get in the U.S., of course, as we can -- as we can expect. But we got operating margins that are certainly viable and supportive of continuing to invest in this region. It's probably closer to a European setup than the U.S. setup.

But definitely driving a lot of growth and a lot of profit and cash flow ultimately. So good place to be in specialty especially when you consider products like cardiovascular products or obesity products that you can deliver in an oral form. And then you're not talking about addressing the needs of patients in the U.S. primarily and a little bit in Europe, but you can address the needs of patients around the world.

And then the volume upside is an almost, as you can see every day with Farxiga and its development or even a Symbicort or Tezspire. So overall, I think it's -- we are very happy to be in the emerging markets. It drives our growth, and the margin aspect is included in our outlook anyway. So Susan, did I give you enough time for the Dato question. Go ahead.

Susan Galbraith

Thank you, Pascal, and thank you for the question. So first of all, just as a reminder, the things that are different about Dato-DXd versus some of the other TROP2 ADCs, is that because we've got a stable linker stable in the peripheral circulation, cleavable in the microenvironment that means that you've got a longer half-life with this drug. And it also means that as the drug is delivered to the cancer cells that express TROP2 that the internalization is an important factor in the activity. What that reflects is lower free payload in the peripheral circulation.

And that leads to lower bone marrow toxicity events. And we've already shown that in multiple trials that you can do in the style comparison. So you've got low discontinuation rates lower bone marrow related adverse events. And that, I think, will also translate through to in terms of the durability on treatment.

Now we have seen already that we know -- and we know that the levels of sensitivity to TROP2-based ADCs is high in the breast cancer setting, particularly in the triple-negative breast cancer setting. So we are optimistic about the results of the TROPION-Breast02 data. And I hope that this will confirm that we have what is a best-in-class TROP2 ADC in that setting and in other settings as well. reminder that, of course, in lung cancer, one of the advantages of that lower bone mower toxicity profile is also that you can combine it with chemotherapy, which I think some of the other TROP2 ADC struggle to do.

So overall, very confident about the profile that we have with this drug and the opportunity for it in multiple settings, not just in lung and breast cancer but other settings as well. And I do think that the biomarker work that we've done in lung cancer is something that will also help us differentiate this molecule across a range of other different indications.

Pascal Soriot

Thank you, Susan. Also a good opportunity to remind everybody that Dato is also under review for the breast cancer indication. And that's included in our outlook for the next few months. The next question is Emmanuel Papdakis at Deutsche Bank.

Emmanuel Papadakis

Thank you for taking the question. Maybe a question on Imfinzi and lot of the advisory committee taking place this week. Just your anticipation on the decision we might see today in light of those agency ADC briefing documents. And in particular, I'm just to understand your -- the company's decision to effectively ignore long-stand the agency advice on that perioperative trial design? And what it might imply in terms of the outlook for the asset in early lung cancer in light of the BR31 mess.

So give us some thoughts in terms of midterm growth indications where we see a negative decision on the approval of the [indiscernible]. And then a quick follow-on for Farxiga. Just your latest expectations on the potential timing and magnitude in terms of range of potential price reduction we could be looking at under VBP inclusion?

Pascal Soriot

Thank you. Susan, do you want to cover the first one? Will you take the second one? Or Leon, if we are sure we have Leon on the line because I can't see him. Right. OK, cool.

Okay. So maybe Susan, you start and Leon will cover the second question.

Susan Galbraith

Yes, sure. Thank you. So as you've noted, Emmanuel, the ODAC, Oncology Drug Advisory Committee for discussing perioperative trial designs is happening later today. So it's probably best not to make too many comments apart from the fact that gene has met its primary endpoint in both pathologic complete response and a statistically significant and clinically meaningful improvement in event-free survival which is also recognized in the briefing document.

I do think there's a discussion that the FDA wants to have about the future design of perioperative child designs, in general, as you have the opportunity for add-on designs and potentially an increase in pathologic complete response rate. Then there's a debate about the relative contribution of continuing combination treatments into the adjuvant setting. The other note I would say is, of course, we've got a very well-established safety profile for Imfinzi in the treatment of early stage lung cancer built off the PACIFIC data that we've had. And so I think the profile for Imfinzi is well established in that setting, and we look forward to the discussion. And I think that will help inform future trial designs.

Pascal Soriot

Very good. Leon, if you're still on the line, can you cover the second question, Farxiga.

Leon Wang

Yes. Yes, I think there's still uncertainty about when Farxiga will have VBP. But if it does come, it should be late this year. So I think there usually will be some price cut, but there's no exact will be different product by product, usually less than 30%, but a different product by product.

Pascal Soriot

All right. Thank you, Leon. The next question is Peter Welford at Jefferies.

Peter Welford

Hi. Yes, thanks for taking my question Two, first of all, just for Brad, if I can, just on the costs. I wonder if you could just talk a little bit about how we should think about the phasing and perhaps not as site specific, but any specific thing in terms of how we should think about the relative weighting of the cost do you think about this year, both SG&A and R&D in the first versus the second half. You gave some helpful commentary on the gross margin for us.

And then secondly, just going back to data. I wonder if we can press Susan, has the FDA definitively said yet there will not be an ADCOM for TL01? Or is that question still open? And I'm wondering if you could just a little bit set the scene for us for AVANZAR, please, going into next year, obviously, potentially an important study for the future of this molecule. You talked a bit about the biomarker work. I guess when you look at that biomarker work, how that sort of impacts your thinking now for the Avanza analysis, there's nothing really changed there.

Pascal Soriot

Susan, do you want to start and then Aradhana?

Susan Galbraith

Yes, sure. So I think, obviously, you're aware of the PDUFA date for Dato-DXd and our experience with the announcement of advisory committees is that, that can happen at any point during the review period. So -- and as I said, I don't have any updates to share with you today on the Dato-DXd filing for TL01. In terms of AVANZAR, I do think this is an important study.

And I do think that we will be sharing at a congress later this year. some of the data from our near COAST 2 trial, which is in the neoadjuvant setting of non-small cell lung cancer including the combination of Dato-DX and Imfinzi. And again, you'd be aware that we've previously shared the data from the BEGONIA study in triple-negative breast cancer, and that combination in that setting had an unprecedented 79% response rate and very durable responses. So those data together with the TL02 and the TL04 data give us encouragement about, first of all, the safety and combined ability, not just with [indiscernible] but also with a platinum-based chemotherapy.

And I think that's important because that can enhance the response rate in that setting. But I also think that the biomarker work is important for because it can potentially give us an opportunity to focus on the optimal benefit risk profile within both the AVANZAR study and the TROPION-Lung10 studies, which obviously looks at the combination with rivagostomake our PD-1 TIGIT molecule. So I am optimistic about the potential for the combination of Dato plus IO in the frontline setting. I'm optimistic about the potential for the optimization of the benefit risk using the biomarker data, and I look forward to the COAST 2 data sharing some of that optimism as we move this combination into the earlier lines.

Pascal Soriot

Thank you, Susan. I would just add that what Susan said in terms of the better or improved benefit risk profile with the biomarker, certainly it would be a great help also in countries where access is more challenging, especially in Europe, where you can show higher value for your medicine. So lots of reasons to expect to need these AVANZAR data in the long run for Dato and the reimbursement. On cost phasing.

Aradhana Sarin

Sure. Thanks for the question. So just to give you a little more color, I talked a little bit about gross margins. And as you know, there are a couple of products that are more seasonal and that have some impact on gross margins.

In terms of R&D, we likely will be on the higher end of the low 20s that we've always signaled. And it's also because we're adding we're accelerating a number of our studies, which you've seen in the clinical trial appendix, but also because we've added a number of projects with the closing of the Amolyt transaction, Fusion, Gracell, etc. And so all of those are accelerating. But again, well within the range that we've always signaled will be included.

So I think you can get there. In terms of SG&A, Again, we -- in terms of the second half, we'll be sort of lockstep with how the revenue growth is driven. We continue to invest behind many of the brands we have launched with Airsupra and Wainua, will also move into new areas like with bladder cancer and NIAGARA, so there will be some market-shaping investments. In addition, the companies we've acquired that I just mentioned, we're also operating them a little bit independently in keeping those capabilities. So there's some SG&A that comes with that.

Pascal Soriot

Thank you, Aradhana. Maybe just a last quick comment is that, if you remember last quarter, we had a sort of a bump in expenses that came as a surprise to some of you. And we don't expect this year to have the same pattern in Q4. The other thing that I would like to add maybe is building on what Aradhana said in terms of study moving well is.

In the last couple of years, the teams have done a lot of work to increase the speed and also look at the cost of the way we conduct clinical trials and that the result of it is that both in oncology and outside of oncology in biopharma, we are also moving very fast with many of our clinical trials that are quite ahead. Now the upside of this is we will launch our medicines earlier if the studies are positive. But of course, it means the costs are more

upfront than we might have expected Overall, I think we should all read this as a positive. Our studies are moving very well and in many cases, much faster than we had expected.

The next question is Seamus Fernandez. Seamus, go ahead.

Seamus Fernandez

Thanks very much for the question. So just one on HER2 and then a second on obesity and the CDMA portfolio. On -- in HER2, Dave, I was hoping you could comment on the growth of in HER2, I think there was some impact in China that you mentioned in the quarter, but historically, I think expectations were for this to be growing to a $10 billion to $15 billion product potentially as additional indications come through. We've seen a number of those indications certainly come through in [indiscernible], but the question, I think, that we're getting from investors is why the growth isn't stronger given the very robust sort of PFS data set.

So I think there's just a little confusion as to where we are in the life cycle of an HER2 and kind of the next drivers that we see going forward. And then the question on obesity is really just more strategic. And this is for Pascal as much as anything, how are you thinking about the overall obesity space strategically? Some are moving very aggressively forward jumping perhaps before really defining the clinical profile of the asset. Others are pushing dosing very aggressively in phase 1 to try to achieve more weight loss.

What do you see as perhaps the problems with some of these development decisions? But separately, how do you think about the broader opportunity for AstraZeneca in this space with your oral programs and your injectables.

Pascal Soriot

Thank you, Seamus. Two great questions. Dave, do you want to cover the first one?

David Fredrickson

Yes. Seamus, I have an outlook for the second half of the year on an HER2 to return to more robust sequential growth. And I can go into why on that in terms of the where we are in the life cycle, I think we're in the early innings. And so I'll go into more on that as well.

for the quarter itself sequentially, we see that the U.S. had underlying growth and sequential demand growth. I think that some of the effects that you see sequentially within the quarter, and you alluded to this, come to that we had quite a bit of destocking happening in China following a stock up in Q1. We talked about that last quarter.

We saw that come through. I expect all of China, Europe and U.S. to be growing as we move into the second half. Now in order to get that growth, I think a couple of things come into play.

We know that we need to continue to move into some of the harder yards with DBO3. We've seen nice progression. We're now probably between 55% and 60% share with DBO3 and need to continue even further into clear standard of care zone. With HER2 low, really nice progression within Europe.

Again, I think that we need to continue to work on changing some of the inertia and embedded behaviors that have existed in the past to get to the share gains that we have. DBO6 has not yet been included in the NCCN guidelines. We expect that when the committee meets that, that's something that will happen. I think that that will be a catalyst I mean then obviously, as we take a look at the road ahead and Susan alluded to this before, in 2025, we have an opportunity for early metastatic and adjuvant readouts with DESTINY-Breast09, DESTINY-Breast11.

We're also in the early innings with outside of breast cancer with the progress that I mentioned on good early awareness on tumor agnostic. And I think that we'll continue to see nice growth there. as well. So in HER2 remains an area where we expect this to be a very important medicine, both for us and also for oncology.

Pascal Soriot

Thanks, Dave. So the -- let me try with your second question, actually, Seamus, a great question and then maybe Ruud or Sharon, if you want to add. So let me just make two overall points, first of all. First of all, we look at this beyond obesity.

We actually look at it in the context of what has been recently called CKM cardiac, kidney, metabolism. So you really have to look at the patients holistically and that is what we have been working on for years. The pipeline we have today, not only for weight management, obesity, but also for hypertension, for kidney disease, etc, is actually a pipeline that we've been working on for quite some time, of course, also the oral PCSK9, which we think has enormous potential. So that's the first comment.

The second is we have a plan. We have a plan for weight management, obesity. And I'm really excited because we have already the plan for phase 2, phase 3. We've approved this plan.

Of course, we will unlock phase 2 at the appropriate time when we see our phase 2 results, but we're very confident we have a plan. I'm also very excited because the person in charge of that plan is the person who built Crestor historically to and develop a fantastic clinical plan and same person who led the team who actually developed Farxiga in renal disease, in heart disease and built it to -- essentially from a clinical viewpoint, of course, built it to what we have today. And now she is going to do with -- together with the team in charge, doing the same. I'm sure is with this franchise.

So going into more details, the way we look at it is that there are really two markets, in our view, in my view. One is what I would call the weight management, weight management is people who have a BMI below 28, 30, that's actually many of us above maybe the edge of 45, 50 we need to lose a few kilos, and maybe people have additional risk factors. It could be hypertension, it could be diabetes, could be dyslipidemia. And these people, they really need a simple regimen, oral regimen with a simple dose and then combine this with a number of medicines we have in development, whether it's back prostate, DAPA, and a number of others, of course.

So that's one part. The other market is what people call obesity and everybody calls the old group of patients or obesity. Obesity is clearly defined. It's people who have a higher BMI.

And in that group, you need a titration up. You need higher doses of GLP-1. You need combinations because you need to improve the quality of the weight loss, more fat loss, less weight loss. And in that context, we need combinations, and that's what Sharon was talking about, we're looking forward to presenting new data, additional data for some of our other products in this franchise.

So really to two separate parts. And then the last part is, of course, diabetes, traditional diabetes for GLP-1. So we have a plan for all those segments. We're ready to go.

Phase 2 will start very soon. And then as soon as we have the results, of course, we unlock phase 3. And our team has proven in the past that they are really excellent at delivering cardiovascular studies. We've done it with [indiscernible] many times.

We've done it before in the old days with Crestor and other medicines, and we are really -- you have a great team to run this. So that's really how we see it. And sort of we have optionality around the pipeline. But really, what we're trying to do is what we presented to you at the Investor Day is leverage the strength of the pipeline.

Some people say you have a broad pipeline. Well, it's on purpose because we want to -- in cardiovascular disease, we want to treat patients holistically, not only help them lose weight but also treat the other factors, the same as we do in oncology. Anything you guys would like to add Ruud or Sharon?

Ruud Dobber

No. The only piece is, and it's obvious, but if you look at the percentage of diagnosed patients with comorbidity and more than 60% of the diagnosed obese, overweight patients have one or more comorbidities. And I think we are somewhat in a unique position with our pipeline with an oral PCSK9 clearly with dapagliflozin. There's more and more scientific evidence that the two mechanisms of action are really synergistic in order to protect the heart, the kidney and the pancreas, hence our enthusiasm bodes combinations.

Pascal Soriot

Thank you. And maybe one last point is that some people I saw have speculated because we talk about risk factors, we are not confident in our GLIP-1. I mean nothing could be further from the truth. We're very confident in the GLP-1 what we want to tell everybody is that we need a simple regimen for the GLP-1 in the weight management segment, people with lower BMI, but still need to lose weight.

And then here, you need a simple regimen in a combination with other agents. The higher BMI group you need to titrate up, you need to combine with other weight loss agent. So those are really two separate segments, and we are addressing both with a very ambitious plan. So moving to the next question, maybe Matt Weston at UBS.

Matthew Weston

Thank you, Pascal. Two questions, please. The first is a follow-up to Aradhana on James question about collaboration income. I understand there may be a degree of uncertainty.

But given that we had a lump sum in our model, is that something we should think about now falling into 2025 or it's something we should just stop considering full stock? And then secondly, either for Dave or Pascal, there continues to be a lot of investor debate on the secondary consequences of Medicare Part D reform as insurers take on 60% of catastrophic risk. Companies that have commented seems to have very different views ranging from no impact to a meaningful increase in rebates. Where does Astra stand based on your current interactions with insurers and PBMs ahead of the January 1st date?

Pascal Soriot

So, Dave, maybe you could cover the second part. I mean, I think maybe a quick comment on this Part D piece actually, Matt, is that I think you're going to hear different responses from different companies based on the type of products, portfolio they have. because it affects more some products than others. And we see this in our own company, different products are affected differently.

So you're going to have low impact to a high impact to major impact. So it really, really depends on the overall portfolio we have. In our case, we have a portfolio that, as you know, covers primary care all the way to more expensive specialty care products. So we are kind of a mix of things.

So maybe, Dave, you want to cover this in more detail. And then Aradhana, will you cover the CR question, collaboration revenue?

David Fredrickson

Matt, on your primary question around how Part D contracting is going. We're still in the midst of finalizing Part D contracting for 2025. I think that within that context, as ever, the importance on a differentiated product profile is the most important element as we enter into those discussions. Certainly, we've seen more focus on the payers on how they think about clinical differentiation and competition.

But again, these are the same discussions that we've always been having with payers and where it's incumbent upon us to make sure that we're differentiating our medicines and showing the clinical value that they can provide. And I think that our oncology portfolio, in particular, is well suited for that. Well, not necessarily part of your question. I think it's also worth noting on Part D that we are seeing the improvements in patient affordability or the reduction in patient out-of-pocket to be translating into more patients being able to have access to medicines within what I would call kind of your normal distribution channels, so outside of free programs.

We're also seeing signs of improvements within abandonment. So I think that these are positive aspects that come out of IRA. And so while in aggregate, I think that I represents a couple of headwinds that we've spoken through. I think that they're manageable, and I think we've got a portfolio that allows us to grow through it.

Pascal Soriot

A couple of additional points, if I may, is that next year, we'll see additional improvements to the challenges that Dave was talking about in terms of access. One is the total co-pay -- annual co-pay will drop to $2,000 from $3,600, I believe, this year or $3,500, so it would drop. The second one, which is I think really meaningful is

you'll have the smoothing. So the $2000 will be delivered by 12 this year, people are still hit by the $3,500 upfront.

So those really changes should further improve access to our medicines. I would hope and that's why we believe, as Dave said, that it's manageable. Aradhana, could you cover collaboration revenue?

Aradhana Sarin

Yes, on the collaboration revenue, again, we're obviously not going to give guidance for 2025. But the upgrade that we did on our guidance is, again, based on the strength of our underlying business and the performance in both product sales and alliance revenue. The collaboration revenue generally includes things like sales-based milestones or potential transactions. And again, they remain uncertain.

Our guidance is -- updated guidance is based on the assumption that there's no increase in CER versus last year. But again, we've considered various scenarios, including a decline, and we've based our revised guidance based on our current best estimates.

Pascal Soriot

Thank you, Aradhana. Next question is from Mattias Haggblom at Handelsbanken.

Mattias Haggblom

Thanks so much for taking the question Which is related to IRA any early effects in terms of development decisions affecting your pipeline. A leading CRO recently called out the in cancellations of large planned clinical trials within big pharma in response to RA. I'm curious if AstraZeneca already at this stage has made similar decisions to sacrifice certain small molecule assets, perhaps at the benefit of a biological or more complex molecule due to IRA. And if so, maybe you could share any concrete examples with us.

But in addition, we talk about how IRA has changed the way you think about business development as well as resource allocation internally.

Pascal Soriot

So maybe let me and this one is that the [indiscernible] challenge was more molecules, there is no question. And -- but as you can see from our pipeline and our investments, what we've communicated, as we move forward, we're investing in biospecifics, cell therapy, ADCs, adioconjugates, and all of those agents are, of course, stating the obvious non-small they're not small molecules. So the in a way we are shifting a little bit away from small molecules. It doesn't mean we're not going to be in small molecules we would be.

Now what I will mean for us is -- and that's really unfortunate, actually, but it will mean we will develop those -- if you think of a product that has a small indication to start with, we will develop these smaller indications. We will launch them around the world, but in the U.S., we will have to wait before we file because we can't start the clock for a small indication that where we would record low sales for a couple of years or three years. In Basel would have been a good example of this. So that's one issue.

The other issue is on the back end of it, if a product is a [indiscernible] medicine, and a new indication will change that status when we consider not launching it in the U.S. So those are some of the implications of the IRA and those are quite unfortunate. But this is what it is, and we're working now to advocate for change for fix to the IRA that would address this issue of what we call orphan indications or orphan diseases. Anything any of you want to add? No? Good? Peter Verdult at Citi.

Peter?

Pete Verdult

Yes. Sorry. hopping from one conference call to another. Peter Verdult from Citi. Thanks for taking my questions. Just two. I think I just want to round out some of the points that you've been making through the day. Just first for Dave, I know it's barely seven weeks since ASCO, and you've not yet got NCCN updates for DESTINY-Breast06.

But are there any early KPI changes you can point to for Tagrisso, Imfinzi, and -- or in HER1 post those planetary data drops? And then lastly for Aradhana, just -- I know you've talked to some of these points, but just so everyone is actually clear. Am I right to assume you've assumed flat collaboration revenue, but risks are probably to the upside for this year. You haven't assumed these gross to net paper dynamics are continuing even though they might. And you have assumed that Farxiga is getting hit by VBP this year.

I know you don't want to probably go through every assumption at [indiscernible], but just any help on those three points would be gratefully received.

Pascal Soriot

Thank you, Peter. Maybe unless you understood Aradhana. The second question, I was not clear about the gross to net, what you actually meant by this.

Pete Verdult

The favorable adjustment -- I think there's some favorable gross-to-net dynamics on Symbicort in the U.S.

Pascal Soriot

I see. OK. Aradhana, do you want to cover that?

Aradhana Sarin

Yes. So as I mentioned, we have assumed that we have flat collaboration revenue. As Leon mentioned, there is still some risk to the Farxiga VBP that we've assumed in our plan. And I think the -- we've again assumed some risk in terms of uncertainty from the Symbicor pricing dynamics as well in our latest guidance.

Pascal Soriot

Thank you. David?

David Fredrickson

So I think that the first point to highlight is that LAURA resulted in guideline changes within 12 days. So I think that's a very first clear indicator of a good response, an outstanding response to one of the key presentations that we had at ASCO. ADRIATIC, we've heard good interest from our medical interactions. Obviously, we're not approved yet for ADRIATIC, and so there's good enthusiasm there.

We're still looking forward to the manuscript being published for that. Similarly, on DBO6, I mentioned before, we're waiting for guidelines to change their I think that those guideline changes will be important elements to seeing a change from an interest and awareness and excitement translating then into KPIs that suggest utilization. I would also say that within the DBO6 setting, we know that based on the DBO4 results, we had already seen utilization happening spontaneously in that setting from others. In fact, it could be as much as one in four to one in five that we're seeing there.

Pascal Soriot

Thank you, Dave. Next question, maybe we'll take the last one with Luisa Hector at Berenberg. Luisa, over to you.

Luisa Hector

OK. Thanks for taking my question. Maybe just a couple left. So you had some phase 2 starts in oncology, where I was curious to just understand the hypothesis.

So that's the fusion asset in prostate cancer and also the anti-folate ADC in ovarian. And I think I'm happy to hear what you hope to show with those trials.

Pascal Soriot

Susan?

Susan Galbraith

Thanks, Luisa. So the folate receptor alpha product is one of the ADCs that we have come out of our own proprietary in-house portfolio of linker and topoisomerase I payload, so we have a B7H4 and the folate receptor alpha and the EGFR met bispecific plus a CD123 for AML in hematologic malignancies. So we're actually seeing encouraging data across all of these projects. We look forward to sharing some of those data in upcoming congress later this year.

Folate is already a validated target in ovarian cancer, and we've shared previously some preclinical data that suggest that we have activity at lower levels of folate receptor alpha expression and the current approved medicine mirvetuximab in that setting. So preclinically, this looks differentiated, and we look forward to showing the clinical data as we're excited about the profile that we've seen. For the lead asset from the Fusion portfolio, which is FPI-2265, this is an alpha emitting actinium-225 radio conjugate with the PSMA target. And again, PSMA is already a validated target in prostate cancer, highly expressed in prostate tissue with the -- obviously, the approval of Pavecto in that setting.

We presented some data from the [indiscernible] data, as I say, our Fusion colleagues presented data from the [indiscernible] data. earlier this year, which showed activity in patients that have had prior Pavecto as well as patients that were naive. And I think this reinforces the confidence that alpha-emitting particles can actually be differentiated and beta. The reason for that, I described a little bit at the Investor Day, but as a reminder, alpha particles are much heavier.

They don't travel as far and they give up their energy over a very short distance, which mean they don't treat as much normal tissue, and they give a lot of the dose to the cancer cells. So we have the opportunity to be different in this space, and that's why we're excited. The phase 2 start there is for a study called Alpha break, which is a phase 2, but potentially fileable from that setting. So this is a very exciting project.

We look forward to showing all of those data in the coming one to two years.

Pascal Soriot

Thank you, Susan. So we'll stop here. And before we close, let me just make a few closing remarks. First of all, is that we are very pleased to upgrade our guidance and it's, as I said before, based only on the strength of our business, and we believe our key medicines will continue to perform well in the second half.

There is some uncertainty around a couple of products, as I mentioned, and the collaborative revenue also could vary. But at this point, we thought this is a reasonable guidance to provide the market. And of course, the things result to the positive on some of those products, we definitely would look to an upside. We're very much on track with our strategic ambitions, whether it's top-line revenue for 2030 or profitability, or the number of NMEs to deliver by 2030, hopefully, this second quarter demonstrate we are on track.

In terms of catalysts, let me comment a little bit on those. First of all, catalysts for the second half of this year. We have TROPION-Breast02 that will read out. We have capivasertib, and we also have -- we haven't talked about this one.

We also have the Tezspire WAYPOINT study that we read out. We'll also present data. And this data, we believe, important. First of all, we'll -- we have TL01 OS.

We also have NIAGARA. We'll also present our QCS biomarker data for Dato, which we believe will create potential substantial value over time because it will definitely differentiate us in the top 2 market with very differentiated strategy in terms of testing. We also will present data with Arbaspecific, Volostomic, and relegostomic in lung cancer and [indiscernible] in gastric at Congress this year. And we also present data with our ADCs, B7H4 and folate receptor alpha.

On the biopharma side, we will also present at a relevant congress related to our visit later this year. We presented the data for our GLP-1, but also additional data for our two injectables, the Amylin and the GLP-1 glucagon. And all of those three together, they represent $5 billion opportunities -- $5 billion big revenue opportunities each. So a very important franchise.

And then if you move forward into 2025, we have AMPLIFY, which I think is a very important indication that is blockbuster indication actually. So we are looking forward to this data. They're very important. We'll have 706, which will give a first view of camizestrant in its potential, a very important product for the future for us.

We'll have AVANZAR results. As Susan mentioned before, a very important set of data. We will have early stage results in -- with HER2, DBO09, and DBO11. And finally, in biopharma, we have baxdrostat in hypertension and controlled health retention.

There's more to the news flow, of course, but those are the most important ones. And as you can see, we have a rich news flow coming up over the next few months. So with this, let me thank you very much and wish you a good rest of the day.